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Comparative Analysis of Vessel Segmentation Techniques in Retinal Images

AZHAR IMRAN[1], JIANQIANG LI[1,2], YAN PEI[3], JI-JIANG YANG[4], AND QING WANG[4]
[1]School of Software Engineering, Beijing University of Technology, Beijing 100024, China
[2]Beijing Engineering Research Center for IoT Software and Systems, Beijing 100124, China
[3]Computer Science Division, University of Aizu, Aizuwakamatsu 965-8580, Japan
[4]Research Institute of Information Technology, Tsinghua University, Beijing 100084, China

Corresponding author: Ji-Jiang Yang (yangjijiang@tsinghua.edu.cn)

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ABSTRACT The blood vessels are the primary anatomical structure that can be visible in retinal images. The segmentation of retinal blood vessels has been accepted worldwide for the diagnosis of both cardiovascular (CVD) and retinal diseases. Thus, it requires an appropriate vessel segmentation method for automatic detection of retinal diseases such as diabetic retinopathy and cataract. The detection of retinal diseases using computer-aided diagnosis (CAD) can help people to avoid the risks of visual impairment and save medical resources. This survey presents a comparative analysis of various machine learning and deep learning-based methods for automated blood vessel segmentation in retinal images. This paper briefly describes fundus photography, publicly available retinal databases, pre-processing and post-processing techniques for retinal vessels segmentation. A comprehensive review of the state of the art supervised and unsupervised blood vessel segmentation methodologies are presented in this paper. The objective of this study is to establish a professional structure to familiarize an individual with up-to-date vessel segmentation techniques. Moreover, we compared these approaches to the dataset, evaluation metrics, pre-processing and post-processing steps, feature extraction, segmentation methods, and induced results.

INDEX TERMS Vessel segmentation, retinal diseases, image segmentation, retinal fundus images, medical imaging.

I. INTRODUCTION

The deep-rooted blood vessel of the eye can only be observed in a non-invasive manner is through the retina. Retinal blood vessels are a main anatomical structure that can be detectable in the retinal fundus image. The structure and feature variations reflect the impact of CVD such as cataract, diabetic retinopathy (DR), and hypertension, etc. A cataract is the most common cause of visual impairment in the industrialized world that accounts for more than half of visual deficiency [1]. Early diagnosis and cure of the cataract can avoid serious effects including blindness. A cataract is a thick, overcast zone that structures in the lens of the eye. A cataract starts when proteins in the eye shape bunches that retain the lens from sending clear pictures to the retina. According to the survey, there will be about 0.075 billion blind people in 2020 [2], [3]. A cataract is majorly categorized into three types based on the location of the retina where it develops i.e. Nuclear Cataract, Posterior Capsular Cataract, and Cortical Cataract. The Nuclear cataract is formed in the centre of the lens and makes the lens yellow which causes a blurry image. The Cortical cataract is formed at the corner of the lens and usually found in the old-age people. Whereas, Posterior Capsular cataract is the severe type of cataract that can damage back of the lens [4]. A cataract is mostly found in the aged people with age above 40 and this ratio increases speedily over the age factor. With this increasing rate, cataract detection and diagnosis is a serious concern for the World Health Organization (WHO). Early diagnosis and cure can decrease the enduring of cataract patients and prevent visual debilitation from visual impairment. The only way to detect retinal diseases is through retinal vessel segmentation but it requires retinal experts for manual vessel detection and segmentation.

A cataract is usually graded into four classes based on the severity of the disease i.e. normal, mild, moderate, and severe [5]. The severity is based on the optic disc and blood vessels which can be either small or large. The schematic

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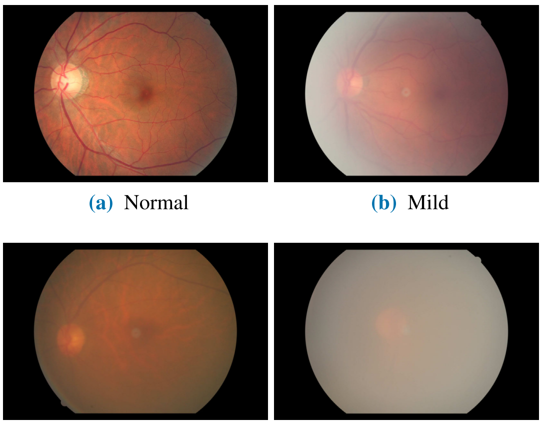
of the cataract classes is given in figure in which Fig. 1 (a) depicts normal patients without cataract, where small and large blood vessel and the optic disc is clearly visible. There are less blood vessel details available for cataract affected the eye in the mild cataract image in Fig. 1 (b), whereas, only large blood vessels and optic disc are available in the moderate cataract image in Fig. 1 (c), and almost nothing is clearly visible in the severe cataract image in Fig. 1 (d). These cataract classes are graded from 0 to 3 respectively as shown in Fig. 1. Cataract detection and classification is heavily dependent upon the blood vessel details and optic disc.



(a) Normal (b) Mild

(c) Moderate (d) Severe

FIGURE 1. Example of various levels of cataract, which develops slowly and make blurry vision and even tends to blindness if not diagnosed and cured at early stages. (a) Normal. (b) Mild. (c) Moderate. (d) Severe.

The manual vessel segmentation and detection is a very tedious approach. There are many vessel segmentation features including length, width, the angle of branches and tortuosity which is extremely difficult to explore manually for early detection and treatment of retinal diseases [6]. Moreover, manual segmentation is very cost consuming and time taking effort as it requires retinal eyes specialist for the segmentation process [7]. Therefore, Automatic extraction and segmentation of the vessels are very necessary for early detection of a cataract by using AI concepts.

This research presents different vessel segmentation techniques of the retinal images. In this research, we tried to cover almost all of the recent and past retinal segmentation researches. As per literature, we classified them into supervised and unsupervised methods that are further distributed into support vector machine-based methods, neural network-based methods, miscellaneous methods, matched filter methods, mathematical morphology methods, model-based methods, and vessel tracking methods. The retinal fundus photography, steps of preprocessing and post-processing, dataset employed, and the evaluation criterion is also presented in this research. The main objective of this research is to highlight the advantages and the drawbacks of the existing research.

This paper is prearranged as follows. The existing methodologies are discussed in section 2. The retinal image processing techniques are illustrated in section 3. Section 4 contains a discussion followed by the conclusion in section 5.

II. LITERATURE REVIEW

There are various methods and techniques available for vessel segmentation of retinal images. These techniques are broadly categorized into two types, i.e. supervised methods and unsupervised methods. Supervised methods are further subdivided into support vector machine-based methods, neural network-based methods and miscellaneous methods. Unsupervised methods are distributed into matcheds filter method, mathematical morphology methods, model-based methods, and vessel tracking methods. In this research, a comprehensive review of various supervised and unsupervised methods of retinal vessel segmentation is presented.

A. SUPERVISED METHODS

Supervised methods have great importance for medical image classification. These methods have two datasets, i.e., trained set and test set. The trained set consists of different images labelled for a specific category e.g. vessels or non-vessels. The test set is the manual annotation of the dataset by expert ophthalmologists. The classification method is targeted at dividing image pixels into the blood vessel and non-vessel types. It uses various supervised classification techniques considering the feature structure of image vessel to achieve blood vessel segmentation. The performance metrics of the support vector machine methods, neural networks methods and miscellaneous methods to its evaluation criteria, dataset, and publication year are given in Table 1, 2, and 3 respectively. Furthermore, Fig. 2, 3, and 4 represent performance measures, and paper decomposition to publication year, respectively.

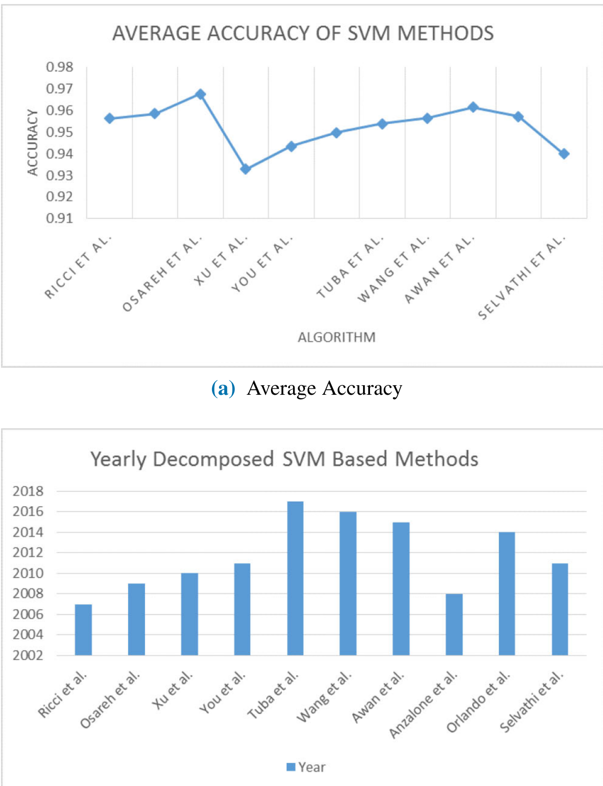
1) SUPPORT VECTOR MACHINE BASED METHODS

Support Vector Machine (SVM) is one of the commonly used algorithms adopted by researchers for supervised classification. SVM was developed by Vapnik in 1990 which works based on labelled data [8]. When both input and output are already given, then the input is used as a training set to classify the data as like output. Different researchers in their researches have used SVM as a classification algorithm [9]–[12].

In [12] a radial projection method based on support vector machine has been used for retinal vessel classification. The proposed SVM method has the advantage to detect narrow vessels with low contrast as it locates the centerlines of the vessels. Complex wavelet is used for the enhancement of vessels while training of the image is performed by SVM. The performance is measured on two public datasets, Structured Analysis of the Retina (STARE) [13] and Digital Retinal Images for Vessel Extraction (DRIVE) [14] datasets. An average accuracy of 0.9434 and 0.9497 is obtained on DRIVE and STARE, respectively. The proposed method falsely detects

TABLE 1. Performance measures of SVM based methods.

Paper #	Algorithm	Year	Dataset	Accuracy	Sensitivity	Specificity	AUC
[9]	Ricci et al.	2007	DRIVE	0.9563	-	-	0.9558
			STARE	0.9584	-	-	0.9602
[10]	Osareh et al.	2009	DRIVE	0.9675	0.9650	0.9710	0.9650
[11]	Xu et al.	2010	DRIVE	0.9328	0.7760	-	-
[12]	You et al.	2011	DRIVE	0.9434	0.7410	0.9751	-
			STARE	0.9497	0.7260	0.9756	-
[15]	Tuba et al.	2017	DRIVE	0.9538	0.6749	0.9773	-
[16]	Wang et al.	2016	DRIVE	0.9564	0.7213	0.9815	-
[17]	Awan et al.	2015	DRIVE	0.9614	0.8280	0.9716	-
			STARE	0.9572	0.8187	0.9689	-
[18]	Anzalone et al.	2008	DRIVE	0.9477	-	0.8069	-
[19]	Orlando et al.	2014	DRIVE	-	0.7850	0.9670	-
[20]	Selvathi et al.	2011	STARE	0.9400	0.6473	0.9673	-



(a) Average Accuracy

(b) Yearly Decomposition

FIGURE 2. Average accuracy of various SVM based methods lies between 0.93 to 0.97 and these algorithms are widely implemented in the period of 2002 to 2018.

the vessels on optic disc border and few narrow vessels are exaggerated due to the noise.

Ricci and Perfetti [9] used a line detector and SVM collectively for the retinal blood vessels segmentation. A line detector is performed on the green channel of the RGB image, where the performance parameters AUC and accuracy for the proposed method have shown decent results as compared to single-line detector method. The performance is evaluated on the commonly available databases of retinal images STARE and DRIVE with an observed AUC (area under the curve) and accuracy score of 0.9563 and 0.9584, respectively. The proposed method has an advantage of easy training, a simple way to extract features and less number of features required.

Osareh and Shadgar [10] proposed a method for automatic detection of blood vessels in the colour images. The feature vector of every image pixel was calculated using the properties of the Gabor filter. The extracted features were classified into vessels and non-vessels based on the Support Vector Machine (SVM) and Gaussian Mixture Model (GMM) classifiers. These experiments were performed on the DRIVE database and author proposed database with 90 normal and fundus images. The method achieved sensitivity, specificity, and AUC of 0.9650, 0.9710 and 0.974, respectively. The proposed method has shown the significant performance for AUC but this has limitation to detect reediest vessels as a result of noise and capricious luminosity.

Image processing based on classification using support vector machine was performed by Xu and Luo [11]. The adaptive threshold value method was suggested for the vessels segmentation in the absence of optic disc. Various features were extracted from the original retinal image by analyzing the wavelets and reedy vessels were recognized with the help of the line detector. Support vector machine was used for the classification of thin vessels along with residual fragments. The vascular network was formed by applying tracking growth on the thin vessels. The evaluation of these experiments is tested on the DRIVE database which has shown above 0.77 of sensitivity and 0.93 of accuracy. The proposed method has the benefit of fewer computations and manual interventions.

Tuba *et al.* [15] proposed an overlapping block-based method characterized by support vector machine classification. The features used in this method for the retinal blood vessel segmentation were discrete cosine transform (DCT) coefficients and chromaticity. This overlapping block-based algorithm was evaluated on the publicly available DRIVE database. The accuracy of the proposed method was evaluated on sensitivity, specificity, and accuracy, which have shown 0.9773, 0.6749 and 0.9548 scores, respectively. This algorithm has an advantage to accurately classify the large retinal vessels but it is scarce to accurately classify thinner vessels.

TABLE 2. Performance measures of NN based methods.

Paper #	Algorithm	Year	Dataset	Accuracy	Sensitivity	Specificity	AUC
[22]	Jin et al.	2019	STARE	0.9641	-	-	0.9832
			DRIVE	0.9566	-	-	0.9802
			HRF	0.9651	-	-	0.9831
			CHASE_DB1	0.9610	-	-	0.9804
[23]	Yang et al.	2019	DRIVE	0.9510	0.9730	0.7970	0.8850
[24]	Guo et al.	2018	STARE	-	0.8212	0.9843	0.9859
			DRIVE	-	0.7891	0.9804	0.9806
[25]	Son et al.	2019	STARE	0.9873	-	-	-
			DRIVE	0.9810	-	-	-
[26]	Hu et al.	2018	DRIVE	0.9533	0.7772	0.9793	0.9759
			STARE	0.9632	0.7543	0.9814	0.9751
[27]	Liskowski et al.	2016	DRIVE	0.9495	-	-	0.9720
			STARE	0.9416	-	-	0.9605
[28]	Wang et al.	2019	DRIVE	0.9511	0.7986	0.9736	0.9740
			STARE	0.9538	0.7914	0.9722	0.9704
[29]	Lin et al.	2018	DRIVE	0.9536	0.7632	-	-
			STARE	0.9603	0.7423	-	-
			CHASE_DB1	0.9587	0.7815	-	-
[30]	Oliveira et al.	2018	STARE	0.9694	-	-	0.9905
			DRIVE	0.9576	-	-	0.9821
			CHASE_DB1	0.9653	-	-	0.9855
[31]	Li et al.	2015	STARE	0.9527	-	-	0.9738
			DRIVE	0.9628	-	-	0.9879
			CHASE_DB1	0.9580	-	-	0.9716
[32]	Guo et al.	2018	DRIVE	0.9613	-	-	0.9737
			STARE	0.9539	-	-	0.9539
[33]	Geng et al.	2019	DRIVE	0.9630	-	-	0.9831
			STARE	0.9620	-	-	0.9830
[34]	Dharmawan et al.	2019	DRIVE	-	0.8314	0.9726	0.9786
			STARE	-	0.7924	0.9827	0.9827
			HRF	-	0.8316	0.9770	0.9821
[35]	Yan et al.	2018	DRIVE	0.9538	0.7631	0.9820	0.9750
			STARE	0.9638	0.7735	0.9846	0.9833
			HRF	0.9607	0.7641	0.9806	0.9776
[36]	Xu et al.	2018	DRIVE	-	-	-	0.9793
			HRF	-	-	-	0.9770
[37]	Hatamizadeh et al.	2019	DRIVE	0.9686	0.8197	0.9819	-
			CHASE_DB1	0.9750	0.8300	0.9848	-
[38]	Fan et al.	2019	DRIVE	0.9661	0.7957	0.9827	0.9818
			STARE	0.9741	0.8164	0.9870	0.9892
			CHASE_DB1	0.9714	0.8020	0.9853	0.9851
			HRF	0.9763	0.8244	0.9874	0.9891
[39]	Ribeiro et al.	2019	DRIVE	0.9569	0.7880	0.9819	-
[40]	Feng et al.	2019	DRIVE	0.9528	0.7625	0.9809	0.9678
			STARE	0.9633	0.7709	0.9848	0.9700
[41]	Noh et al.	2019	DRIVE	0.9569	0.9746	0.8354	0.9820
			STARE	0.9764	0.9864	0.8537	0.9921
			CHASE_DB1	0.9778	0.9871	0.8523	0.9916
[42]	Soomro et al.	2019	DRIVE	0.951	0.822	0.979	0.976
			STARE	0.953	0.809	0.974	0.972
			HRF	0.948	0.786	0.964	0.965
			CHASE_DB1	0.891	0.8020	0.968	0.974
[43]	Jin et al.	2017	DRIVE	0.9628	-	-	0.9764

TABLE 2. *(Continued.)* **Performance measures of NN based methods.**

			STARE	0.9690	-	-	0.9844
[44]	Lu et al.	2018	DRIVE	0.9559	0.7812	0.9814	0.9790
[45]	Xia et al.	2018	DRIVE	0.9685	0.7979	0.9857	-
[46]	Jiang et al.	2019	DRIVE	0.9709	0.7839	0.9890	0.9864
			STARE	0.9781	0.8249	0.9904	0.9927
[47]	Thangaraj et al.	2017	DRIVE	0.9606	0.8014	0.9753	0.8884
			STARE	0.9435	0.8339	0.9536	0.8938
			CHASE_DB1	0.9468	0.6288	0.9728	0.7971
[48]	Feng et al.	2017	DRIVE	0.9560	0.7811	0.9839	0.9792
[49]	Soomro et al.	2017	DRIVE	0.947	0.746	0.917	0.831
			STARE	0.948	0.748	0.922	0.835
[50]	Song et al.	2017	DRIVE	0.9499	0.7501	0.9795	-
[51]	Ngo et al.	2017	DRIVE	0.9533	0.7464	0.9836	0.9752
[52]	Dasgupta et al.	2017	DRIVE	0.9533	0.7691	0.9801	0.9744
[53]	Fan et al.	2017	DRIVE	0.9612	0.7814	0.9788	-
			STARE	0.9614	0.7834	0.9799	-
			CHASE_DB1	0.9761	0.9702	0.9702	-
[54]	Yao et al.	2016	DRIVE	0.9360	0.7731	0.9603	-
[55]	Luo et al.	2016	DRIVE	0.9471	-	-	0.9682
[56]	Khalaf et al.	2016	DRIVE	0.9456	0.8397	0.9562	-
[57]	Mahua et al.	2012	DRIVE	0.9616	-	-	-
[58]	Ghaderi et al.	2007	DRIVE	-	-	-	0.9668
[59]	Sengur et al.	2017	DRIVE	0.9178	-	-	0.9674

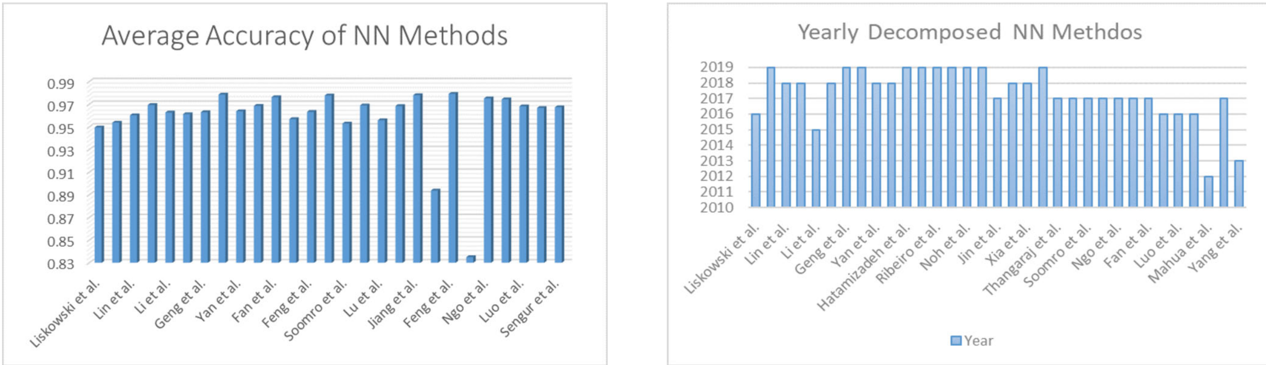
TABLE 3. **Performance measures of miscellaneous methods.**

Paper #	Algorithm	Year	Dataset	Accuracy	Sensitivity	Specificity	AUC
[14]	Staal et al.	2004	DRIVE	0.9442	-	-	0.952
			STARE	0.9516	-	-	0.9614
[60]	Niemeijer et al.	2004	DRIVE	0.9416	0.7145	-	0.9294
[61]		2006	DRIVE	0.9466	-	-	0.9614
			STARE	0.9480	-	-	0.9671
[62]	Lupascu et al.	2010	DRIVE	0.9597	0.72	-	0.9561
[63]	Memari et al.	2017	DRIVE	0.9722	0.8726	0.9884	0.9795
			STARE	0.9514	0.8085	0.9798	0.9701
			CHASE_DB1	0.9482	0.8192	0.9591	0.9436
[64]	Fraz et al.	2011	DRIVE	0.9476	0.7525	0.9722	0.9616
			STARE	0.9579	0.7604	0.9812	0.9734

Wang *et al.* [16] proposed a novel algorithm based on a supervised method for the retinal vessels segmentation. A vector containing 30 features of every pixel of the retinal image was formed containing features in Gaussian scale space, multiscale Gabor filter, and the vector field divergence. Support Vector Machine classifiers were used for the vessels classifications based on the input of feature vector and manual segmentation. The proposed method was evaluated on the DRIVE database with performance metrics, accuracy, sensitivity, and specificity. The average measured scores were 0.956, 0.721 and 0.982, respectively. The segmentation performance and reduced running time were the salient features of the proposed method.

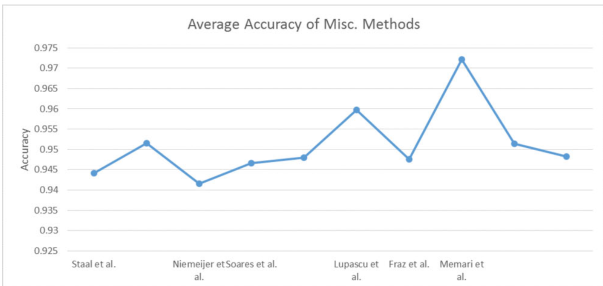
In [17], the authors proposed a robust method for the retinal blood vessels segmentation task. This method consists of three main points to correctly classify the vessels, i.e. the feature extraction based on the region, feature selection from the candidate region and applying support vector machine classifier. The proposed method was evaluated on three databases DRIVE, STARE and AFIO (Armed Forces Institute of Ophthalmology) and the performance of this method was assessed using sensitivity, specificity and accuracy measures. The average scores of these measures were 82.80, 97.16, and 96.14, respectively. This method has an advantage to truly classify the vessels even in the presence of lesions while that was limited to when non-vessels appear as the disconnected region from vessels.

The vessels segmentation has performed by the modular supervised method presented by Anzalone *et al.* [18]. The author has carried out two main steps to execute the proposed methods i.e. image binarization was performed by the threshold method and vessels enhancement was completed using

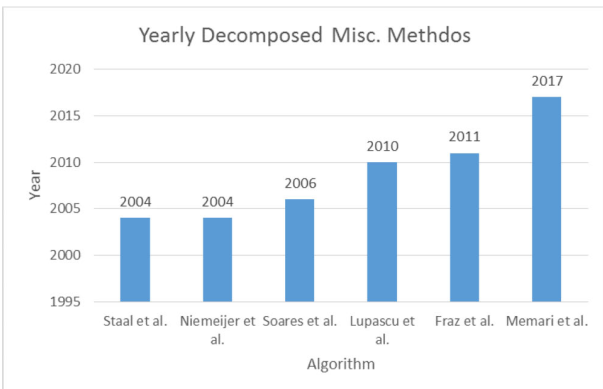


(a) Average Accuracy (b) Yearly Decomposition

FIGURE 3. Neural network based methods: Average accuracy is about 0.96 which is higher than other algorithms and accuracy of some algorithms approaching 0.97 to 0.98. The NN based algorithms are mostly used in 2015 to onwards.



(a) Average Accuracy



(b) Yearly Decomposition

FIGURE 4. Miscellaneous methods: These methods are mostly evaluated from 2004 to 2017 on STARE and DRIVE dataset with average accuracy and AUC is about 0.94 and 0.96 respectively.

the scale-space theorem. The performance is evaluated on the DRIVE database with 20 images are used for the test set and train set. The average accuracy, K value, and specificity are 0.9587, 0.8069 and 0.9477, respectively. The proposed method is flexible to remove all or multiple features required for any application by updating reference measures of performance (MOP) while there is some tradeoff between the quality, computation time and complexity of the algorithm.

Orlando and Blaschko [19] presented a supervised learning algorithm constructed from structural support vector machine for the retinal blood vessels. The proposed method was deeply rooted from fully connected conditional random field (FC-CRF). This method was evaluated on DRIVE, STARE, CHASE_DB1 (Child Heart and Health Study in England) and HRF (High-Resolution Fundus) public databases and tested on both quantitative and qualitative approaches. The performance was evaluated against the different perfromance measures such as sensitivity, Matthew's correlation, G-mean, and F1-score coefficients. Although, this method has outperformed others to properly segment the thin vessels and attains good accuracy. Moreover, this method has shown some limitations to misclassify the main blood vessels in the HRF and CHASE_DB1 database with high-resolution images.

Selvathi and Vaishnavi [20] proposed a kernel-based technique for the segmentation of retinal blood vessels in the fundus images. The method used SVM classifier to discriminate the vessels and the non-vessels. A feature vector was created that contains green channel extraction, pixel's intensity and Gabor wavelet responses as its features. STARE database was used to perform experiments. The performance of these experiments was measured for normal and abnormal images separately against the commonly used measures sensitivity, specificity, and accuracy. The accuracy score of 0.944 and 0.947 was obtained for normal and abnormal retinal images respectively. This method has shown decent results even on a smaller dataset, but these results may improve by using larger dataset.

2) NEURAL NETWORK-BASED METHODS

Artificial neural networks (ANNs) are processing frameworks ambiguously propelled by the natural neural systems. Such frameworks "learn" to perform errands by thinking about cases. ANN depends on the likelihood of making arrangement choices [21]. To prepare the system, ANN utilizes the preparation set which contains information sources and target yields and the principles for learning. By the change of preparing inputs with the information of known yields makes the system to permit retraining.

Jin *et al.* [22] introduced deformable U-Net (DUNet) model based on CNN for retinal vessel segmentation, which exploits the local features of retinal vessels. The up-sampling operators are used in DUNet to improve the output resolution, capture the contextual information, and to facilitate specific localization by combing both high and low-level features. The various image preprocessing steps are used to enhance the vessel details. A single-channel of RGB image is extracted as it retains more vessel-background contrast; CLAHE is used to improve the vessel details and background; gamma correction is employed to improve the image quality. The technique extracts the retinal vessel at different scales and shapes by regulating the receptive field accordingly. The method is evaluated on STARE, DRIVE, HRF, CHASE_DB1 datasets and achieves the highest accuracy of 0.9651 on HRF and AUC of 0.9832 on STARE database.

Yang *et al.* [23] presented an improved deep CNN model for retinal vessel segmentation. The technique is based on three steps: data augmentation is used to improve the generalization of training dataset by rotating and mirroring the image at different angles, image preprocessing such as CLAHE is used to reduce noise and improve image quality, and deep CNN combined with U-Net and Dense-Net is employed to segment retinal blood vessels. The method is evaluated on DRIVE, achieving an average accuracy, sensitivity, specificity, and AUC of 0.951, 0.973, 0.797, 0.885, respectively.

A multi-scale deeply supervised neural network with a bottom-top short connection (BTS-DSN) is proposed by Guo *et al.* [24] for vessel segmentation. The method employs short connections for the transference of semantic information among the side output layers. The proposed method uses two types of short connections i.e. top-bottom and bottom-top, in which the semantic information is passed accordingly for refining results and reduces noises in either direction. They used ResNet-101, and VGGNet model to perform experimentation, achieving 0.8212/0.7891, 0.9843/0.9804, 0.9859/0.9806, 0.8421/0.8249 of sensitivity, specificity, AUC, and F1-score on STARE and DRIVE, respectively. However, the proposed model is limited to accurately segment the micro-vessel with one to several pixels wide.

A Generative Adversarial Networks (GAN) has been applied for the retinal vessel segmentation tasks to leverage the capability of CNN model [25]. GAN is designed with a U-Net style generator and various discriminators. The discriminators distinguish between output and the gold standard, while the generator creates realistic output. The method is evaluated on two public databases DRIVE and STARE, achieving an accuracy of 0.9810 and 0.9873, respectively. The segmentation results can be improved in the future by combing the anatomical knowledge of the vascular structure and the optic disc and applying post-processing steps to remove noise.

Hu *et al.* [26] presented a retinal vessel segmentation method based on CNN and fully connected conditional random fields (CRFs). The segmentation is based on two steps: firstly, a multiscale CNN with an improved cross-entropy loss function is used to create probability map and multiscale network combining the feature map of each layer is constructed to extract more details of retinal vessels. Secondly, the final binary segmentation is obtained by using CRFs. The method in combination with multiscale and loss function achieved 0.7772/0.7543, 0.9793/0.9814, 0.9533/0.9632, 0.9759/0.9751 of sensitivity, specificity, accuracy, and AUC on DRIVE and STARE datasets, respectively. This method is presentable to cope with the issues of locating vascular edges and tiny thin vessels.

A deep neural network-based method is presented for retinal blood vessel segmentation [27]. The fundus images are preprocessed with zero-phase component analysis and global contrast normalization and augmented using gamma correction and geometric transformations. The method is evaluated on two public datasets DRIVE and STARE with several variants including structured prediction. The proposed method achieved an average accuracy of 0.9495/0.9416 and AUC of 0.9720/0.9605, respectively. The results of this study can be improved by adopting various training parameters.

Wang *et al.* [28] proposed a Dense U-Net based on patch-based learning method for retinal vessel segmentation. In model training, the training patches are extracted randomly, U-Net is implemented as a training network, and the dataset is augmented using random transformations, while in the testing phase, images are divided into patches, training model is used to predict test patches, and the segmentation results are created by applying overlapping-patches sequential method. The method is evaluated on DRIVE and STARE dataset and achieved 0.7986/0.7914, 0.9736/0.9722, 0.9511/0.9538, 0.9740/0.9704 values of sensitivity, specificity, accuracy, and AUC, respectively. The splintering of fine blood vessels is formed in the proposed method during the binarization course, which can be improved by applying post-processing steps.

A deep learning method based on deep supervision and smoothness regularization network (DSSRN) is proposed for retinal vessel segmentation [29]. The method is created in combination with holistically-nested edge detector (HED) using VGG network, and global smoothness regularization from conditional random fields (CRFs). DSSRN is a pixel-to-pixel and end-to-end deep network, which is evaluated on three public datasets achieving apical accuracy of 0.9603 and sensitivity of 0.7423 on STARE retinal images. The proposed method achieved state of the art results of accuracy, but the overall sensitivity is low as compared to other traditional methods, which can be improved using model fine-tuning.

Oliveira *et al.* [30] performed retinal vessel segmentation using a novel method based on Stationary Wavelet Transform (SWT) with Multiscale Fully Convolutional Neural Network (FCN). The method is designed to handle variable width and direction of the vessel structure within the retina. Furthermore, new channels are added into FCN through the SWT decomposition. The rotation operation is used to discover the information learned in the training phase to enhance the segmentation for both data augmentation and prediction. The method achieved an average accuracy of 0.9694, 0.9576, 0.9653 and AUC of 0.9905, 0.9821, 0.9855 on the STARE, DRIVE, and CHASE_DB1 datasets, respectively. The method is presentable for the robust training set, faster GPU implementation, and inter-rater variability. The other wavelet families like curvelets, increase the data volume and deep learning in combination with domain knowledge can be used to obtain optimal performance.

A new supervised method advert as a Cross-Modality Learning Approach for retinal vessel segmentation was proposed by Li *et al.* [31]. The method overhauls the segmentation task to data transformation from retinal fundus image to vessel map. A deep learning model with solid induction ability is used for model transformation along with robust training procedure is conferred. The network is designed to output the label map all the pixels of the image patch, rather than focusing on a single label of the centre pixel. The method is verified on DRIVE, STARE, and CHASE_DB1 databases and achieved maximum accuracy and AUC of 0.9628 and 0.9879 on STARE database. The average 70 seconds is required to segment a single retinal image, which is very high and can be considered as the potential limitation of the method.

Guo *et al.* [32] proposed multiple deep CNN (MDCNN) for retinal vessel classification, which is designed and trained on retinal images with limited contrast. The incremental learning technique is used in MDCNN to boost the networks' performance. The majority voting procedure is used to obtain the final classification results. Two public retinal datasets DRIVE and STARE are used to evaluate the method, achieving an accuracy and AUC scores of 0.9613/0.9539 and 0.9737/0.9539, respectively. The proposed MDCNN yields better segmentation performance as there is no preprocessing steps are employed, and the colour retinal images are directly fed into CNN.

A method for retinal vessel segmentation based on FCN with channel weighting and depthwise separable convolution was proposed by Geng *et al.* [33]. The method is composed of three steps: image preprocessing, image segmentation and model formation. First, the green channel of the colour fundus image is extracted, along with CLAHE and gamma correction are used to enhance the contrast. Second, the enhanced image is divided into patches to expand the data for network training. Finally, the proposed depthwise separable convolution method is used to increase the network width, instead of the standard convolution method. Moreover, the channel weighting is used to enhance the distinguishability of the features. The method achieved an accuracy of 0.9630/0.9620, and AUC of 0.9831/0.9830, on DRIVE and STARE databases, respectively.

Dharmawan *et al.* [34] presented a hybrid algorithm for vessel segmentation, which combines the retinal vessels enhancement method and CNN derived from U-Net. The retinal vessels enhancement method is established on multiscale orientation modified Dolph-Chebyshev Type-I matched filtered function (MDCF-I). The training and testing of the method was performed on DRIVE, STARE and HRF database and achieved significant results on DRIVE with 0.8314 of sensitivity, 0.9726 of specificity and 0.9786 of AUC. The proposed method is helpful to deal with low contrast vessels, vessels detection in the presence of pathologies and vessels with centre reflex.

A novel method to segment both the thick and thin vessels separately was proposed by Yan *et al.* [35]. The method is a three-step deep learning model: thick vessel segmentation, thin vessel segmentation, and vessel fusion. Both the thick and thin vessels are segmented individually to overcome the imbalance problem and low segmentation accuracy. The vessel fusion is applied to refine the results by distinguishing that the pixel belongs to vessel or non-vessel. The hybrid method evaluated on DRIVE, STARE and CHASE_DB1 databases and attained best scores of 0.7735, 0.9820, 0.9538 and 0.9750 on STARE for sensitivity, specificity, accuracy, and AUC, respectively.

Xu *et al.* [36] presented a method for vessel segmentation based on a multiscale deeply guided neural network with boundary refinement (MDGN-BR). The method is utilized to deal with the variant structure of vessels which hinders to extract tinny vessels in the presence of ophthalmic diseases. The network is implemented on the encoder-decoder scheme in which training of features is performed using deep supervision. Moreover, skip connections are used in scaled layer to fuse feature maps along with vessel boundaries are refined via residual-based boundary refinement module. MDGN-BR is evaluated on DRIVE and HRF achieving 0.9793 and 0.9770 of AUC, respectively.

A deep dilated convolutional network based on encoder-decoder architecture has been proposed for retinal vessel segmentation [37]. The dilated spatial pyramid pooling along with various dilation rates are used to recuperate the lost content in an encoder, and multiscale contextual information is added in the decoder. The width of blood vessels is identified by using segmentation predictions, in which the whole image is fed to the network rather than a patch-wise approach. The method achieved state-of-the-art performance on sensitivity, specificity, and accuracy with values 0.8197/0.8300, 0.9819/0.9848, 0.9686/0.9750 on DRIVE and CHASE_DB1, respectively.

Fan *et al.* [38] presented encoder-decoder based octave CNN model for accurate blood vessel segmentation. The method adopts octave convolution, unlike the traditional deep learning methods in which vanilla convolution is used for features extraction, which is propitious for multiple-spatial frequency features. The multi-frequency features are decoded via octave transposed convolution. Furthermore, an octave U-Net characterized from encoder-decoder based FCN is proposed to generate accurate vessel segmentation in single forward feeding. Octave U-Net is used to extract hierarchical features, and the training of the method is performed in an end to end manner without any pre-or-post processing steps. The method is verified on DRIVE, STARE, CHASE_DB1, and HRF databases and achieved promising results for accuracy, sensitivity, specificity and AUC of 0.9763, 0.8244, 0.9874 and 0.9891 on STARE database.

Retinal vessel segmentation is performed by using baseline network architecture based on the U-Net model, and two ensemble learning techniques, Stochastic Weighting Average (SWA) and Snapshot Ensembles (SE) [39]. The proposed method is evaluated on public dataset DRIVE and it achieves optimal performance in terms of accuracy, sensitivity, and specificity with values 0.9569, 0.7880 and 0.9819, respectively.

Feng *et al.* [40] presented cross-connected network (CcNet) based on the convolutional neural network using multiscale features for retinal vessel segmentation. The convolution layers of the CcNet extract the informative features and predict the pixel classes with respect to these features. The green channel of the retinal images is extracted to train and test the proposed model. The cross-connection is employed amongst primary and secondary path to fuse the multiscale features. CcNet achieves an average accuracy of 0.9528 and sensitivity of 0.7625 on DRIVE dataset.

Blood vessels are segmented using convolutional neural network structure incorporated with scale-space theory in [41]. The proposed scale-space approximated network (SSANet) is designed by combining upsampling, downsampling and residual blocks. The method evaluated on DRIVE, STARE and CHASE_DB1 databases, in which optimal results of accuracy, sensitivity, specificity, and AUC are achieved on CHASE_DB1 with values 0.9778, 0.9871, 0.8523 and 0.9916. SSA network has great potential for the segmentation of thin vessels and localization of vessel boundaries.

Soomro *et al.* [42] presented a strided-CNN method based on deep CNN for the segmentation of retinal vessels including tiny vessels. The model is established on the encoder-decoder scheme, where the pooling layers are replaced with strided convolutional layers. The images of the training dataset are preprocessed by using morphological operations in combination with principal component analysis (PCA). Moreover, the skip connections are applied that combines the features from encoder and decoder part to improve vessel details especially the tiny vessels. The method achieved best results of sensitivity, specificity, accuracy, and AUC of 0.822, 0.979, 0.951 and 0.976 on DRIVE dataset as compared to STARE, HRF and CHASE_DB1 databases.

The automated segmentation model based on CNN has been developed for the segmentation of retinal blood vessels [43]. First, the image preprocessing steps are used to improve the quality of retinal image including green channel extraction, CLAHE and gamma correction. Next, to adapt low contrast and various scale images, a set of layers are introduced in the proposed network to create one-size patches for all the models. Finally, the five pre-trained models are modified for the retinal vessel segmentation such as LeNet, AlexNet, ZF-Net, VGG, and Deformable-ConvNet. The highest AUC of 0.9764 (ZF-Net) and 0.9844 (AlexNet) is obtained on DRIVE and STARE, respectively.

RetNet: an encoder-decoder architecture based on CNN was proposed by Lu *et al.* [44] for the segmentation of retinal blood vessels. The encoder part is used to extract hierarchical features and the decoder part is used as a pathway to restructure the full-size input. The two skip connections are adopted to extract more semantic and contextual information and to improve the localization and classification of the RetNet without any post-preprocessing steps. The model is evaluated on DRIVE dataset and achieves 0.7812, 0.9814, 0.9559, 0.9790 of sensitivity, specificity, accuracy, and AUC, respectively.

A coarse-to-fine method based on CNN (CTF-Net) has been presented for retinal vessel segmentation [45]. The method has a cascaded architecture composed of many encoder-decoder networks based on the adaptation of U-Net. Some amendments are made for assembling that distinguish the proposed model with U-Net such as eliminating max-pooling operation, reducing succeeding convolutions and feature maps of middle layers. The ensemble strategy is employed that combines the input image with outputs of basic network sequentially to improve the feature propagation of model. CTF-Net is evaluated on public dataset DRIVE and achieves 0.9685, 0.7979, 0.9857 of accuracy, sensitivity and specificity, respectively.

Jiang *et al.* [46] proposed deep CNN method (D-Net) for retinal vessel segmentation. In the encoder part, the feature loss is reduced by reducing the downsampling factor for tiny vessel segmentation. The combined dilated convolution is used to amplify the receptive field of the model and lessen the grid problem within dilated convolution. A multiscale information fusion (MSIF) component comprises of parallel convolution layers with varying dilatation rates is used to extract deep feature and better retinal vessel information. In the decoder part, the skip connection is used to proliferate contextual information to higher resolution layers. D-Net is verified on DRIVE and STARE dataset and achieves 0.7839/0.8249, 0.9890/0.9904, 0.9709/0.9781, 0.9864/0.9927 of sensitivity, specificity, accuracy, and AUC, respectively.

Thangaraj *et al.* [47] presented a novel technique for the retinal vessel segmentation with the help of the neural network. A 13D feature vector with essential features is formed comprising Hu moment invariants (excluded for better performance), Gabor filter responses, local binary pattern, gray-level co-occurrence matrix (GLCM), and Frangi's vesselness measure were used. These features were used as input to train the neural network. The model was evaluated on the openly accessible databases, CHASE_DB1, STARE, and DRIVE. The performance of the proposed method was tested against the different measures i.e. accuracy, sensitivity, specificity and AUC which has shown significant results for the blood vessels segmentation. This method has an advantage to accurately classify both the normal and fundus images with better performance but still, it needs high-level features for the segmentation of children dataset.

Feng et al. [48] proposed patch-based fully Convolutional Neural Network method for the segmentation of blood vessels in the retinal image. The local entropy sampling and a skip connection for CNN were used in this method to fasten the speed of fully CNN architecture. The experiments were performed on DRIVE and the proposed method achieved 0.8736 0.9839, 0.8736, 0.7811, and 0.9792 scores of accuracy, specificity, precision, sensitivity, and AUC respectively. Robustness and learning hierarchical structure without explicitly feeding the domain knowledge distinguish this method from others. The effectiveness of this method can be improved by experimenting on cross databases and also by improving the sensitivity score.

In [49], a method based on CNN was proposed to detect tiny vessels from low contrast image. The preprocessing and post-processing were applied to the network to remove extra noise so that sensitivity can be improved. DRIVE and STARE database was used to evaluate the proposed method and achieved 0.75, 0.947 of sensitivity, and accuracy. This method has the advantage to detect tiny vessels because of boosted sensitivity and removed uneven illumination, but its results can be improved by evaluating on multiple datasets with improved preprocessing techniques.

Song and Lee [50] proposed a model using a CNN with pixel-wise path based implementation. This method has consisted of different convolutional and up-sampling layers. A feature vector was created and used as an input for the pixel-wise prediction of vessels. The performance of the proposed method was evaluated on DRIVE dataset with a sensitivity, specificity and accuracy scores of 0.750, 0.979, and 0.950, respectively. This method has an advantage of decent performance measures but the entire spatial blood vessels information was not included in this method.

Ngo and Han [51] proposed a neural network method based on multi-levels for the blood vessels segmentation. The blood vessels were accurately classified using the max-resizing technique. In this technique, the dropout and spatial dropout were combined and implanted on the deep neural network for the better segmentation. A publicly available DRIVE database was used to evaluate the method achieving 0.9533 of accuracy and 0.9752 of AUC. Whereas, this method cannot detect tiny vessels as sensitivity results can further be improved in the future.

Dasgupta and Singh formulated the vessels segmentation tasks by combing the features of fully CNN and structured prediction [52]. This novel approach was multi-label inference problem that helped to detect dependencies of neighbouring pixels which are used in the segmentation. The performance of this method was tested on DRIVE dataset with a learning rate of 0.0001 and RMSprop algorithm is adjusted at a value of 0.7. The proposed method has achieved 0.8498, 0.7691, 0.9801, 0.9533 and 0.9744 scores of precision, sensitivity, specificity, accuracy, and AUC, respectively.

The use of deep neural network and de-noising auto-encoder (DAEs) has been verified by Fan et al. [53]. The segmentation of vessel in the retinal fundus images has been performed using the deep neural network. This multi-level approach was prepared by DAEs and by applying the backpropagation (BP) algorithm. The proposed method was evaluated on 3 different databases DRIVE, STARE and CHASE_DB1 with performance measures i.e. accuracy 0.961, 0.961, 0676, sensitivity 0.781, 0.723, 0.970, and specificity 0.979, 0.980, 0.970 respectively.

Yao et al. [54] proposed a method based on CNN for the blood vessels segmentation in the retinal images. The local binarization and heuristic morphological operations were used to refine the output of CNN based segmented images. The method was tested on DRIVE dataset. The performance of the proposed method was calculated using different measures i.e. sensitivity, specificity and accuracy with 0.773, 0.960, and 0.935 scores respectively. This method can also be improved by applying deep CNN to diagnose each pixel's detail at various scales.

A size invariant fully convolutional network (SIFCN) was employed in [55] for the retinal blood vessels segmentation. This method was designed so that the image patches and pixel-wise labels could be used as an input. The training steps for the vessel segmentation include pooling layers and consecutive convolutional layers on the input. The features height, width, padding and pooling stride of each layer were stored to kept spatial information instead of up-sampling. The lost is determined by using the cross-entropy function and patch edge is detected using the overlap approach. Both the overlap and non-overlap approaches of SIFCN are tested on DRIVE database in which overlapped approach achieved 0.947 of accuracy and 0.968 of AUC while the non-overlap approach was the most efficient in terms of time (3.68s/image). The proposed method used patches of the image as the training set while whole image training could have improved the processing time for overlapped SIFCN.

In [56], the author has been employed a novel deep Convolutional Neural Network (DCNN) for automatic retinal blood vessels segmentation. This method was used to differentiate the large vessels, small vessels, and background areas. The performance measures sensitivity and specificity have been improved by combining different kernel with different sizes. Three convolutional layers were used in the architecture along with a single subsampling was used after every third layer. The green channel of the retinal fundus image was extracted and histogram equalization and top hat transformation were performed to improve the vessels visibility. DRIVE dataset was used to test the suggested method and achieved 0.839 of sensitivity, 0.956 of specificity and 0.945 of accuracy is achieved. The results of the proposed method could also be improved by using CNN without subsampling layers that could have helped in lessen the error rate of the background areas of the vessels.

The Gabor filter and the Artificial Neural Network (ANN) were used to segment the retinal blood vessels [57]. The author proposed a 2D Gabor filter bank based on entropy. The output of the ANN-based classifier was based on the features of the Gabor filter, which was evaluated on both normal and abnormal retinal fundus images. The open retinal database DRIVE was used to test the segmentation results. AUC of both the normal and abnormal retinal images showed 0.961 of accuracy. This method has the advantage to overcome computational and large feature space.

Ghaderi et al. [58] proposed a novel approach for the retinal vessel segmentation. A feature vector was created from the retinal image to categorize the pixels as vessel and non-vessel. A multilayered feed-forward neural network was used to classify the vessels and non-vessels. The feature of this method consisted of the pixel's intensity and 2D Morlet wavelet transformation. The DRIVE dataset has been used for evaluation of this method which achieved an accuracy score of 0.967. The method is advantageous to remove noise and vessel enhancement because of Morlet wavelet transformation.

A CNN-based approach has been employed for the retinal blood vessels segmentation task in [59]. The CNN method has used two layers; each for convolution and pooling and one layer for dropout and loss. The method achieved an accuracy of 0.918 and AUC of 0.967 for retinal vessel segmentation task evaluated on publicly available retinal database DRIVE. The colour fundus images were used as an input for CNN without applying preprocessing steps, thus better results can be obtained by using preprocessing steps.

3) MISCELLANEOUS METHODS

Miscellaneous approaches contain different supervised techniques for the automatic detection and classification of the retinal fundus images. Although, we created the separate category for the hybrid approaches but sometime, a technique may fall in more than one category so we have cross-listed their reference. The techniques like ridge based, feature-based, and 2D Gabor wavelet, etc. are discussed in this section.

Staal *et al.* [14] proposed a ridge based method for the vessels segmentation in 2D retinal color images. The image ridges were extracted in the presented method, which overlaps with vessel centerlines. The primitives were created using ridges as line components which were further used to partition an image into patches by transferring every pixel to the closest line component. A local coordinated frame in every patch was created, which extracted features of each pixel. A feature vector with 27 features was created using a k-NN algorithm and feedforward method. The technique was evaluated on Hoover's (STARE) and Utrecht (collected from the Netherlands) database. The performance was evaluated using AUC and accuracy scores of 0.952 and 0.961 respectively. The proposed method has also shown the state of the art results than the rule-based methods.

The use of Gaussian matched the filter and their derivatives were explained by Niemijer *et al.* [60]. The author proposed a pixel classification approach for vessels segmentation. A feature vector was formed for every pixel to train the classifier. The filter's output and pixel value were the two features evaluated for experiments. The k-NN classifier was used to classify pixels as vessels and non-vessels. The experiments were tested on DRIVE dataset which achieved an AUC and accuracy score of 0.929 and 0.942, respectively.

Soares *et al.* [61] has been proposed a 2D Gabor wavelet and supervised classification method for the blood vessels classification. A feature vector consists of 2D Gabor wavelet transform and pixel's intensity was constructed for each pixel. The response of transformation was recorded at different scales. The classification of pixels as vessels and non-vessels was carried out by classifier called the Gaussian mixture model. The proposed technique was tested on both STARE and DRIVE publically available datasets and 0.947 and 0.948 of accuracy and 0.961 and 0.967 of AUC scores were achieved. As this technique is limited to local image information regardless of shapes and structures so, this gives false vessels detection with non-uniform illumination.

Lupas *et al.* [62] presented a feature-based AdaBoost classifier (FABC) for retinal vessel segmentation task. A feature vector with 41 features is constructed for each pixel in FOV of the image including local intensity structure spatial properties, geometry at various scales ($\sqrt{2}$, 2, $2\sqrt{2}$, and 4), and the output of various filters i.e. Gaussian, 2D Gabor, Matched, etc. For the classification of vessel and non-vessel, 789914 benchmark samples were used to train the classifier. The classifier was evaluated on DRIVE and FABC datasets and attained accuracy and AUC of 0.9597 and 0.9561 respectively. The advantage of the proposed method was as follows, it contained information of locally restricted spatial scales, shape, and structure, etc. in the feature vector. The broken vessel segments and some local ambiguities due to twisted vessels were also not covered in FABC.

Matched filtered technique in combination with AdaBoost classifier was used for the vessel segmentation in [63]. The preprocessing of the retinal image involves different steps i.e. the morphological process was used to enhance the image, the contrast was improved using limited adaptive histogram equalization, Retinex was applied to adjust the inhomogeneity, and the amalgamation of Frangi matched-filter and B-COSFIRE were utilized to improve retinal vessels. Using the sliding window on the preprocessed image, various pixel-wise statistical features were extracted to train the AdaBoost classifier. An mRMR feature selection process was used to keep the tinny vessels. The segmentation method was evaluated on DRIVE, STARE and CHASE_DB1 datasets with an average accuracy of 0.972, 0.951, and 0.948 respectively. The proposed method has shown acceptable accuracy for vessel segmentation with low levels of noise and segmentation artefacts. Degrading the practicality of the classification, the advantage of this method can be seen in retinal images where vessel pixels can be recognized as non-vessels.

Fraz *et al.* [64] proposed a supervised method for ocular fundus images. A 7-D vector was created using the features of morphological linear operators, Gabor filter at various scales, spatial intensity measures and line strengths. The GMM was used to classify the pixels as vessel and non-vessel. DRIVE and STARE datasets were used to test the proposed method. The performance was evaluated on different measures i.e.

TABLE 4. Matched filtered methods.

Paper #	Algorithm	Year	Dataset	Accuracy	Sensitivity	Specificity	AUC
[67]	Sofka et al.	2006	DRIVE	-	-	-	-
			STARE	-	-	-	-
[68]	Kumar et al.	2016	DRIVE	0.9626	0.7006	0.9871	-
			STARE	0.9637	0.7675	0.9799	-
			HRF	0.9450	0.7574	-	-
[69]	Chaudhuri et al.	1989	DRIVE	0.8773	-	-	0.7878
[70]	Gang et al.	2002	-	-	-	-	-
[71]	Odstrcilik et al.	2013	DRIVE	0.9340	0.7060	0.9693	0.9519
			STARE	0.9341	0.7847	0.9512	0.9569
			HRF	0.9445	0.7463	0.9619	0.9589
[72]	Yavuz et al.	2010	STARE-MF	-	0.7189	-	-
			STARE-GF)	-	0.8185	–	-
[73]	Dharmawan et al.	2017	DRIVE	0.954	0.756	0.973	-
			STARE	0.953	0.731	0.972	-
[74]	Gao et al.	2017	DRIVE	0.9636	0.7802	0.9876	0.9772
[75]	Zhang et al.	2010	STARE	0.9382	0.7120	0.9724	-
[76]	Elson et al.	2017	DRIVE	0.9657	0.7221	0.9775	-

TABLE 5. Mathematical morphology methods.

Paper #	Algorithm	Year	Dataset	Accuracy	Sensitivity	Specificity	AUC
[79]	Monga et al.	1995	-	-	-	-	-
[80]	Nisha et al.	2017	-	-	-	-	-
[81]	kumar et al.	2017	DRIVE	-	-	-	-
			STARE	-	-	-	-
[82]	Rodrigues et al.	2016	DRIVE	0.9565	0.7323	0.9783	-
			STARE	0.9568	0.6699	0.9797	-
[83]	Fraz et al.	2011	DRIVE	0.9419	0.6879	0.9798	-
			STARE	0.9434	0.7925	0.9670	-
[84]	Singh et al.	2014	DRIVE	0.9460	0.7138	0.9801	-
			STARE	0.9521	0.7036	0.9800	-
[85]	Zana et al.	1999	-	-	-	-	-
[86]	Zana et al.	2001	-	-	-	-	-
[87]	Sun et al.	2009	-	-	-	-	-
[88]	Miri et al.	2011	DRIVE	0.9458	0.7352	0.9795	-
[89]	Fraz et al.˙	2008	DRIVE	0.9326	-	-	-
			STARE	0.9349	-	-	-

accuracy, sensitivity, specificity, and AUC. The accuracy scores of 0.9579 and 0.9476 were achieved using DRIVE and STARE dataset respectively.

B. UNSUPERVISED METHODS

The unsupervised method is used to discover hidden patterns of a blood vessel from the retinal image and it doesn't require any previous knowledge e.g. ground truth images to classify the pixel is a vessel or not. It is further utilized for the clustering of data. The data used in unsupervised learning is not labelled (training data) along with a number of classes are not certain to classify the image data [65]. The unsupervised method can be further divided into matched filtered methods, mathematical morphology methods, vessel tracking methods, and model-based methods.

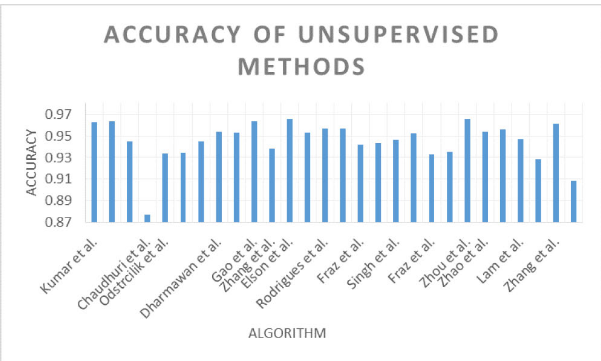
The features of multi-scale line detection were employed for the retinal vessels segmentation in colour fundus image [66]. In this unsupervised method, the line detector is calculated by varying the length of the line detector. The segmentation is attained by linearly combining the line response at different scales. The method has shown significant results of segmentation accuracy at the region around the vessel. This method is tested on three datasets DRIVE, STARE, and Retinal Vessel Image set for Estimation of Widths (REVIEW). The proposed method has shown high local accuracy and marked correct vessel segmentation on DRIVE and STARE datasets. The vessel width measurement is achieved using the segmentation of the suggested method. The main advantage of this method includes simplicity, faster segmentation results, and scalability to pass high- resolution images. The performance measure of each category along with the graph of unsupervised average accuracy is given in this section. The performance measure of matched filtered, mathematical morphology, and model-based methods are illustrated in table 4, 5, and 6 respectively. The graphical schematic of unsupervised methods is given in Fig.5. in which 5(a) represents the average accuracy of these methods which falls between 0.86 to 0.96 and the yearly decomposition is given in 5(b).

1) MATCHED FILTERED METHODS

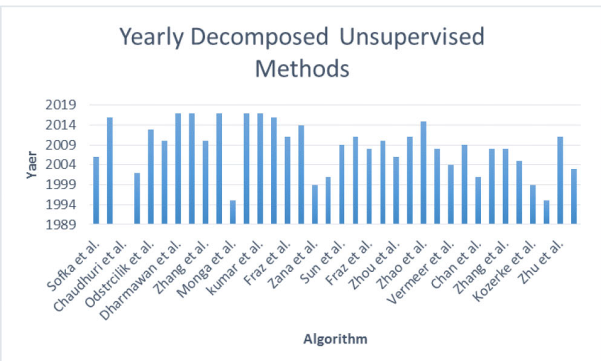
The matched-filtered (MF) methods are used to extract the vessel outlines. The kernel tuned at different locations to find an image feature at anonymous location and direction and

TABLE 6. Model based methods.

Paper #	Algorithm	Year	Dataset	Accuracy	Sensitivity	Specificity	AUC
[90]	Yu et al.	2010	-	-	-	-	-
[91]	Zhou et al.	2006	CT Images	0.9659	-	-	-
[92]	Tagizaheh et al.	2011	X-Ray Angiogram	-	-	-	-
[93]	Zhao et al.	2015	DRIVE	0.954	0.742	0.982	0.862
			STARE	0.956	0.782	0.978	0.874
[94]	Lam et al.	2008	STARE	0.9474	0.8215	-	-
[95]	Vermeer et al.	2004	GD_X	-	0.924	0.921	-
			STARE	0.9287	-	-	0.9187
[96]	Al-Diri et al.	2009	DRIVE	-	0.7282	0.9551	-
			STARE	-	0.7521	0.9681	-
[97]	Chan et al.	2001	-	-	-	-	-
[98]	Sum et al.	2008	-	-	-	-	-
[99]	Zhang et al.	2008	DRIVE	0.9610	-	0.9772	-
			STARE	0.9087	0.7373	0.9736	-
[100]	Tong et al.	2005	-	-	-	-	-
[101]	Rueckert et al.	1995	MR Images	-	-	-	-
[102]	Zhu et al.	2011	ARIA	-	-	-	-
[103]	Kovesi et al.	2003	-	-	-	-	-
[104]	Kozerke et al.	1999	Flow Phantom	-	-	-	-



(a) Average Accuracy



(b) Yearly Decomposition

FIGURE 5. Unsupervised Methods: Average accuracy of unsupervised methods which falls between 0.86 to 0.96 and these algorithms are employed from the period of 2002 to 2018.

matched filter response plays a vital role to detect the vessel contours. The matched filter methods convolve a 2D kernel with retinal fundus image for the detection of the vessel. Usually, three features are associated with kernel designing: vessel have restricted curve and can be approached using linear segments, the diameter in the optic disk is higher and it decreases in the outer region, the pixels' strength of linear segments estimates the Gaussian curve [67]. The convolutional kernel is used to remove the computational overhead. The vessels which are specified by the kernel and with equal standard deviation (SD) of Gaussian function are well treated by kernel unlike the kernel with different standard deviation. The retinal image has various different backgrounds and the existence of pathologies in the image may lead to misclassifying the vessel form the background. The matched filtering approach works better in combination with other approaches i.e. Memari et al. have used a matched filter with AdaBoost classifier in [63].

The author has been proposed 2-D matched filter for the blood vessel detection in the retinal image. CLAHE (Contrast Limited Adaptive Histogram Equalization) was used to enhance the vessels [68]. The LoG (Laplacian of Gaussian) filter was applied to avoid non-vasculature misclassification. The vessels were extracted from the retinal image using the inherent property of LoG along with MF. The proposed method was evaluated on DRIVE, HRF and STARE databases. The method has an advantage of easy implementation, less computation time, simplicity, and effectiveness to extract vessel regardless of the pathological condition of the retina.

In [69], the solution of accurately locating the vessels in the retinal image was discussed. The author created an operator based on the spatial and optical properties of the object for the feature selection. The Gaussian-shaped curve was used to approximate blood vessel. A 2-D MF was introduced to detect the vessel in the retinal image based on piecewise linear segmentation. The 12 templates were construed in this method which was used to detect vessel segments in every direction. The strong point of the proposed method was its computational simplicity and model-based edge detection. This method has shown decent results to detect vessels even in fluorescein angiogram image.

Gang *et al.* [70] proposed amplitude modified second-order Gaussian filter for the blood vessel detection task. The width of the vessel in a linear relationship was measured by "spreading factor" of the MF when the magnitude coefficient was suitably assigned for the Gaussian filter. The pre-calibrated line can be used to find out the vessel diameter absolute value. The results of this study have proved that width measurement was not only used for blood vessel size but it could also be used for optimizing the MF response for the accurate detection of vessels.

The task of retinal vessels segmentation was achieved by improving the matched filter in [71]. The segmentation was performed by varying diameter of the vessel in high-resolution retinal images of the new database. The binary vessel tree was extracted using minimum error thresholding and MF. Five kernels were designed in view of five width classes of the retinal vessel with a reliable resolution of the width. The proposed method has an advantage to segment vessel with specular reflection.

The features of Gabor filter (GF) and 2-D matched filter (MF) were analyzed for blood vessels segmentation [72]. The 2D Gabor filter and MF were applied to the retinal image to enhance blood vessel. The Otsu and P-tile thresholding techniques were used for binary transformation of vessel segmentation. The results of this study have shown remarkable results for binary transformation. STARE dataset was used for the evaluation task. Gabor and 2D MF have shown 0.8185 and 0.7189 true positive rate respectively.

In [73], a novel 2D matched filter based on modified Chebyshev Type-I function has been proposed for retinal vessel detection. The proposed method substitutes the Gaussian probability in the traditional MF. The CLAHE was used to enhance vessel contrast and the background normalization was performed by replacing the lesion pixel with background pixel. The post-processing steps were applied to detect low noise vessel image. The performance was evaluated on STARE and DRIVE databases.

Gao *et al.* [74] proposed a method based on Gaussian matched filter and U-net (fully convolutional neural network) for the prediction of vessel segmentation. The thin vessels were strengthened using the Gaussian matched filter while U-net was used for end-end automatic retinal vessel segmentation. The DRIVE dataset was used to evaluate the performance of the proposed method and achieved an accuracy score of 0.9636.

Zhang *et al.* [75] proposed a matched filtered first-order derivative of Gaussian method (MF-FDOG) for the accurate retinal vessel extraction. The method was based on an original matched filter approach along with first-order derivate and zero-mean Gaussian function. The MF-FDOG accurately detects vessels edges, unlike MF which was used to extract both vessel and non-vessel edges. The thresholding of the fundus image to the MF was used to extract vessels, where image response to the FDOG was used to adjust the threshold value. The proposed method has an advantage of simplicity, to deal with pathological retinal images and to detect tinny vessels.

A Multi-Scale Matched Filter (MSMF) approach was used for the automatic extraction of the vessel [76]. An MSMF originated from Social Group Optimization (SGO) was used to extract retinal blood vessels. The most commonly used datasets STARE and DRIVE were used to evaluate the proposed approach. The optimum filter values for MSMF were achieved to improve the accuracy of vessel extraction. The SGO based MSMF has shown significant results to detect vessels.

2) MATHEMATICAL MORPHOLOGY METHODS

Mathematical morphology methods are used to extract the structure of the image (image features). This is the well-known approach for the segmentation of image [77]. It is used to extract the image components for recognition of specific shape i.e. boundaries, skeleton, features, and convexity. The basic operators used for mathematical morphology to deduce top hat transformation are closing, opening, dilation, and the erosion. This technique was initially established for a binary image which was further extended for greyscale images. Top-hat transformation and watershed transformations are two algorithms closely related to mathematical morphology processing methods [78].

Mathematical morphology and linear processing techniques were implemented for vessel segmentation in [79]. The proposed model used the geometric model to extract the vessel from non-vessel. The bright round peaks were removed that permits angiogram to be segmented from micro-aneurisms. The main strength of the proposed techniques was based on the combination of different operators and mathematical morphology. Various shape features like curvature were calculated with Laplacian filter and basic features and linear bright shapes were extracted by mathematical morphology operators. The curvature differentiation was used to extract vessels.

Nisha *et al.* [80] proposed a novel approach for vessel segmentation in infant's retinal images. The approach was based on mathematical morphology and fusion of structure adaptive filtering (Coherent-Enhancing Diffusion Filter and Guided Filter). In the proposed method thicker and thinner vessel were extracted. The top-hat transformation was used to extract thicker vessels, while guided filter-based suppression technique was used to extract a thinner vessel. The modified morphological closing operation was used as a post-processing step which keeps the tinny vessel in segmented output that can be used to find pertinent feature for the analysis of Retinopathy of Prematurity.

In [81], the morphological operation detection approach has been used for automated segmentation of the retinal vessel. In the vessel filling stage, the vessel centerlines have been determined. The output of the four directional differential operators has been analyzed to find out the candidate connected set. The vessel derived features were used to classify candidate points into centerline pixels. The region growing method was used to obtain vessel segmentation. In this proposed method, vessel centerlines used region growing technique (that is used to grow point in the vessel segmented image using Top-hat transformation). The cleaning operator was used to remove all unnecessary pixels near the vessel points for final vessel segmentation.

The features of the morphological and topological vessel extractor method for automated vessel segmentation had discussed in [82]. The parallel greyscale skeletonization method has been employed with mathematical morphological operators to obtain better segmentation results. The morphological and topological extractors were used to extract pixel belonging to a vessel tree and to find out the topological vessel features and connectivity respectively. The proposed method obtained accurate retinal vessel tree by removing the spurious objects and smoothing the vessel borders. The DRIVE and STARE dataset were used to evaluate the classifier.

Fraz *et al.* [83] employed a morphological curvature, adapted hysteresis thresholding based on morphological reconstruction method for the retinal vasculature network. The Top-hat transform and maximum principal curvature calculation at different points were used to enhance the blood vessel. The centerlines of the vessel were computed using non-maximal suppression, morphological reconstruction and adapted hysteresis thresholding. The vessel skeleton map was constructed using double threshold curvature image and morphological reconstruction which was used to obtain retinal vessel segmentation. The DRIVE and STARE datasets were used to evaluate the proposed method.

A novel approach for the blood vessel extraction from retinal images has been proposed in [84]. The approach was based on morphological (bottom-hat transformation) operations with phase preservative noise-removal method which was utilized for vessel enhancement and background elimination. The vessel outlines were extracted using the fixed threshold method. The refined vessel was obtained in a post-processing step by removing irrelevant regions and spur pixels. The proposed method has shown significant result evaluated on DRIVE and STARE database.

Zana and Klein [85], [86] employed the morphological filters followed with cross-curvature evaluation for the segmentation of the vessels. Mathematical morphology was used to highlight the vessel in the unicolor retinal image because the vessel was connected, linear, and their curvature was smooth along the crest line. The cross curvature evaluation was used to identify the vasculature in the retinal image for linear coherent curvature images. The proposed method has four steps for the detection of vessel i.e. linear pattern with a Gaussian-like profile, linear filtering, cross curvature evaluation, and noise reduction. Three different image types were used to evaluate the proposed method: grayscale images, RGB images without a filter and fluoro-angiograms images.

The mathematical morphological multiscale enhancement, watershed transformation, and fuzzy filter were used in the combine to extract vasculature tree in the angiogram [87]. The opening operator of nonlinear multiscale morphology with varying size of structure element on every pixel was used to determine the background. The contrast normalization was performed by subtracting the estimated background image with the original image. The combined fuzzy morphological operation was used to process the normalized angiogram with 12 linear structuring elements altered at every 150 from 00 to 1800 with the length of 9 pixels each. The vessel region was identified by making the filtered image as a baseline proceed to form thinning operation to estimate vessel centerlines. Watershed technique was used to find out the boundaries of the vessel with the obtained centerlines. The proposed method was evaluated on the image set of seven patients.

Miri et al. proposed multi-structure mathematical morphology and fast discrete curvelets transform (FDCT) for the retinal vessel detection in [88]. The multi-structure mathematical morphology was used to detect the edge of the vessel while FDCT was applied for contrast enhancement. The unnecessary vessel edges were eliminated using morphological opening operator and the length of the detected vasculature was computed using adaptive connected component analysis method so that a complete vascular tree can be obtained. The proposed method was evaluated on DRIVE dataset and has achieved state of the art accuracy comparing with others.

The combination of vessel centerlines and morphological processing has been proposed for the retinal vessel segmentation task in [89]. The performance comparison of two retinal vessel segmentation techniques was presented in that paper which was based on the combination of morphological bit plane slicing and multiscale morphological reconstruction. The proposed method was evaluated on STARE and DRIVE considering accuracy and processing time as performance metrics. The bit plane slicing techniques have outperformed others in terms of processing time and accuracy.

3) MODEL BASED METHODS

Model-based approaches use explicit vessel models for the extraction of the retinal blood vessel. These approaches help to deal with both pathological and normal retinas. Model-based methods include deformable models and vessel profile models. The deformable models can be either parametric (active contour) or geometric. Whereas, the vessel intensity profile models were used to approximate the Gaussian shape. The cubic splines, second-order derivative Gaussian or Hermit polynomic profile were freely replaced. The inclusion of bright and dark lesions (non-vessel features) and background properties in difficult imaging condition was a complex procedure for vessel detection and improve segmentation accuracy. It was assumed to have a flat background in some profile models for the vessel detection task.

Yu and Sun [90] proposed a deformable model based on morphology features for the extraction of the vessel on angiogram. The deformable model has been developed to address the issues of low contrast angiogram images and complex vessel shape. The proposed method used region-based active contours for the vessels segmentation task in which morphology region measures were implemented as a stop criterion curve rather than gray intensity and its gradient to avoid from the issue of inhomogeneity caused by gray intensity. The model has been evaluated on both real and synthetic images.

The features of the deformable model and ridge scan conversion for the vessel boundary extraction and automated bifurcation points detection has been presented in [91]. The proposed method was implemented using pre-selection of the tubular structure and vessel tracing based on Eigen analysis of the Hessian matrix. This gives the advantage of estimated vessel direction and a cross-sectional plane orthogonal to the vessel. The bifurcation vessel points were detected using Scan-Conversion method. The deformable model was used to identify and reconstruct the vessels. This method has shown significant success rate to extract the vessel boundary.

Tagizaheh *et al.* [92] used a novel approach for coronary vessels segmentation in X-ray angiogram images. The artefacts were omitted by registering the angiogram in the first step, then geometric active contours were utilized for the vessel segmentation. The tracking method was used to detect the vessel centerlines which helps to converge the active contours. The main strength of the proposed method detects thinner and low contrast vessels successfully.

The infinite active contour model based on the hybrid region image information for automated vessel segmentation in the retinal images has been presented in [93]. The infinite perimeter regularizer (developed using a Lebesgue measure of the neighbouring boundaries) gives the advantage of better detection of small oscillatory structure than the former models like Hausdorff measure which was based on the length of feature's boundaries. The multiple types of region information i.e. combination of local phase-based enhancement map and intensity information were used in a proposed method to obtain better segmentation results. The intensity information was used for accurate features segmentation while the superiority in vessel edges was preserved using local phase-based enhancement map. The proposed method was evaluated on three datasets which have outperformed others.

In [94], an algorithm based on the divergence of a vector field was presented for vessel segmentation in pathological retinal images. Firstly, the normalized gradient vector field was used to detect the vessel centerlines then gradient vector field was used to identify the blood vessels. The falsely identified blood vessel-like objects were pruned with respect to detected centerlines distance. The proposed method was evaluated on STARE dataset which yields an accuracy of 0.9474.

Vermeer *et al.* [95] used a Laplacian vessel profile to find the central vessel reflex. The 2D Laplacian kernel was used to convolve the retinal image and the smaller objects in the images were pruned in order to connect the aligned vessel fragments in the matched-filter-response (MFR) image. The morphological closing operation was used to detect the inner parts of the vessel to produce candidate objects. The proposed method was evaluated on GDx created images and has shown 0.924 of TPR, and 0.079 of FPR.

The segment profiles of retinal blood vessels were extracted by a method proposed by Al-Diri *et al.* [96]. The segmentation of vessel and the measurement of width characterized by the Ribbon of Twin active contours were incorporated in this method. The tramline filter was used in the first step to trace the vessel segment centerline pixels. The growing algorithm was used to transform the tramline pixel map as a segment set including a series of profiles and removing false positive pixels. The segment growing algorithm used an active contour model ROT to capture the vessel edges followed by junction resolution algorithm which resolve various joining and junctions. The proposed method was evaluated on STARE, DRIVE, and REVIEW publicly available datasets.

The Chan and Vese vessel segmentation method [97] was modified by Sum and Cheung [98]. The local image contrast was incorporated into active contours based on the level set in the proposed method. The main strength of the method was to deal with non-uniform illumination. The performance of the modified method was evaluated on both the clinical and synthetic angiogram images.

Zhang *et al.* [99] proposed a novel method based on nonlinear projections for vessel detection. The surface structure in the image was captured using a nonlinear projection. Firstly, the green channel of the RGB image was projected into a closed convex set containing zero mean oscillating function. Then the oscillating components of retinal images were used to capture the blood vessel properties. Finally, an adaptive thresholding method characterized by variational image binarization algorithm [100] was used to achieve the segmented vessel tree along with morphological post-processing was also applied to obtain a better binary image.

The vessel segmentation in cine MR image was performed using an adaptive snake model which includes both probabilistic and stochastic relaxation methods [101]. The Simulated Annealing stochastic relaxation technique was used in the first frame of the proposed method to find the minimum global energy in the adaptive snake for vessel segmentation task. The fast probabilistic relaxation technique in other frames segmentation. The previous frame segmentation results were used to initiate the snake in subsequent frames. This method was similar to the Geometrical Deformable Models and modelled as 1D Markow Random Field, which has shown significant results.

Zhu [102] proposed a general representation of the cross-sectional vessel profile in the Fourier domain. The universal representation was characterized using phase congruency. The Fourier domain adjusts the upward and downward of cross-sectional profiles with varying sharpness and considers the inner part of the vessel. A 24 log Gabor filter was used to transform the input image at six directions along with four scales (symmetric and asymmetric pairs). The Kovesi phase congruency model [103] and the scale-invariant property was employed to measure the symmetry and asymmetry of local Fourier components. The SVD (singular value decomposition) was used to discover maximum and minimum eigenvalues). The nonlinear point features i.e. crossovers and bifurcation were used to identify the point feature location and among them, non-vessel are excluded.

A methodology based on active contours models for automated vessel segmentation in cine phase-contrast flow measurement was proposed by Kozerke *et al.* [104]. The user-selected vessel from a random image frame was used as an input of the method. The system matched the phase image consistent to initial systolic acceleration of the blood movement that confirms the robust segmentation of the initial image frame. Firstly, a Gaussian mask convolves each image frame to lessen noise. Then all those pixels were detected which surpass the half of the maximum phase and the isolated pixels were eliminated and filled with connectivity information. Finally, the phase image was selected whose area was above half of the maximum phase. The resulting contours of the former frame were used to process the remaining frames. The proposed method had the advantage to deal with the image distortion as it incorporated the phase image and the magnitude image.

4) VESSEL TRACKING METHODS

Vessel tracking methods are used to track the vessel by keeping the eye on the centerline of the vessel. The centerline of the vessel is determined including various properties i.e. tortuosity and intensity. These methods divide a vessel among two points using single vessel details (instead of the whole vasculature) and local information. This is further intended to find the local information and a vessel profile model path in which not only vessel centerline but the width of every vessel is extracted correctly. Vessel tracking methods usually work with matched filters of morphological operators as in [105]. The detail of the individual vessel and accurate vessel width is the major advantage of this method.

In [106], a graph theory-based method was proposed to extract vessel outlines in angiogram images by tracking two edges. The blood vessel properties i.e. section size, position, and the curvature of the segment have been utilized for formal structure blood vessel model. The heuristic search approach [107] was used to detect the possible edges in the retinal image. The best-detected edge was further used as an optimum path in the graph representation. This method used the node concept in which two opposite edges were kept together for the representation of vessel segmentation.

The combination of sequential tracking method, watersheds, and morphological tools of the homotopy was used to extract arteries into angiogram image [108]. The recursive sequential tracking method was originated from circular template analysis, which was used for segmentation of artery tree skeleton and to estimate the width of arteries at different scales. The watershed transformation and the morphology of the homotopy modification were employed to investigate the artery segment for the correct extraction of the border.

A Fuzzy C-Means (FCM) clustering technique has been presented in [109]. The proposed method used the linguistic features i.e. vessel and non-vessel to track the blood vessel in the angiogram images. The only fuzzy image intensity information was encoded in the algorithm without considering the vessel shape. This method performed four major steps to track the vessel: (1) the optic nerve was detected and used as an initial point in retinal image, (2) the optic nerve bonding circle was identified, (3) FCM was applied and the bonding circle points were segmented into vessel and non-vessel, (4) on each candidate's vessel, the fuzzy vessel tracking algorithm was employed. The main strength of this algorithm was that it reduced the noise effect in vessel tracking because it didn't use any edge information to locate the vessel.

Li *et al.* [110] employed a retinal vessel tracking technique using a maximum posterior probability. The principal component analysis (PCA) method was used to detect the optic disk, while the intensity gradient co-occurrence matrix and Gaussian filter were applied to detect retinal vessel. The segmentation results were used to identify the vessel starting points around the optic disk. The Bayesian theory was used to track the individual vessel. According to the vessel width, curvature, and mobile direction, a semi-ellipse was introduced as a search region. The candidates of the subsequent vessel edge points were selected in this search region. The vessel structures were categorized into the normal vessel, vessel crossing, and vessel branching. The probabilities of all the possible candidate points were approximated and the vessel structure and edge points were calculated with Bayesian theory. The proposed method has shown good tracking results.

In [111], the author proposed a method to detect retinopathy in retinal images based on matched filtering approach that uses the prior information of retinal vessel properties. The proposed method was iterative and forms the profile of the vessel using the Gaussian function. The spatial properties of the vessel were also included in the method to enhance the computational performance in a region where the segments were comparatively straight. The method required manual information to locate the starting and ending search region and vessel direction.

The retinal blood vessels in fundus image were detected using a tracking approach with Kalman and Gaussian filters [112]. The average vessel centerline was approximated using a second-order Gaussian filter and the vessel tracking was initiated around the optic disc circumference. The Kalman filter was used to approximate the location of the next vessel segment based on both current and previous segments. The detection of the vessel branches was tracked using the branch detection approach.

Can *et al.* [113] proposed a method based on recursively vessel tracking beginning from early seed points using directional templates. The maximum response of the edge in a specific direction was obtained using the directional template. The templates were employed on candidate vessel point at various locations. The edges that give the most of the responses of the templates were highlighted at candidate points. This method used the iterative procedure in maximum response direction and at every new point, the same procedure was recorded. The retinal features i.e. crossover points or branching were approximated once the segmentation of the vessel was performed. The main strength of the proposed method was its robustness.

The model-based tracking algorithm for the vessel segmentation was proposed by Delibasis *et al.* [114]. The proposed model used vessels parametric model consists of the stripe. The similarity between the input image and the model was identified using a measure of the match (MoM). The seed pixels were initialized using multiscale vessels filter, arbitrary picking non zero seed pixel, and splitting the binary result into non-intersecting square blocks. The tracking of the vessel was performed using optimum strip matching results based on strip orientation, seed point, strip width and MoM. The method seeks vessel bifurcation without the user's involvement when vessel tracking was terminated. The DRIVE dataset has been used to evaluate the proposed method.

A novel approach to extract the central axis which helps to search the minimum cost path was employed by Wink et al. [115]. The extraction in the proposed method was based on a multiscale vector value feature representation. The Eigen decomposition of the Hessian matrix was used to construct the vessel segment at various levels and the response of vector-valued was transformed into a 3D cost image. The transformation process has given the advantage of lower-cost path searching for a wave-front propagation in two or more user-defined points to extract the central axis of the retinal vessels. The proposed method was evaluated on real and synthetic images and it has shown decent results to cope with different imaging artefacts.

Liu and Sun [116] proposed adaptive tracking for vasculature detection in the retinal angiogram. The approximation of vessel trajectories was based on indicating vessel point in the vessel. After the segment tracking, it was removed from the angiogram image by increasing deletion intension value over gray level indicating vessel. These experiments were carried out recursively to excerpt the vessel tree. The starting points were manually specified by the user in this algorithm.

III. RETINAL IMAGE PROCESSING

The processing of retinal fundus image is the preliminary step for vessel segmentation task. It involves different steps, i.e. capturing a photo of the eye containing vessel, vessel enhancement, removing noise, and evaluating performance using different measures, etc.

A. FUNDUS PHOTOGRAPHY

Fundus photography uses specialized fundus camera to capture the photo of the retina (back of the eye). The intricate microscope is attached to flash enabled fundus cameras. Fundus camera uses special filters and dyes to capture the main structure of the eye i.e. optic disc, macula, and central and peripheral retina [117]. The fundus photography has been decomposed into different modes i.e. colour, red-free, angiography, and simultaneous stereo fundus photography. The retina is brightened using white light and examined in full colour in colour photography. In red-free fundus photos, special filter i.e. a green filter with 540-570nm wavelength is used to observe superficial lesion and remove red light. In the process of angiography, a fluorescent dye is injected into the bloodstream to capture the photos. Sodium fluorescein angiography uses the blue light of 490 and fluoresces 530 of yellow light. This is highly acceptable photography for diabetic retinopathy. Indocyanine green angiography is used to observe choroidal vessel and utilized an infrared diode laser of 805nm.

B. DATASETS

There is a number of public retinal datasets available with blood vessel details. It is the key step for blood vessel segmentation to train and test the classifier on the retinal database. Some databases i.e. STARE and DRIVE etc. are publically available for the researchers along with the ground truth images of the vessels. The performance of the classifier can be evaluated using these datasets.

1) STARE

[1]STARE stands for Structured Analysis of the Retina. This dataset consists of 400 retinal images, captured using TOPCON TRV-50 fundus camera with additional settings of 35° field of view (FOV) and 8bits/colour channel at 605*700 pixels. The average diameter of the FOV is 650*700. STARE has 20 vessel ground truth images used for blood vessel segmentation in which 9 are healthier while rest of them has shown a different type of retinal diseases. Two experts have manually segmented these images in which the first expert segmented 10.4% vessel pixel, while the second expert segmented 14.9 % of the thinner vessel. Generally, the segmentation of the first observer used to compute the performance as the ground truth.

2) DRIVE

[2]Digital Retinal Images for Vessel Extraction (DRIVE) is one of the commonly used datasets for retinal blood vessel segmentation. DRIVE consists of 40 retinal images, in which 33 are healthier images while 7 have shown sign of mild diabetic retinopathy. Canon CR5 non-mydriatic camera with 45° FOV and 8 bit per colour channel at 768*584 pixels have been used to capture the images in JPEG format. Every image has a circular FOV with 540 pixels' diameter. DRIVE dataset has been divided into training and test set with 20 images each. In the training set, 14 images were segmented by first expert and 6 images were segmented by the second expert. In the test set, segmentation has been performed twice in two cases. In case1, first and second expert segmented 13 and 7 images respectively while the case2 has been performed by the third expert. In case1 and case2, the observers marked 12.7% and 12.3% pixels as vessel respectively.

[1]http://cecas.clemson.edu/~ahoover/stare/
[2]https://www.isi.uu.nl/Research/Databases/DRIVE/

3) CHASE_DB1

[3]Child Health and Heart Studies in England (CHASE) contains images of different diseases in which retinal images along with ground truth vessel can be found in the first database entitled CHASE_DB1 [118]. The images were captured with NM-200D fundus camera with 35° FOV, 1280 by 960pixels resolution and in TIF format. The images were captured under full-field illumination and around the centre of the optic disc. The CHASE DB1 database incorporated 28 pictures altogether, which were gathered from the left and right eyes of 14 kids. The vessel ground truth pictures were physically sectioned by two experts. There was no record of the disease of the 28 retinal pictures, however, they are all in great quality and differentiation.

4) HRF

[4]This is the database of high-resolution fundus images created by Jan Odstrcilik to perform a comparative analysis on automatic segmentation algorithms. HRF database contains 45 photographs including 15 of normal patients, 15 images of the patient with glaucomatous and 15 of diabetic retinopathy patients. The images in this dataset have 3504*2336 resolutions, which is higher than other retinal databases. Binary gold standard images are available for each image and these ground truth images are manually segmented by the experts in the retinal image analysis field. Canon CR-1 camera was used to capture fundus images along with 45° FOV and different acquisition settings [119].

5) MESSIDOR

This is the project of the French Ministry of Research and Defense to perform comparison studies on different segmentation algorithms for retinal fundus images [120]. [5]Messidor is the largest dataset with 1200 retinal images captured using non-mydriatic Topcon TRC NW6. The 3 ophthalmologic departments acquired images with additional settings of 45° field of view and 8 bit per colour channel 2304*1536, 2240*1488 and 1440*936 pixels' resolution in TIFF format. 400 pictures of this dataset were acquired without pupil dilation while rests of them were captured with dilation. For each image in the dataset, two diagnoses have been suggested by the experts i.e. risk of macular oedema and retinopathy grade.

6) REVIEW

[6]REVIEW [121] with 16 mydriatic images and 193 vessels segments, is the retinal vessels reference database. REVIEW is the abbreviation for retinal vessel images for estimation of width, this dataset was created by the University of Lincoln, UK in 2008. A special drawing tool has been used by three experts to mark the edges of the vessels. This dataset has been segmented into four sets i.e. high-resolution images, central light reflex images, vascular disease images and kicks point images with 8, 2, 4, and 2 images respectively.

7) ImageRet

[7]ImageRet is the project of FinnWell Technology for diabetic retinopathy (DR) and was open access in 2008 [122]. This dataset contains 219 retinal images, which is sectioned into two sets i.e. DIARETDB0 and DIARETDB1. There are 130 images (110 Normal, 20 DR affected) in DIARETDB0 set while the DIARETDB1 has 89 images (5 Normal, 84 DR affected). The images were captured with fundus camera at 50 degrees of field of view and 1500 by 1152 resolution in PNG format.

8) ROC MICRO-ANEURYSM

[8]Retinopathy Online Challenge (ROC) was held in University of Lowa in 2009 for micro-aneurysm detection. A dataset of 100 images was created for ROC, which was divided into two sets i.e. test set and training set with 50 images each. The gold standard representing micro-aneurysm locations are available in the training set. The images are captured with TopCon NW100 and Canon CR5-45NM fundus camera in JPEG format at a 45-degree field of view and 1058*1061, 1389*1383 and 768*576 resolutions [123].

9) ARIA

[9]Automatic Retinal Image Analysis (ARIA) is the database created by the joint collaboration of the University of Liverpool and the Royal Liverpool University Hospital Trust, the UK in 2006 [124]. The dataset has three images subset i.e. diabetes images (59), control group images (61), and age-related muscular degeneration images (92). The images were captured with Zeiss fundus camera FF450 at 50o FOV, 8 bit per colour plane, 768*576 pixels' resolution and stored in TIFF format. The ground truth details of the blood vessel location, fovea location, and the optic disc were marked by two observers.

10) VICAVR

[10]VICAVR [125] dataset consists of 58 retinal images. The dataset was used to compute the artery/vein ratio and the images are captured using NW-100 TopCon nonmydriatic camera with centred optic disc and 768*584 pixels' resolution. The database contains the details of the vessel measured from the optic disc at different radii along with the type of vessel (A/V ratio). The ground truth details were observed by three image analysis experts.

C. PREPROCESSING STEPS

The preprocessing of the image is the key concept for the better segmentation process of the retinal vessel before the

[3]https://blogs.kingston.ac.uk/retinal/chasedb1/
[4]https://www5.cs.fau.de/research/data/fundus-images/
[5]http://www.adcis.net/en/third-party/messidor/
[6]http://www.aldiri.info/Image%20Datasets/Review.aspx/
[7]http://www.it.lut.fi/project/imageret/
[8]http://webeye.ophth.uiowa.edu/ROC/
[9]http://www.aria-database.com/
[10]http://www.varpa.es/research/ophtalmology.html#vicavr/

classifier training and testing phase. This step may involve different steps and techniques depending on the requirements of the classifier. This is usually performed for noise reduction, vessel enhancement, and outlier deletion, etc. We have mentioned some of the commonly used preprocessing steps in the subsequent section.

1) IMAGE TRANSFORMATION

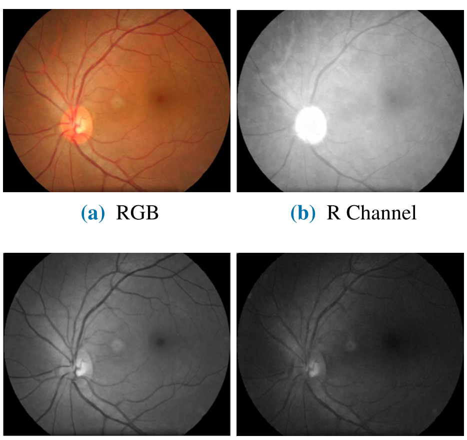
The main objective of image transformation is to transform the retinal fundus image into a grayscale image. This preprocessing step was employed by most of the researchers for a better understanding of the image [48], [49]. The grayscale image has an only one-dimension image, unlike the RGB which has three-dimension images as in Fig.6.

(a) Color Image (b) Grayscale Image

FIGURE 6. RGB image (3-dimensions image) is converted into grayscale format for better understanding of the image which has only one dimension.

2) GREEN CHANNEL EXTRACTION

The retinal colour image (RGB) has three channels that are red (R), green (G) and blue (B). The green channel holds the maximum contrast and minimum noise to extract the accurate vessels as mentioned in [13], [61], [85], unlike the blue and red channel which are filled with the background texture. Whereas, it is difficult in the blue and red channel to determine whether the thinner pixels are a vessel or not as shown in Fig.7.



(a) RGB (b) R Channel (c) G Channel (d) B Channel

FIGURE 7. Retinal Image RGB has three channels red (Red), green (g), and blue (B). The optic disc and blood vessel details are clearly visible in green channel.

3) KNOWLEDGE-BASED PROCESSING

Knowledge-based (KB) approach is used to address the problem of image acquiring and image processing. KB helps to get the specific information from the image by adjusting parameters accordingly. This technique also facilitates in extracting the semantics within an image that can be comprised of the recognition of an object or scenario [126].

4) IMAGE ENHANCEMENT

Image enhancement is the technique to improve the quality of the retinal image so that the blood vessel can properly be visible for the training and testing of the classifier. There are various approaches in digital image processing for image enhancement. Like, Dong et al. used maximum entropy transformation to boost the quality of the fundus image. The iterative algorithm was employed to approximate the gray level optimal classification threshold. Yang *et al.* [127] and Li et al. [128] used the histogram equalization method to improve image quality. Histogram equalization uses grayscale transformation to adjust the contrast quality of the image.

5) FILTERING

Image filtering technique is used to modify an image. It is applied to the fundus image to retain specific features by discarding other features. The various filters have been employed in the task of retinal vessel detection i.e. Gabor filter [10], [61], Gaussian filter [62], [70], matched filter [69], linear filter [86], median filter [129] and fuzzy filter [105] etc.

6) IMAGE SEGMENTATION

Image segmentation is the process of dividing the image into multiple segments so that it can easily be analyzed. It is intended to locate various objects and boundaries i.e. line, circle, and curve, etc. The image segmentation (retinal vessel segmentation) decides whether a specific pixel belongs to a vessel or non-vessel. Fraz *et al.* [64], [83] applied morphological features and line strength for the retinal vessel segmentation.

7) FEATURE EXTRACTION

The feature extraction technique is used to reduce data dimensionality. It is usually applied when there is a large amount of redundant data. A feature vector is created which have to reduce the set of features specific to the requirements as in [130]. The Lupas *et al.* [62] created 41-D features vector and Xu and Luo [11] created a 12-D feature vector for the vessel segmentation in the retinal images.

8) FEATURE SELECTION

The major aim of the feature selection is to choose relevant features for developing the classifier. The feature selection technique is usually employed by researchers as it gives the advantage of lesser training time, reduces overfitting, avoids the curse of dimensionality and makes the model simple. The term feature selection is different from feature extraction as features selection is used to give a subset of the features while new features are created using feature extraction [14], [61].

9) IMAGE RESTORATION

The image restoration is used to recover resolution loss and reduce noise. The image restoration takes a noisy image and estimates the clean. The deconvolution is the simplest image restoration technique which is applied in the frequency domain after calculating the Fourier transform of the image. It is used to remove the degradation effects, unlike the image enhancement. Walter et al. used an image restoration technique because of poor quality images due to cataract for the diagnosis of DR [131].

D. POST PROCESSING

Post-processing is the last step for retinal vessel segmentation. It is usually applied on the segmented vessel output to remove noise, erroneous artefacts and the overlapping vessel. The main aim of the post-processing step is to obtain better segmentation accuracy of retinal images as in [69], [99], [129].

1) DILATION AND EROSION

Dilation and erosion are the basic operations to refine the retinal images by adding and removing pixels to the object boundaries respectively. The addition and the removal of pixels are based on the shape and the size of the structuring element [77].

2) MORPHOLOGICAL OPENING AND CLOSING

Morphological opening and closing operations are based on dilation and erosion. In the opening, the erosion is followed by dilation and the dilation has been followed by erosion in closing operation. The opening operator is used to detect false edges [88] and to estimate the background [87]. The vessel inner parts are detected with closing operation in [95].

E. EVALUATION CRITERIA

The retinal vessel classification is based on the correctly classified vessel (TP: true positive) and non-vessel (TN: true negative) and incorrectly classified vessel (FP: false positive) and non-vessel (FN: false negative). TP identifies that pixel is a vessel in both the segmented and ground truth image while in TN, the pixel is non-vessel in segmented and ground truth images. FP identifies that pixel is a vessel in the segmented image but non-vessel in observer marked image, also in FN, the pixel is a vessel in ground truth while non-vessel in the segmented image. These terms are used to evaluate performance. True positive rate (TPR) identifies the number of pixels correctly marked as a vessel. False-positive rate (FPR) identifies the number of pixels erroneously marked as a vessel. Sensitivity (Sn) also called as a recall is a probability to identify vessel pixels. Specificity (Sp) represents the ability to identify non-vessel pixel. Accuracy (ACC) is the ratio between the correctly classified pixels (TP+TN) and the total pixel in an image FOV. Precision also called a positive predicted value (PPV) is the measure of ability that pixel identified as the vessel is truly positive.

The area under the curve (AUC) is the ratio between TPR and FPR. The formulas to calculate these metrics are given in equations (1)-(7).

$$TPR = \frac{TP}{Number\ of\ pixels\ marked\ as\ vessel} \tag{1}$$

$$FPR = \frac{FP}{Number\ of\ pixels\ marked\ as\ non-vessel} \tag{2}$$

$$Sp = \frac{TN}{TN + FP} \tag{3}$$

$$Sn = \frac{TP}{TP + FN} \tag{4}$$

$$Acc = \frac{TP + FN}{FOV\ Pixel\ Count} \tag{5}$$

$$PPV = \frac{TP}{TP + FP} \tag{6}$$

$$AUC = \frac{1}{2}(\frac{TP}{TP + FN} + \frac{TN}{TN + FP}) \tag{7}$$

IV. DISCUSSION

The various algorithms have been proposed by researchers for the blood vessel segmentation in the retinal fundus images. Usually, the steps performed for the vessel segmentation are image preprocessing, feature selection, developing a classifier, testing and training the dataset and evaluate performance on different metrics i.e. sensitivity, specificity, accuracy, and AUC, etc. The performance evaluation of these methods is tested on various retinal datasets i.e. STARE, DRIVE, CHASE_DB1, etc. Most of the authors evaluated their classifier on commonly available STARE and DRIVE datasets. You et al. evaluated their radial projection method on DRIVE and STARE [12]. Some of the authors cross-validated their classifier on multiple datasets i.e. Orlando et al. tested the method on STARE, DRIVE, HRF, and CHASE_DB1 for the better evaluation of a classifier.

We have categorized the various vessel segmentation techniques into supervised and unsupervised based methods. Supervised based methods are those methods in which input and ground truth images indicate the pixel is a vessel or are not included in the training set. Unsupervised learning mainly involves clustering and anomaly detection task, where, there is no as such ground truth data is required for the vessel segmentation task. These methods are further sub-categorized based on their features. The supervised method is divided into a support vector machine method, neural network method, and miscellaneous method. Unsupervised methods are sectioned into template matching filters method, mathematical morphology method, fuzzy-based method, and vessel tracking method. Some of the authors proposed more than one method, therefore, we have added them into one category and put the reference into another category.

Although, many authors have applied preprocessing steps i.e. green channel extraction, histogram equalization, and improve top-bottom hat transformation as in [132], which are employed to remove noise, enhance vessel details and eliminate uneven illumination. In [49], Soomro et al. used the morphological operation to remove noise and non-uniform illumination and employed principal component analysis (PCA) to convert RGB image into the grayscale image as their preprocessing steps but Sengür *et al.* [59] used classifier without applying the preprocessing step. Most of the segmentation papers established feature vector to train the classifier [16], [47], [133]. The performance of the classifier is evaluated mostly on STARE and DRIVE using various platforms [9], [64].

It has been observed that some segmentation methodologies have shown the significant result on sensitivity measure but not good to give high accuracy i.e. Fan & Mo achieved 97% sensitivity on CHASE_DB1 with 67.6% accuracy which is very low for the vessel segmentation. Ghaderi *et al.* [58] have achieved the best accuracy of 96.7%, Dasgupta et al. achieved 98.01% of specificity [52] and NGO et al. attained 97.52% of AUC, which has outperformed others. The performance of any retinal vessel segmentation method is based on different measures i.e. precision, processing time, accuracy, sensitivity, specificity, and AUC, etc. The suggestion to adopt any method for retinal vessel segmentation along with its pros and cons are also described in this review. The performance matrices based on the dataset (STARE, DRIVE or either local dataset), accuracy, sensitivity, specificity, and AUC is mentioned in Table 1 to 6. The performance measure of supervised methods i.e. SVM based methods, NN based methods, and miscellaneous methods are given in Table 1, 2, and 3 respectively. The performance measures of matched filtered methods, morphological processing methods, and model-based methods are presented in Table 4, 5, and 6 respectively.

V. CONCLUSION

Retinal diseases can only be observed through retinal vessel segmentation by retinal experts. The physical examination of retinal diseases is a very tedious task as it requires retinal experts, high cost and more time for the detection and segmentation of the vessels. Automatic extraction and segmentation of vessels are very necessary for early detection of retinal diseases by using AI concepts.

Many researchers have employed various algorithms for the retinal vessel segmentation task. We distributed these algorithms into two categories i.e. supervised and unsupervised methods. These vessel segmentation algorithms are further divided into sub-categories. The SVM based methods, NN based methods, and miscellaneous methods are given in a supervised method. Whereas, unsupervised methods are further distributed into matched filter methods, vessel tracking methods, mathematical processing methods, and model-based methods. We presented the comparison of existing vessel segmentation techniques, dataset employed, fundus photography, preprocessing and post-processing methods, and the evaluation criteria.

Although these algorithms are efficient enough to diagnose retinal disease, they aren't supposed to be the alternative of retinal experts. They are designed to diminish the workload of human experts. Due to advancement in technology, it is getting better and better to obtain retinal imaging using fundus cameras with high resolution. The segmentation of these high-quality images will reduce the chances of pixel identification (marked as a vessel or not). The average accuracy of deep learning methods is reaching around 98% that is strong evidence that these algorithms can be employed for the retinal vessel segmentation tasks to prevent the victims at an early stage.

This paper presents a literature review of machine learning (ML) and deep learning (DL) methods for vessel segmentation methodologies. we tried our best to cover all of the current and existing approaches of vessel segmentation in this review. Each approach to implementing a vessel segmentation has its own advantages and the drawbacks. Thus, to choose a specific method for retinal vessel segmentation is very difficult. We covered the various issues regarding the selection of any method. The year-wise decomposition of the papers with respect to its category is also given in the graphical format to highlight the latest work in this field. Moreover, we tried to establish a professional structure to familiarize an individual with up-to-date vessel segmentation techniques.

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AZHAR IMRAN received the B.S. degree in software engineering and the M.S. degree in computer science from the University of Sargodha, Pakistan, in 2012 and 2016, respectively. He is currently pursuing the Ph.D. degree with the Beijing University of Technology, Beijing, China.

From 2012 to 2017, he was a Lecturer with the Department of Computer Science, University of Sargodha, Pakistan. His research interests include machine learning, image processing, medical imaging, and data mining. He has received awards and honors from the China Scholarship Council (CSC), China, including the Star Contribution Award for the Best Researcher from the Beijing University of Technology, China.

JIANQIANG LI received the B.S. degree in mechatronics from the Beijing Institute of Technology, Beijing, China, in 1996, and the M.S. and Ph.D. degrees in control science and engineering from Tsinghua University, Beijing, in 2001 and 2004, respectively. He was a Researcher with the Digital Enterprise Research Institute, National University of Ireland, Galway, from 2004 to 2005. From 2005 to 2013, he was with NEC Labs, China, as a Researcher, and with the Department of Computer Science, Stanford University, as a Visiting Scholar, from 2009 to 2010. He joined the Beijing University of Technology and the Beijing Engineering Research Center for IoT Software and Systems, Beijing, in 2013, as a Beijing Distinguished Professor. He has over 40 publications, including one book and more than ten journal papers, and holds 37 international patent applications (19 of them have been granted in China, U.S., or Japan). His research interests include Petri nets, enterprise information systems, business process, data mining, information retrieval, semantic web, privacy protection, and big data. He served as a PC Member of multiple international conferences and organized the IEEE workshop on medical computing. He served as a Guest Editor to organize a special issue on information technology for enhanced healthcare service in computer in industry.

YAN PEI received the B.Eng. and M.Eng. degrees from Northeastern University, Shenyang, China, and the Dr.Eng. degree from Kyushu University, Fukuoka, Japan, He is currently an Associate Professor with the University of Aizu. His research interests include evolutionary computation, machine learning, and software engineering.

JI-JIANG YANG received the B.S. and M.S. degrees from Tsinghua University, and the Ph.D. degree from the National University of Ireland, Galway. He is currently an Associate Professor with Tsinghua University. He was with Computer Integrated Manufacturing System/Engineering Research Center (CIMS/ERC), Tsinghua University, from 1995 to 1999. He had joined or been in charge of different projects supported by the State Hi-Tech Program (863 programs), the NSF, China, and the European Union. Since 2009, his main focus is on e-health and medical service. He has undertaken a few projects of the National Science and Technology Supporting Program about digital medical service model and key technologies. He is also collaborating with a lot of medical institutions and hospitals. He is a member of the Expert Committee of the Internet of Things (IoT) in Health, Chinese Electronic Association, the Expert Committee of Remote Medicine and Cloud Computing, and Chinese Medicine Informatics Association. He has published over 60 papers on professional journals and conferences. His research interests include e-health, e-government/e-commerce, privacy-preserving, information resource management, data mining, and cloud computing.

QING WANG received the Ph.D. degree from Tsinghua University. He is currently a Researcher with the Research Institute of Information Technology, Tsinghua University. His research interests include web service technology, data mining, and machine learning, especially in the healthcare area. His current research mainly focuses on big data technology applied in the medical service area.