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Diabetic retinopathy techniques in retinal images: A review

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ABSTRACT

The diabetic retinopathy is the main reason of vision loss in people. Medical experts recognize some clinical, geometrical and haemodynamic features of diabetic retinopathy. These features include the blood vessel area, exudates, microaneurysm, hemorrhages and neovascularization, etc. In Computer Aided Diagnosis (CAD) systems, these features are detected in fundus images using computer vision techniques. In this paper, we review the methods of low, middle and high level vision for automatic detection and classification of diabetic retinopathy.We give a detailed review of 79 algorithms for detecting different features of diabetic retinopathy during the last eight years.

1. Introduction

Diabetes complications that influence the ocular perceivers and affect veins of light-delicate tissues at the back of ocular perceiver, are known as Diabetic Retinopathy (DR) [79].The DR is caused because of many reasons such as oxidative injury, enzymatic activations, osmoticlysis of cells, increase of toxins, stimulation of Harmon's, different growth factors and carbonic metabolites. The common symptoms of DR are blurred vision, floaters and flashes, and sudden loss of vision [62]. Identification of these causes is helpful to treat DR with different types of therapies and medicine for recovery from diabetes [85].

The DR has many consequences such as Diabetic Macular Edema (DME), cataract and glaucoma at the retina. This also affects nonvascular pathology, such as hypertension, diabetes, cardiovascular diseases [23]. All these mechanisms cause harm to retinal cells and grow microaneurysm, cotton wool spots, hemorrhages and many types of lesions. This also causes morphological changes such as change in diameter, length, branching angles or tortuosity for vascular. Thus, blood vessels provide important information, and this information can be used for diagnosis, evaluation of ocular and systemic disease. In some cases, creation of new blood vessels commences in the retina region, which causes visual impairment [47]. Thus, blood vessel detection and segmentation are an important phase in DR detection and classification or grading.

In this paper, we analyzed the algorithms for automated detection and grading of the DR algorithms. First of all, we described the features and types of DR and then essential image preprocessing terms used in these algorithms were described. We categorized DR algorithms into several categories according to their sequence order in algorithmic application in CAD systems. These categories include optic disc detection and localization, blood vessels segmentation, clinical & geometric and haemodynamics features and detection & grading of DR. This work is helpful for researchers choosing fundus image analysis for DR detection as their future research area. We provided details of approaches used which can help researchers understanding impact of these methods. We also showed summarized contribution of algorithms in tabular form along with their results helping researchers understanding the advantages and shortcomings of these algorithms.

1.1. Features (symptoms) of diabetic retinopathy

The microaneurysms and neovascularization, intra-retinal hemorrhages, exudates, red lesion, area, perimeter, width and branching angles, etc. are important DR clinical geometrical & haemodynamic features. The clinical features are:

- Microaneurysms: The microaneurysms (MAs) are deformations in walls of blood vessels. These are marked as balloon-shaped deformations induced by permeability of vasculature due to hyperglycemia [63]. The number of MAs is directly proportional to level or stage of DR. The area of MAs is 1 - 3 pixels in different fundus image databases.
- Hemorrhages:The hemorrhages (HMAs) are formed due to leakage of blood from the damaged capillaries. The HMAs are divided into three categories: dot, flame and blot. The dot HMAs are dark red spots. These

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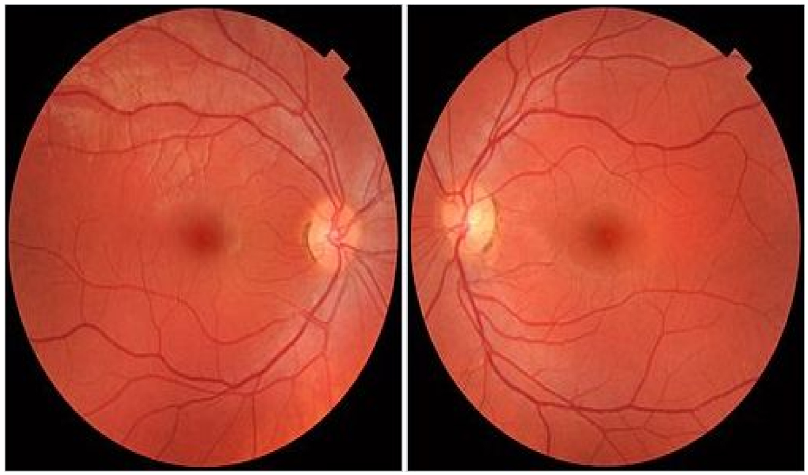


Fig. 1. Normal fundus eye images for both left and right eye.

are hard to distinguish from MAs in color properties, but these are larger in size. Flame HMAs are distinguished by their flame shape. These are formed due to blood leakage in alignment with the nerve fibers. Blot HMAs usually have irregular shape and larger in size [103].

- Hard Exudates: Hard exudates are bright yellow or white colored objects on the retina. These objects have waxy appearance and sharp edges against the background from blood vessels. Hard exudates are developed due to blood leakage from veins and exudates have circular shape around vessels.
- Soft Exudates: Soft exudates or Cotton Wool Spots (CWS) occur due to occlusion of arteriole. The reduced blood flow to retina causes ischemia of the Retinal Nerve Fibre Layer (RNFL) which affects the axoplasmic flow and causes accumulation of axoplasmic debris in retinal ganglion cell axons. The debris accumulation appears as fluffy white lesions in the RNFL called CWS.

The fundus image of the left and right eye is shown in Fig. 1

These features are shown in Fig. 2. Blood vessels are shown in Fig. 2(a) and optic disc, clinical DR features are mentioned in Fig. 2(b).

1.2. Types & levels of diabetic retinopathy

The types of DR are based on damage of blood vessels, number of MAs and HMAs at the retina and formation of abnormal new blood vessels. Stages of diabetic retinopathy depend upon the presence of certain number of features and the severeness/density of these features [96].

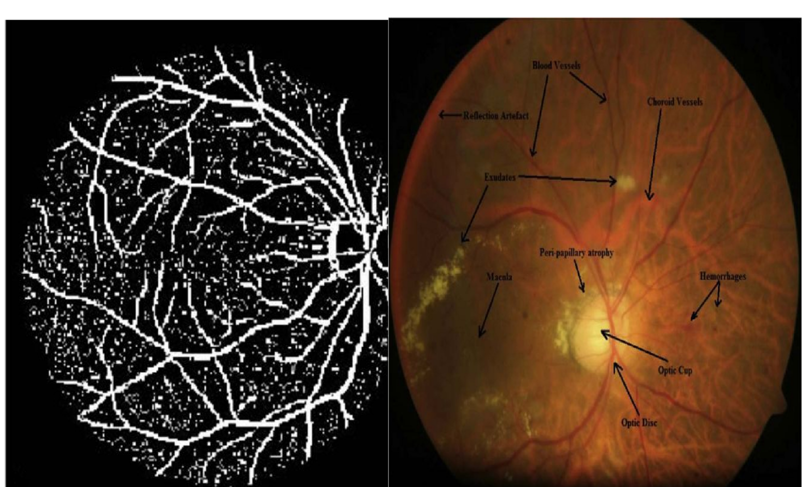
The non proliferative DR type is described in terms of sensitivity and number of MAs and HMAs as normal, mild, moderate, and sever DR. This type of DR is further divided into following levels of DR.

- Normal:If no DR sign is observed, this class is called Normal
- Mild: Only MAs are found in mild DR.
- Moderate DR: If the number of MAs, haemorrhages less than 20 in each quadrant, hard exudates(white lesion, cotton wool
- Severe DR: MAs, more than 20 haemorrhages in each quadrant, Venous beading in more than two quadrants, exudates, red lesion

The type proliferates diabetic retinopathy (PDR) is characterized by neovascularization (NV), which is the formation of abnormal new blood vessels. It is the sever stage of retinopathy and new blood vessels start growing anywhere in eye. Therefore, MA and NV are two clinically important types of lesion [90] and fluid in DR is categorized as exudates and non-exudates [66].

1.3. Computer aided diagnosis (CAD) of diabetic retinopathy

The DR level can be detected by fundus eye image analysis, hence fundus image processing, and feature extraction is an integral part of



(a) blood vessels (b) DR features

Fig. 2. Blood vessels and diabetic retinopathy features in fundus image [25]. In 2 (a), blood vessels are shown in binary image and DR features are shown in 2 (b) in RGB image.

automatic detection and classification of DR. Low, middle and high level computer vision methods are required for fundus image processing such as localization and segmentation of OD, blood vessels, microaneurysms, hemorrhages, vessels branching angles and other features [14,56,7,103,81]. The other features include microaneurysms [71], optical disc [22], angiography [31,86], colorogrms [91], reflection features [39],etc. Blood vessels are used for the fovea and lesion detection and these vessels are affected by systemic or local ocular disease. In image, the width of the vessels ranges from 2 to 10 pixels as it is 36–180 μm in actual measures. The vessels with 2 or 3 pixels width are known as small or thin vessel and remain vessels are called as large vessels.

The Computer Aided Diagnostic Systems (CAD) are used for detection and classification of DR. The computer based methods detect changes in normal and effected eye images and use these changes to develop feature space. The combination of these features defines type and level or grade of DR. Many CAD systems have been proposed in literature for early detection of DR and lesions related to DR [67,4,74]. Every CAD system is the concatenation of two algorithms i.e. feature extraction and classification algorithm. Efficiency of the first algorithm has an impact on the efficiency of the lateral algorithm and the overall CAD system.

1.3.1. Image preprocessing

The quality of a fundus image may vary due to factors such as eye movement, media opacity, small pupils, nonalignment of the camera, problems in camera focusing and noise at the image acquisition stages. These factors actually affect image contrast, illumination and color. Therefore, fundus image preprocessing is quite mandatory step in CAD systems [64]. Steps of image preprocessing are explained below:

- Fundus images are in RGB color space. The green image plane is used due to fact that blood vessels are prominent, and noise is represented by red and blue pixels. The other color spaces are also used for better segmentation results. For this purpose, the RGB image is converted into other spaces. These color spaces are YC_bC_r model consists of *Y* (luma component), *Cb* (the chroma of the blue difference) and the *Cr* (the chroma of the red difference) components. Gaussian Space, HSI (Hue saturation and intensity) *Lab*, lightness and *a* and *b* for the color opponents green-red and blue-yellow.
- Contrast Enhancement and De-noising techniques are implemented to improve image quality. Most of the image enhancement techniques are application based. These include Contrast Limited Adaptive Histogram Equalization (CLAHE), Mean, Median and Gaussian and Gabour Variance Filters.
- In image preprocessing step, many image filtering techniques are applied for separation of background and foreground images, edge enhancement etc. This includes the filtering technique such as Matching,Laplacian and Sobel filters. The transformation method includes the Curvelet, shearlet and scale invariant transformation. The mathematical morphology is an other tool which can be used for De-noising, edge or contrast enhancement and background & foreground separation.
- The Mathematical morphology is a nonlinear tool for analysis of size, shape and inner structure of objects using set theory. It is used for both contrast enhancement and background subtraction. Following is the morphological operators
  - ○ Structure Elements: In mathematical morphology, grey level images are studied with the help of families of special sets *B*. These sets are known a priori, called structuring element, and can be adopted according to our need in terms of size, shape, orientation, etc. In practice, circular, elliptical and linear structure elements are used. It is simply a binary image or mask generated by the user for a particular task
  - ○ Dilation: It is a simplest operator, translation of a pixel value. Let *B* be a structure element and *X* be a binary image a subset of *E*. The translate of *X* by $p \in E$ is the set $X_p = \{x + p | x \in X\}$. Here *p* defines a translation vector. The morphological dilation of *X*by a set *B* will be:

    $$\delta_B(X) = X \oplus B = \bigcup_{b \in B} X_b = \bigcup_{x \in X} B_x = \{x + b | x \in X,\, b \in B\}$$

    It is translation of pixel *x* by every element of *B*. Dilation enlarge the pixel *x* by set *B*.
  - ○ Erosion: The erosion operator also depends upon structure element. The morphological erosion ε of an image *X* with the structure element *B* will be

    $$\varepsilon_B(X) = X \ominus B = \bigcap_{b \in B} X_{-b} = \{p \in E, \text{forevery}\, B_p \subset X\}$$

    The erosion of *X* by *B* is the locus of points *p* such that B_p is entirely included in *X*. An erosion shrinks the sets. Erosion is dual of dilation, i.e., Eroding foreground pixels is equivalent to dilating the background pixels. The dilation and erosion operator are used for edges and boundaries detection.
  - ○ Opening: The morphological opening operator is the concatenation of two operators. It is erosion followed by dilation. This combination of operators acts as a shape filter and removes the objects smaller than structure element. It is used for background approximation in an image. The image enhancement is complement of opened image and opening of set *X* is denoted by O_X. For example, opening of a set *X* by structure element *B*

    $$O_X = X \circ B = (X \ominus B) \oplus B$$

  - ○ Closing: Closing is the dual operator of opening operator. It is dilation followed by erosion operator and it resembles to dilation morphological operator. The objective of operator is to preserve the background region whose shape matches with the structuring element and all other elements are removed from background. Closing operator is represented by C_X for set *X*, it can be written as

    $$C_X = X \bullet B = (X \oplus B) \ominus B$$

    These operators are used in binary images.These Morphological operators are discussed with detail in book [80]. Top Hat Transformation is the inter pixel difference in original and processed image. The white top-hat is the pixel wise distance between opened and original image. Similarly, black top-hat (bottom hat transformation) is the difference of pixels between original and closed image. This transformation is implemented to detect top hills or peaks and valleys in image regions. For detailed examples see [95].

1.4. Our contribution

There already exist on reviews and surveys such as [15,30,25,37,63] during years 2012 and 2016 respectively and a comprehensive survey is found in [97] during 2009. In this review, we highlight the works published on DR from 2010 till 2018. We divide all these algorithms in categories of optic disc detection segmentation, blood vessels segmentation, extraction of DR features for classification of diabetic retinopathy and algorithms for the detection and classification of diabetic retinopathy.

This paper is arranged as, Section 1.3.1 covers the basic definitions, terminology used in this review and some necessary definitions. Section 2 summarizes the selected research papers included in this study. The methods for optic disc localization and segmentation are summarized in Section 3. The methods for blood vessels segmentation are gathered in Section 4 and Section 5 cover the methods for clinical features extraction. The section 6 consists of methods which are used for detection and classification algorithms and Section 7 concludes the paper.

2. Review structure & related work classification

In this review, we considered 78 major works on DR published from 2010 to date and categorized them as below according to nature of their work:

- Optic Disc localization and segmentation
- Segmentation of blood vessels
- Clinical, geometirc & haemodynamic features
- Diabetic retinopathy detection and classification

The optic disc localization is also important to detect the changes in blood vessels and for features such as area and perimeter of blood vessels, detection of exudates MAs and HMAs, etc. Similarly, the detection of clinical, geometrical and haemodynamics features are also used for the diabetic retinopathy detection and classification of algorithms. Table 1 summarizes all the methods which are applicable at different image analysis stages in fundus image analysis for detection of DR. These methods were reported during the survey period.

As we can see in the table, 18 algorithms are relevant to optic disc localization and 22 algorithms are relevant to blood vessel detection. There are 21 algorithms that are related to DR features extraction and 16 detection and screening algorithms are reported. Stage wise processing data is represented in Fig. 3. This shows that the blood vessel detection and optic disc detection has gained the equal importance during these years. Relatively less work (only 4%) is done in the area of pre-processing in medical images.

Fig. 4 shows the year wise research work published from 2010 to onward. This shows that the quantity of research increases every year.

Most of the data collections used in application of algorithms are the research data collections for testing the algorithms related to blood vessels, exudates and other diabetic retinopathy features. Only a few of these are actually taken from research hospitals. The online research data collections such as

- DIARTDB: This database is provided by a research group Tomi Kauppi et al. and can be downloaded from http://www.it.lut.fi/project/imageret/ and freely available for research purpose. Images were captured with a 50 degree field-of-view digital fundus camera. This has two levels, which are: DIARTDB0, consists of 130 color fundus images and 20 are normal and 110 contain signs of the diabetic retinopathy. These signs include hard exudates, soft exudates, MAS, HMAS and NV and this data set is referred as ”calibration level 0 fundus images. The second database is called DIARTDB1, consist of 89 indexed fundus images out of which 84 contain at least mild non-proliferative signs (MAs) of DR, and 5 are normal without DR. This data set is referred as ”calibration level 1 fundus images”.
- HRF is introduced as the High-Resolution Fundus (HRF) image database for comparative studies of the segmentation algorithms on retinal fundus images. These images were taken using a Canon CR-1 fundus camera with multiple image acquisition setting and 45 degree field of view. Currently, this database consists of 15images in each category for healthy 15 with diabetic retinopathy and glaucomatous patients. It also contains the blood vessel segmentation images along the mask of field of view (FOV). This data in database is generated by a group of experts working in the field of retinal image analysis and clinicians from the cooperated ophthalmology clinics.
- STARE: The STructured Analysis of the Retina (STARE) is a University of California, San Diego project and images are provided by the Shiley Eye Center at the University of California. It consists of 400 images.
- KAGGLE: A set of high resolution fundus images are provided by the Kaggle platform. These images are taken under the variety of spatial conditions. These images are indexed by an experienced pathologist according to scale from 0 to 4 according to No DR, Mild, Moderate, Severe and Proliferative DR.
- ROC: Retinopathy Online Challenge (ROC) is a database developed for enabling medical image analysis research groups to develop diabetic retinopathy CAD algorithms and it aims to provide a platform for algorithms comparison.
- DERIVE: The DRIVE database has been established from a diabetic retinopathy screening program in the Netherlands. It consists of 40

Table 1
The methods for diabetic retinopathy in fundus images applicable to detect the features of diabetic retinopathy at different stages of image processing in CAD systems.

Image processing stage in CAD	Methodology	Author name with citation for each algorithms
Optic disc localization and segmentation		Baisheng Dai et al. [18], Sangita Bharkad [16], Balazs Harangi and Andras Hajdu [36], Rashmi Panda et al. [70], Lesay et al. [55], S. B. Akhade et al. [3], Muhammad Alshayeji [9], Rashid Jalal Qureshi et al. [75], Beiji Zou et al. [107], Sa'ed Abed et al. [1], Li Xiong and Huiqi Li [99], M. Partha Sarathi et al. [78], Esmaeili et al. [22], Shilpa Joshi and P.T. Karule [42], Daniel Welfer et al. [95], Kemal Akyol et al. [43], S. Lu [58],A. Basit and Muhammad Moazam Fraz [12]
Segmentation of blood vessels	Thresholding method	R. GeethaRamani and Lakshmi Balasubramanian [32] Jyotiprava Dash and Nilamani Bhoi [19], Zhun Fan, Jiewei Lu and Wenji Li [24], Chengzhang Zhu et al. [105], Luiz Câmara Neto et al.[64]
	Tracking method	Ming Zhang [103], Lili Xu and Shuqian Luo [56], Uyen T.V. Nguyen et al. [65], Mohammed Al-Rawi et al. [7], Soorya M. et al.[60]
	Machine trained classifiers	Luiz Carlos Rodrigues et al. [76], Lei Zhang et al. [102], Mehdi Hassan et al. [38], Shahab Aslani and Haldun Sarnel [11], S. Wilfred Franklin and S. Edward Rajan [27], Roberto Vega et al. [89] M.M. Fraz et al. [29], S. Wilfred Franklin and S. Edward Rajan [26], D. Marin et al. [61],L. Shyam and G. S. Kumar [81], M. Usman Akram and Shoab Ahmad Khan [6], Amna Waheed et al. [94]
Clinical, geometric &haemodynamic features	Red Lesion (MAs, HMAs)	G. Quellec et al. [74], Ruchir Srivastava et al. [83], Bo Wu et al. [98], Carla Pereira et al. [71], M. Usman Akram et al. [4], Niladri Sekhar Datta et al. [20] Bo Wu et al. [98]
	Hard and soft exudates	Sharib Ali et al. [8], Jaskirat Kaur and Deepti Mittal [46], Qing Liu et al.[57], C. JayaKumari and R. Maruthi [41], Xiwei Zhang et al. [104], José Ignacio Orlando et al. [68], Doaa Youssef and Nahed H. Solouma [101], Elaheh Imani and Hamid-Reza Pourreza [40], M. Moazam Fraz et al. [28], Julian Zilly et al.[106], Javeria Amin et al. [10]
	Geometric and haemodynamics features	G. Leontidis et al. [53],Francesco Calivá et al. [17], Maged S Habib et al. [35]
Diabetic retinopathy detection & classification	DR, Non DR	Jen Hong Tan et al. [84], Joel E.W. Koh [48],GG. Gardner et al.[33], S. Saranya Rubini and A. Kunthavai [77], Gulshan V. et al. [88], Cemal KöSe et al. [49], Yehui Yang et al. [100], Dilip Sisodia et al. [82]
	NPDR, PDR	Harry Pratt et al. [73], R. Venkatesan et al.[92], M. Usman Akram et al. [5], K. Verma et al.[93], P.N. Sharath Kumar et al. [50], Gupta et al.[34], Sudeshna Sil Kar and Santi P. Maity [45], Georgios Leontidis [54]

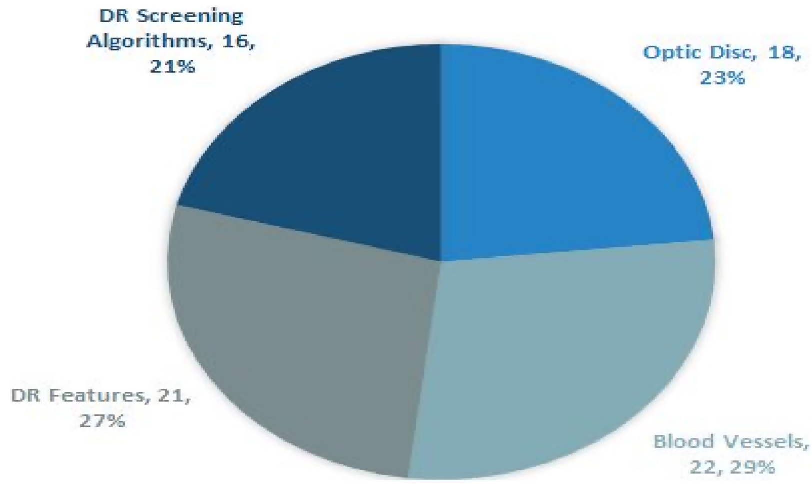


Fig. 3. The percentage contribution of algorithms for optic disc segmentation, blood vessel segmentation detection of features of diabetic retinopathy and screening and classification algorithms.

images out of which, 33 are without signs of DR and 7 show signs of mild early diabetic retinopathy. The images were acquired using a Canon CR5 non-mydriatic 3CCD camera with a 45 degree field of view (FOV).

- MESSIDOR is a research program funded by the French Ministry of Research and Defense within a 2004 TECHNO-VISION program. It consists of 1200 eye fundus color numerical images. These images are acquired by 3 ophthalmologic departments using a color video 3CCD camera on a Topcon TRC NW6 non-mydriatic retinograph with a 45 degree field of view. The images were captured using 8 bits per color plane at 1440 × 960, 2240 × 1488 or 2304 × 1536 pixels.
- E OPTHIA: The OPHDIAT Tele-medical network for DR screening established a colored image database for DR, called E ophtha. The database is made of retinal images with different types of lesions (exudates and microaneurysms) manually annotated by ophthalmology experts [21]. It contains e-ophtha-MA (MicroAneurysms), and e-ophtha-EX (EXudates). The e-ophtha-EX contains 47 images with exudates and 35 images with no lesion and e-ophtha-MA consist of 148 images with microaneurysms or small hemorrhages and 233 images with no lesion.
- DRIONS: A benchmarking database for optic nerve head segmentation from digital retinal images. It consists of 110 images belonging to the Ophthalmology Service at Miguel Servet Hospital, Saragossa (Spain). The samples are 46.2 % male and 53.8 % female from Caucasian ethnicity. The images were acquired with a colour analogical fundus camera.
- CHASEDB1:It is a fundus eye image database freely downloadable from https://blogs.kingston.ac.uk/retinal/chasedb1/.
- HEI Med: The Hamilton Eye Institute Macular Edema Dataset (HEI-MED) is a test data images for algorithms for the detection of exudates and diabetic macular edema. It consists of 169 fundus images. The images are segmented manually by an expert ophthalmologist.
- Others: These are the small databases developed by individual researchers such as ONHCD,RFC,KMC, DMED,ARIA,Eyepack,VIER, REVIEW,RIS,SHIFA and AFIO

The percentage use of these database in algorithms are shown in Fig. 5.

The algorithms are compared with the state of the art algorithms through the statistical measures. Meanwhile, efficiency of a classifier is measured in terms of receiving operator curve, area under the curve, accuracy, precision and sensitivity. These are explained as:

- Receiving Operator Curve (ROC): A graphical representation of the performance of a classification algorithm for all thresholds. This

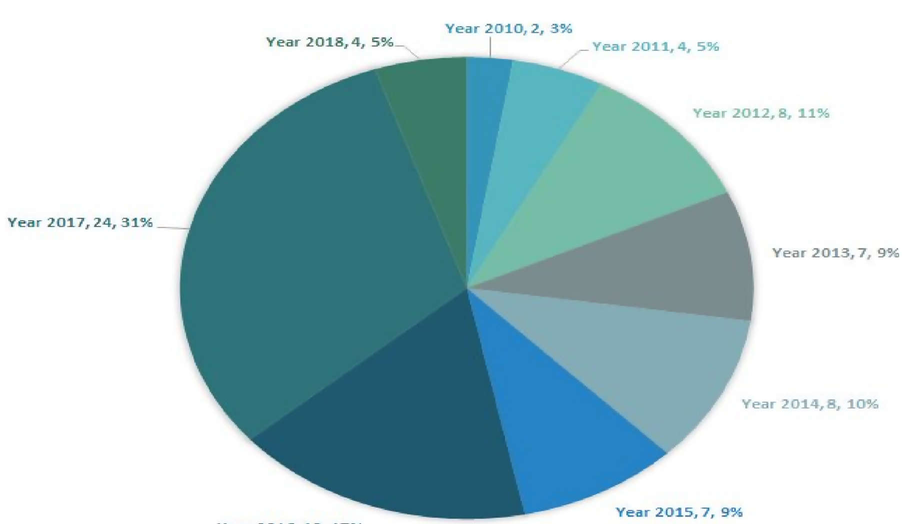


Fig. 4. Year wise contribution of algorithms.

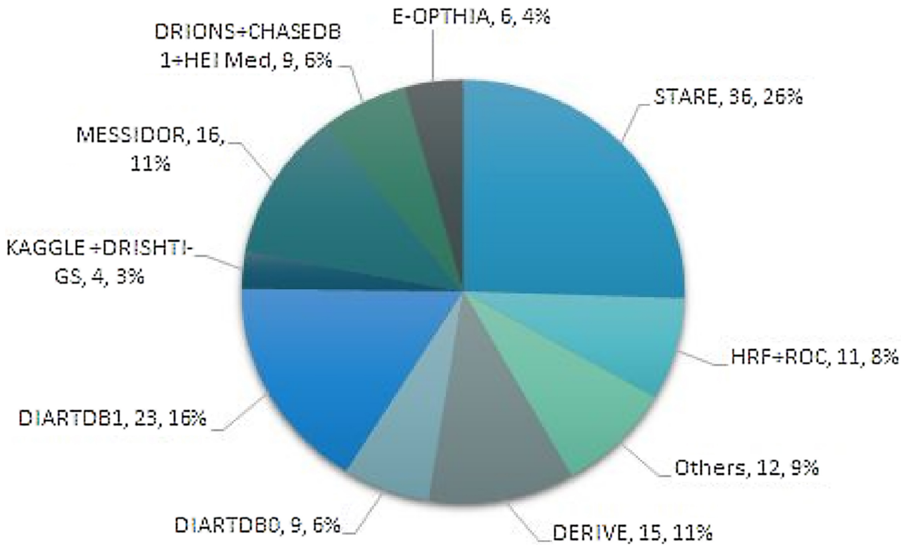


Fig. 5. The Fundus eye image research databases used in algorithms.

curve uses two parameters namely, true positive and false positive rate or sensitivity and specificity. These are defined as

$$\text{TruePositiveRate} = \frac{\text{TP}}{\text{TP} + \text{FN}}$$

$$\text{FalsePositiveRate} = \frac{\text{FP}}{\text{FP} + \text{TN}}$$

where *TP*, *TN*, *FP* and *FN* stands for true positive, true negative, false positive and false negative respectively. True positive are the positive predictions and classifier also marked them positive. False positive are predictions which are negative but classifier marked these predictions as positive. Similarly, true negative are negative predictions and classifier also marked them negative and false negative are values which are positive but classifier decide them negative.

- Area Under the Curve (AUC): Area under the receiving operator curve is commonly denoted by AUC, it represents degree or measure of separability. It is a numerical value and higher the AUC, better the model is at predicting. The classifier efficiency can be graded as (i) 0.90–1 = excellent, (ii) 0.80–0.90 = good (iii) 0.70–0.80 = fair, (iv) 0.60–0.70 = poor (v) 0.50–0.60 = fail (F)
- Accuracy (Acc.) Accuracy is the overall performance of the classifier. Mathematically

$$\text{Acc} = \frac{\text{TP} + \text{TN}}{P + N}$$

- Specifity (Spec). It is the proportion actually negative classes which are classified as negative by the model. True negative rate is called specifity. Mathematically, it is

$$\text{SPC} = \frac{\text{TN}}{N}$$

- Sensitivity (Sen): It is the proportion of positive classes to positively marked classes. It is also known as Recall or TPR stands for True Positive Rate (TPR). Mathematically

$$\text{Sen} = \frac{\text{TP}}{P}$$

where P and N are known as positive and negative predictions respectively.

- Overlapping Score: The overlapping score between the manually segmented optic disc (true OD) and optic disc segmented by proposed method. Mathematically an overlapping score is calculated using formula:

$$S_o = A_m \cap A_p$$

where A_m and A_p are the manually segmented and segmented by model area of OD.

In the following sections, we will discuss each category (as mentioned above) in detail.

3. Optical disc localization and segmentation

The bright oval structure in retina is called optic disk. It is the starting point of optic nerve head and is the entry point for major blood vessels to eye [27]. Optical disc localization and segmentation is a fundamental part of DR studies. It is generally defined as a circular or elliptical object in the fundus image. In most of the literature, it is defined as a circle center at the origin. The segmentation of optic disc is usually known as contour detection of the disk. Optic disk segmentation is the prerequisite for blood vessel segmentation algorithms and its dimensions are used for determining the location of center of vision.

3.1. Optical disc characterization

The retina lesions are detected and quantified after the removal of Optic Disc (OD) and blood vessels. So, detection and segmentation of OD is an important step in diabetic screening algorithms. The macula and fova are also important features. These parts are used for vision tasks such as reading and fova is the center of macula, is the reference point for sharpen vision [75]. It is a bright yellowish in color and all vessels & nerves initiate from this point.

3.2. Algorithms for optic disc localization & segmentation

The detection and segmentation of OD is important in many feature extraction algorithms. The diabetes may weaken blood vessels and these blood vessels can leak, this forms the small, dot hemorrhages. The leakage in blood vessels is the main cause of swelling in retina. It affects the human vision system. Detection of blood vessels is important to measure the area, perimeter, troisity features of the blood vessels. For all this, we have to subtract the OD area from the blood vessels. Following subsection covers the algorithms for the detection and segmentation of OD.

Rashid Jalal Qureshi et al. in [75], introduced a shape-based algorithm for detection of OD. A pyramidal decomposition is applied to green image plan. The candidate regions are selected by comparing low and high intensity pixel values. The smoothing is implemented to each bright region. Each bright pixel is considered as the center of circular region and continuous regions are merged into each other. Fundus image is in RGB color space so it is converted into HSI space. Noise removal and image contrast enhancement is achieved by median filter and CLAHE. The OD is detected by entropy filter and hough transformation. Blood vessels are obtained by applying the closing morphological operators after smoothing the green image plane. Features such as intensity, vessels, vessel size, standard deviation, orientation, maximum width, density, and average image intensity, measured under and around a circular template are computed.

Daniel Welfer et al. in [95] use *LUV* image space and image is enhanced by morphological enhancement techniques. Top-hat transformation is computed by opening and closing operators to separate the brightest and darkest regions. Then this is followed by erosion and dilation and image details are enhanced. The center of circular region is an option. Minimization is performed and noise is removed by separating the back ground and foreground images. The background image is reconstructed and difference between the minima and maxima of this image is computed. This transformation removes all the connected peaks and it contains only a few basin structure elements and subtraction decrease contrast outside the optic disc. This finds the local optic disc. Then this region is gradually improved in second phase. The authors claim 100 % and 97.75% for accuracy.

A probablistic method for detecting OD is introduced by Balazs Harangi and Andras Hajdu in [36]. An ensemble based single object detection system is used for localization of the center and each pixel is considered to be the center. A probability map (PM) for the input image is defined by confidence values. This information is merged on majority vote bases for OD localization. Another method for optic disc localization in fundus images is proposed by Lesay et al.[55]. In this method, morphological opening, closing, dilation and erosion operators are used. Image smoothing is achieved by median filter and hough transformation is applied to green image plan. At the next step, gaussian filter is applied to smoothen the edges and a high intensity region is extracted by adaptive threshold method. After that, three methods (i) Fast Radial Symmetry Transform, (ii) Hough transformation (iii) and histogram matching are implemented for optic disc localization and segmentation. The accuracy 92.38%, 89.47% and 71.24% is claimed.

An automatic detection of optic disc is introduced by Kemal Akyol et al. [43]. Image smoothing is performed by CLAHE on the inverted green image plane. Key points are extracted using the morphological operators and the BLP operator. Next, the visual dictionary is prepared. Sa'ed Abed et al. introduces a swarm intelligence based algorithm in [1]. In this method, image is re scaled and resized. Image smoothing is implemented by median filter and contrast is improved using adaptive histogram method. A median filter with large kernel is employed for background estimation excluding the OD. The local maxima and minima is obtained through optimization algorithm. A power factor transformation is applied to enhance the grey scale value. To remove the pixels outside the region of interest, image masking is performed. This two dimensional function is optimized by the optimization algorithm. This results as the segmentation of optic disc. Four swarm artificial intelligence algorithms are tested and each of them reach to 100% accuracy.

The method proposed by Joshi et al. in [42] has two steps. First of all, the image smoothing is performed and foreground and background images are extracted. Then region of interest is defined and circular features are determined by hough transformation. The average accuracy of method is 94.7 percentage as reported by authors. The OD detection by employing the edge sensitive Digital Curvelet Transform (DCUT) has introduced by Mahdad Esmaeili [22]. The histogram equalization is performed on green and red image planes on square image and these histograms are adjusted. The image is enhanced using mean intensity values. The coefficients of curvelet transformation are obtained by applying the curvelet transformation on the enhanced images. The canny edge detection filter is implemented on the inverse coefficients of curvelet transformation and OD is obtained by employing dilation and erode morphological transformation. The transformation can be implemented by two ways, i.e., the un equispaced FFT transform and the wrapping transform. Both algorithms have same output. The authors report the 94.51%, 90.41% and 93.42% accuracy.

Li Xiong and Huiqi Li proposed the method for Location of OD [99]. The morphological opening, closing, and erosion operators are applied with square kernels to generate the ROI mask in red image channel. The ROI mask is shrunk to avoid effects of pixels near edges of ROI on the localization of OD. The holes in ROI, which are generated due to illumination changes are filled by a hole filling algorithm. The vertical, horizontal and OD edges are used for searching the candidate region. Then two features are defined using the green image plan and the horizontal and vertical edges. The maximum value of these two features locate the position of OD center. Median filter is implemented for image smoothing then morphological dilation operation are performed with circular structuring element. The method accuracy is 95.8% to 100% as reported by authors.

M. Partha Sarathi et al. introduced a method for OD localization and segmentation by blood vessel inpainting [78]. A kaiser window operator is applied to obtain coordinate pixels with maximum intensity. The red and green image planes are combined. In this approach, more weightage is given to red image, this preserves the OD region. Efficiency and robustness of the method is increased using inpainting technique for blood vessels. A variational model for OD segmentation is proposed by Baisheng Dai et al. in [18]. The OD is localized and SIFT and HoG features reflect the shape, texture and color characters of image patch and these features are used in training data. To remove the blood vessels, a foreground image is obtained by applying morphological closing followed by a morphological opening to the ROI. The problem of OD segmentation is considered as energy minimization problem in variational models. The OD is a circular or elliptical object. To model the prior OD shape is constructed by principal components analysis (PCA). This prior knowledge about shape of OD can be exploited to guide the curve evolution and OD is segmented.

Sangita Bharkad proposed a method for automatic OD segmentation [16]. Blood vessels are blurred and optic disc is enhanced by the equiripple low pass filter. The optimized order of filter is 83 with design parameters. The low pass equiripple filters are tuned for better results and empirically computed variable are used. This choice provides better results in suppressing blood vessels and lesion while enhancing the OD portion in fundus image. The maximum intensity values are selected for the OD region and center of that region marked as the OD center. The square region around the center is cropped from green plane. The image enhancement is performed by morphological dilation along with the disc structuring element. The OD region is segmented by implementing the median filter. Finally, the segmented OD region is replaced in original retinal image to obtain actual position of the OD and its boundary. Authors mention the accuracy of 96.92% to 100% for different databases.

In method, proposed by Rashmi Panda et al., convergence point of vessels as OD center [70]. The blood vessels are obtained by segmentation method. The morphological erosion operation is used to remove the minor vessels and get the foreground image of major vessels. Lines passing through the center of masses are used. The line orientation is taken from 0 to 180 with the variation of 5 degree and partial hausdorff distance measure is defined. The blood vessels in retina image have unique random distribution. Vessel Symmetry Line (VSL) is computed and line sets are computed on edge pixels. Symmetry lines are drawn by vessel component count. The number of major blood vessel components converging around the OD center is more than any other location in fundus image. This property is existent in many fundus images irrespective of the health of retina. The Vessel Component Count (VCC) is defined using two semi-annular masks centered on each pixel of symmetry lines. The mass center of vessel map inside the region is considered as OD center.

S. B. Akhade et al., investigated the red and green channel [3]. The blood vessels are removed by implementing the mathematical closing morphological operator and this is followed by watershed transformation to obtain the location of optic disc. Muhammad Alshayeji proposed Gravitational law based optic disc detection algorithm in [9]. The image is re-sampled to 128 × 128 to reduce the computation time for algorithm. The colored fundus image is converted to a gray scale image. A scheme proposed by Perona and Malik [72] is applied for image smoothing and resultant image is subjected to adaptive edge detection algorithm. The edges are detected following the gravitational law and edge map filter is implemented. Pixels outside the circular region are dropped out. Finally, a 5 pixels square region is removed from the edge map center. This step is used for masking operation. A binary image is obtained by thresholding and optical disc is found by trail and error method. Accuracy of the method is mentioned from 92.90% to 100%, for different data sets.

Beiji Zou et al. introduced a method for OD localization [107]. The green channel is selected and contrast enhancement is achieved by applying median filter. The region of interest is chosen and pixels in this region have effective information. Two images are reconstructed using dilation operators with two structural elements and images are subtracted. The brightest area is selected by threshold method, and a binary image is obtained. There may be multiple areas due to lesion and exudates. The ratio or the major and minor axis is computed and all areas whose ratio is outside the selected band are dropped. Calculate the area of connected domains and drop all the objects whose area is less than one third of the selected area. The model is checked through the model verification. The authors mentioned 96.3% and 100% accuracy.

3.3. Results comparison of optic disc algorithms

In these studies, we find a total of 16 papers in the area of optic disc localization during survey period. Table (2) represents summary of the results. The databases for which these methods are tested and compared to other algorithms are also mentioned in 6^{th} column of the table, and these are measured in terms of accuracy (acc), sensitivity (sen) and specifity (sp). The last column represents the accuracy of detection and segmentation of optic disc as reported by authors.

4. Segmentation of blood vessels

Blood vessels are important structures in the retina.. These vessels have high contrast values in fundus images. The fundus images contain a wide range of blood vessel structures such as capillary, short, narrow, large and long vessels, and bleeding areas. The bleeding areas are known as lesion such as MAs and HMAs and these lesions are an early stages of DR. The accurate segmentation of blood vessel parts is an essential part of diabetic screening algorithms. Many blood vessel related features like diameter, length, area, perimeter and branching angles are used directly in computation of features of DR algorithms. The blood vessel detection algorithms are classified into four types:

1 Adaptive threshold algorithms
2 Blood vessel tracking algorithms
3 Machine trained classifier algorithms
4 Algorithms for Large and small vessel detection

In the next subsections, we describe the methods in each class separately.

4.1. Adaptive threshold algorithms

In these methods, background and foreground images are separated by implementing a threshold technique. For this purpose, Laplacian, Sobel, Gaussian filters and Wavelet transformations are implemented and cross-sectional area of blood vessels is assessed from the foreground images.

Mehdi Hassan et al. [38] proposed an adaptive technique for blood vessel detection. In this method, Hidden Markov Model (HMM) and morphological operators are implemented for preprocessing. The image smoothing is achieved by median filter on green image plane and this image is subtracted from original image for normalization. Background and foreground are separated by a binary threshold. The HMM is implemented at second stage for predicting vessel pixel. The HMM classify pixels into vessel and non vessel, where the pixel intensities are considered as a sequence of observations. In training of HMM, every pixel is accessed multi-directionally. The mean square error of five intensity values is used in construction of feature vector. Finally, these three images are combined using the OR operator. The small objects which are not part of blood vessels are removed by morphological opening operator and refined blood vessels are reconstructed by morphological dilation operator with circular structure element. The authors reported that method has accuracy more than 95 %. In algorithm proposed by Jyotiprava Dash and Nilamani Bhoi [19], the CLAHE and median filter are used for contrast enhancement and noise removal respectively at preprocessing step. This is followed by image smoothing. Then image is transferred to binary image using c-mean clustering. Blood vessels are the differences of binary and enhanced image.

4.1.1. Tracking algorithms

Uyen T.V. Nguyen et al. [65], introduced an algorithm for segmentation of blood vessel. The lines are drawn through central pixel at the rotation of 15 degree in green image plan and average of gray level values of pixels along each line is computed. The line with maximum value is called winning line and line response for each pixel is computed as difference between winning and average line. Background and foreground images are separated using response line and a balancing parameter. Multi-line detectors are used to handle the misclassification of pixels. The image is enhanced by applying gaussian filter with zero mean and unit standard deviation distribution. A standardization and normalization are performed to improve background image contrast before combining the images. Images are combined using weighted average and segmentation is a linear combination of line responses at different scales.

R. GeethaRamani and Lakshmi Balasubramanian [32] proposed an algorithm for automatically segmentation of blood vessels. First of all, the region of interest is obtained by image cropping, this minimizes computational cost. For contrast enhancement, the CLAHE and gabor filters are used on Green, Y, L and G_1 channels from RGB, *YCbCr*, *La b* and Gaussian color space respectively. These filters are applied with the orientation of 15 degree to capture all the vessels. Gabor filtering is operated on four contrast enhanced images yielding 12 gabor response images. The adaptive filtering is performed using the half wave rectification and this results in 12 images. These images along with green channel of contrast image formulate the feature space. Principal component analysis is applied to 13 dimensional feature vector to arrive at a new set of more representative and 13 dimensional features represented as Eigen vectors. It is a binary classification problem and Manhattan distance is used for this classification in PCA. The pixels in vessel cluster are finalized as vessel pixels. The root guided decision tree (RGDT) classifier is used for classification and this is trained by the training data.

In Hierarchical Image Matting Model for blood vessel segmentation, introduced by Zhun Fan, Jiewei Lu and Wenji Li [24], regional features of blood vessels are used for segmentation. Area, Bounding box, Extent, Vratio, Convex hull and Solidity are regional features of blood vessels.

Table 2
Total number of methods introduced which are analyzed in survey period. These methods are separated based on features and processing and classification of DR.

Year	Authors with citation &Publication title	Image Plane	Denoisng, smoothing &Enhancement	Seg. Method	Databases	Accuracy.
2012	Mahdad Esmaeili et al. [22], Automatic Optic Disk Boundary Extraction by the Use of Curvelet Transform and Deformable Variational Level Set Model	Red and Green Image	Mean intensity value, Curvelet transformation, canny edge detection	Mathematical morphology	STARE, DRIVE, DIARETDB1	acc) = 94.51%, 90.41%, 93.42%
2012	Rashid Jalal Qureshi et al.[75],Combining algorithms for automatic detection of optic disc and macula in fundus images	Green	Median Filter, CLAHE	Entropy and hough transformation	DIARETDB0, DIARETDB1, DRIVE	Performance compared as Euclidean error
2012	Shilpa Joshi and P.T. Karule [42], Localization of Optic Disc in Color Fundus Images	Red and green	contrast enhancement	ROI, hough transformation	DRIVE, DIARETDB0, DIARETDB1 and live images	acc) = 94.7%
2013	Daniel Welfer et al. [95], A morphologic two-stage approach for automated optic disk detection in color eye fundus images	Luv	Mathematical Morphology	Mathematical Morphology	DRIVE, DIARETDB1	sen. = 92.51% spec. = 99.76%
2015	Balazs Harangi and Andras Hajdu [36], Detection of the optic disc in fundus images by combining probability models	Grey	Gaussian filter	ROI, Probablistic model and agumented Naive based aggregation	DIARETDB0, DIARETDB1, DRIVE, MESSIDOR	acc)= 82.64%, 99.98%
2016	Lesay et al. [55], Optic disc localization in fundus images	Green	Median, gaussain filter	Hough transformation and adaptive threshold	MESSIDOR	acc)= 94.38%, 95.00% 90.00%
2016	Kemal Akyol et al. [43],Automatic Detection of Optic Disc in Retinal Image by Using Keypoint Detection, Texture Analysis, and Visual Dictionary Techniques	Green	CLAHE, Morphological operator	BLP operators	DIARETDB1, DRIVE,ROC	acc)= 94.38%, 95.00% 90.00%
2016	Sa'ed Abed et al.[1],Effective optic disc detection method based on swarm intelligence techniques and novel pre-processing steps	Grey	Median filter, adaptive histogram, power factor transformation	Image mask and optimization	DRIVE,DIARETDB1, DMED, STARE	acc)= 100%
2016	Li Xiong and Huiqi Li [99],An approach to locate optic disc in retinal images with pathological changes	Red and green	Median filter, Mathematical morphology	ROI, hole filling algo.	DRIVE, STARE, DIARETDB0. DIARETDB1	acc)= 95.8% to 100%
2016	M. Partha Sarathi et al. [78], Blood vessel inpainting based technique for efficient localization and segmentation of optic disc in digital fundus images	Red and green	Kaiser window operator	Blood vessels inpainting	MESSIDOR, DRIVE	Overlap secore = 89 %
2016	Baisheng Dai et al.[18], Optic disc segmentation based on variational model with multiple energies	Grey	Mathematical morphology	ROI,hough transformation, PCA	MESSIDOR, ONHSD, DRIONS	acc)= 99.17%, 100%
2017	Sangita Bharkad [16], Automatic segmentation of optic disk in retinal images	Green	Equiripple low pass filter	Median filter	DRIVE, DIRATEDB0, DIRATEDB1, DRIONS	acc)= 100%, 96.92%, 98.98%, 100%
2017	Rashmi Panda et al. [70],Robust and accurate optic disk localization using vessel symmetry line measure in fundus images	Grey	Convergence of blood vessels	Mathematical morphology and vessel symmetry line	DRISHTI-GS,DRIONS-DB, E-OPHTHA-EX, MESSIDOR, DIARETDB1, DIARETDB0, DRIVE, HRF, ROC, STARE.	acc)= 97.75% to 100 %
2014	S. B. Akhade et al. [3], Automatic optic disc detection in digital fundus images using image processing techniques	Red and green	Mathematical morphology	watershed	MESSIDOR	not mentioned
2017	Muhammad Alshayeji [9],Optic disc detection in retinal fundus images using gravitational law-based edge detection	Grey	Perona and Malik	Adaptive edge detection, gravitational law and edge map filter	DERIVE, DMED, STAR, DIARETDB1	acc)= 100%, 92.90%, 90%, 95%, 97.75%
2018	Beiji Zou et al. [107],Classified optic disc localization algorithm based on verification model	Green	Median filter	Mathematical morphology, model checking	STARE, DERIVE, DIARETDB0, DIARETDB1	acc)= 96.3%, 100%
2011	S. Lu [58]Accurate and Efficient Optic Disc Detection and Segmentation by a Circular Transformation	Red and green	Median filter	circular transformation, Probability map, B-spline curve fitting	STARE, ARIA,DERIVE	acc)= 99.75%, 97.5%, 98.77%
2015	A. Basit and Muhammad Moazam Fraz [12] Optic disc detection and boundary extraction in retinal images	Green	Median filter,mathematical morphology	Watershed transformation	DRIVE, Shifa, CHASEDB1, DIARETDB1	acc)= 100 %, 100%, 100%, 98.9%

Objective of image segmentation is to divide the input image into three classes: the vessel (foreground), background and unknown regions. The enhanced vessel image I_{mr} is segmented into background, unknown and vessel regions. The unknown region is further investigated and hierarchical image matting model labels the pixels of unknown regions as vessels or background in an incremental way. The method stratifying pixels of unknown region into a hierarchies. The method consists of two steps: Stratify pixels in unknown regions into different hierarchies and update in the hierarchical. This assigns new labels (V for vessel or B for background) to pixels in each hierarchy.

4.1.2. Machine trained classifier algorithms

This class of algorithms use feature vectors derived from fundus images. The features are computed for each pixel, and feed into classifier. The classifier divides pixels into vessel and non vessel class of pixels.

The algorithm proposed by S. Wilfred Franklin and S. Edward Rajan [27] is a class of machine trained classifier. In this algorithm, multilayer perceptron neural networks are used for identification of blood vessels. The gabour filters at rotation of 15 degree are applied to detect the oriented profiles of blood vessels and small vessels are detected by applying multiscale gabor filters using the key points as proposed by Lei Zhang et al. [102]. The set of gabour filter bank is used as input in scale invariant feature transform (SIFT) to detect key points and low contrast key points are removed by thresholding. The spatial coordinates and scale of remaining points are assigned one or more orientations based on gradients of surrounding local image and k-mean clustering algorithm is used to cluster training images. The filter responses from key points are used to initiate k-means algorithm. This algorithm is run iteratively to achieve the convergence or maximum required iterations.

In S. Wilfred Franklin and S. Edward Rajan [26] employed ANN in retinal blood vessel segmentation. The features like haemorrhages, exudates and presence of retinopathy are detected using the artificial neural networks. The RGB fundus image is converted into HSL color space and mean filter to the Luminance space is applied for background estimation. Background and foreground images are separated and normalization is performed on foreground image only. Then image is converted back into RGB space. Gabour features are obtained by gabour filter after the image enhancement and merging the small objects.

These features along with some moment invariant based features are used as input nodes in ANN. The pixels are classified into vessel and non vessel classes. A five layered feed forward neural network is implemented, where output layer contains a single neuron. The pixel samples are taken from vessel and non-vessel regions in network training phase. The intermediate processing such as Histogram equalization, conversion of image into HSL and RGB spaces and image enhancement are performed at the hidden layers. A copulative distribution function is used for contrast enhancement. The blood vessels are used to detect the abnormalities in retina using image processing techniques.

Shahab Aslani and Haldun Sarnel [11], proposed a supervised learning algorithm for retinal vessel segmentation based on robust hybrid features. Machine learning algorithms are used for pixel classification. A feature vector is constructed using local features and feature extraction algorithms is used for extraction of features. The pixels are distributed in vessel and non vessel classes. In training phase, manual labeling of pixel sets are used. The green plan is used for further processing. A 17 dimensional feature vector is constructed and this vector includes blood vessel features such as intensity, vesselness measure, intensity of morphological top-hat transformed image, multi-scale gabor features, and response of B-COSFIRE filter. A FOV area extension and image contrast is enhanced using the CLAHE before feature extraction.

An unsupervised blood vessel segmentation algorithm is presented by Luiz Câmara Neto et al. [64]. Gaussian smoothing for noise removal, a top-hat operator and contrast enhancement are performed on inverted green image plan. The blood vessels are enhanced using mathematical morphological top hat transformation with a circular structured element. The coarse blood vessels are detected using local thresholding scheme. This scheme uses both, grey level intensity and spatial dependency of pixels. An adaptive labeling rule is used for labeling pixels to vessel or non vessel regions. This is called coarse segmentation map. This map presents a connective tree with both large and thin vessels. This connective tree may contain the artificial vessel as a result, the coarse segmentation negatively affects visual perception.

A post-processing step is applied to remove these structures, by creating a curvature map that is combined with local coarse segmentation in a morphological reconstruction approach. Image is a 3D differentiable function which consist of homogenous and non homogenous subregions. Background areas on retinal surface tend to present slight variations, these areas is considered as homogeneous regions with lower curvature values and higher gray level intensities that cause the peaks on the surface are non homogenous. A binary morphological reconstruction operator is used for the reconstruction of refined vessel maps. This improves vessel detection on the coarse vessel segmentation by removing unconnected artificial vessels. The coarse segmentation is assumed to be the mask-image since it contains a noisy vessel tree where most of the vessel pixels are present. Authors claimed the balanced accuracy of the method is 87.87, 86.16 %.

Carmen Alina Lupasçu et al. [59] introduced a method for retinal vessels segmentation. A 41 dimensional feature vector which consists of the output of filters, vesselness, and ridgeness measures based on eigen value decomposition of hessian matrix, and output of a 2-D gabor wavelet transform taken at multiple scales. The classification is performed using the AdaBoost classifier. This classifier divides the pixels into vessel and non vessel pixels.

Another method proposed by Luiz Carlos Rodrigues et al. [76] uses wavelets and Hessian-based multi-scale filtering for segmentation of blood vessels. Initially two images are selected and histogram of image is computed for color band selection by histogram analysis. The red band is selected for optic disc segmentation and image enhancement is achieved by employing a white top hat transformation with circular structuring element. At the next step, image is decomposed into approximate frequencies up to four levels by Haar wavelet and fifth level is then resized to original binary image. The optic disc is segmented by thresholding and blood vessels are detected by scale space analysis. The Hessian is also a discrete function and it is approximated using 2-dimensional Gaussian filter and convolution differentiation property. The vessels are enhanced by filtering through Hessian matrix and Eigen values are computed for contrast and directional information of a pixel. The vesselness and a genome function is developed. The initialization, mutation, crossover and elitism are fundamental operations in a genome. The elitism is a function which passes well fitted individual number from one generation to the next generation without any change. The objective function is defined at next stage and objective function consists of the comparison between manual segmentation of image dataset and result of the segmentation obtained by the Hessian-based filter on Gaussian scale-spaces.

A method for Retinal vessel segmentation using Extreme Learning Machine is proposed by Chengzhang Zhu et al. [105]. The green image plan is used for processing and features vector is computed. A 39 directional feature vector which consist of blood vessel profile, Gaussian filters, mathematical morphological transformation, phase congruency, Hessian matrix and gradient vector field for a pixel is constructed. The morphological openings and closings operators results in top-hat and bottom-hat transformations. These transformed images are subtracted and this combined image is used for computing the morphological features. The bright objects with dark background are detected by top-hat transformation. Its converse is computed by bottom-hat transform. These features are fed into extreme learning machine for further processing. It is a binary classification algorithm and segmentation is achieved through optimization.

Roberto Vega et al. [89] introduced the method for vessel extraction using lattice neural networks with dendritic processing. After image acquisition, the preprocessing is performed for central light reflection removal with the application of morphological opening. The mean filters are implemented for background subtraction and enhancement of blood vessels is achieved. A 7-dimensional feature vector is computed as described by D. Marin et al. in [61], which composed of gray-levels and moment invariants for pixel representation. The network is trained using a lattice neural network with dendritic processing. The noise and misclassified pixels are removed by post processing applications.

M. Usman Akram and Shoab Ahmad Khan in [6] present a multi-layered thresholding-based blood vessel segmentation method. A 2-D gabor wavelet is applied on inverted green channel for vessel enhancement and a binary mask is created using multi-layer and adaptive thresholding for blood vessel segmentation. Then binary image classification is performed. Another method for blood vessel segmentation, proposed by Amna Waheed et al.[94]. This is an extended version of the above method. The extracted vascular pattern obtained after applying technique in [6] are used in next step to cater false structures precisely. The candidate regions are extracted through connected component analysis. Each connected segment in vessel map is considered as a region. The morphological and intensity values are used as features. A seven dimensional feature vector is formulated for each candidate region. These features are fed into the Localized Fisher Discriminant Analysis (LFDA) for pixel classification. The method accuracy is 95.81% reported.

4.2. Algorithms for large and small vessel detection

In DR screening algorithms, blood vessel area and perimeter related features are used. The accuracy of an algorithm is directly related to the detection of blood vessels. At starting point of a vessel, it has much more visually clear picture and then branching occurs, its size decreases. As a result, a single choice of threshold doesn't work and some basic information is lost. To overcome this difficulty, two or more segmentation algorithms are combined. The large size blood vessels are segmented an algorithm then a separate algorithm is used to determine the small size vessels. In STARE database, the system of blood vessels is divided into two categories: large and thin(small) blood vessels. The vessels with the diameter greater than 3 pixels are considered as large blood vessels and those with diameter less than or equal to 3 pixels are called small vessels. The following subsection covers the methods which can detect both large and small vessels.

Lili Xu introduced an algorithm for determination of large and small vessels [56]. The large vessels are determined using adaptive thresholds technique. Background image is approximated by median filter and image normalization is performed by subtracting background image from the green image plan. The large connected component are considered as large blood vessels and a pair of local gradient along the blood vessel profile is obtained by sobel filter, whereas optic disc is surrounded by a single min max. The optical disk is located and its edges are creased form the binary image. The residual fragments of binary image are classified using the support vector machine. Wavelets and curvelets are best point and line features detectors. These transformations are used to extract the features from feature space for thin vessels. As thin vessels, can be considered as line features with width of 3 pixels. Eight line detectors are used along eight directions.

M.M. Fraz et al. in [29], introduced an algorithm for localization of retinal blood vessels. The statistical measures are used for determining the directional candidates for each pixel. The matching and mean filters are implemented for vessel line determination and background extraction respectively. Image is normalized by subtracting an estimated background from the image. In second technique, maximum principal curvature of blood vessels is computed and line strength is generated by implementing line detector technique. Then first order difference of Gaussian is computed for a line and contrast enhancement is achieved by morphological operators. The shape and orientation of blood vessels is determined by bit plane slicing. The binary vascular map is produced using vessel center line. In this algorithm, RGB, HIS, the luminance channel of NTSC(YIQ) color space and *L ab* color space are used. Finally vessel center lines, shape and orientation are reconstructed using the seed algorithm. The centerline image is used as seed point. The aggregation operators are used for region growing. Authors reported Acc. 95.52% of the method.

4.2.1. Detection of glaucoma

Distortion in optical nerve system and vision loss is called the glaucoma [81]. The bright region in fundus eye image is called optic nerve head region. This region composed of optic disc and optic cup. Flat structured optic disc can become a non flat region due to intraocular pressure (IOP). The IOP creates an inward force on retina and an optic disc cupping starts. This cupping of disc is termed as optic cup. Glaucoma is a disease which is related to optic nerve head and its neighboring regions and glaucoma is a diabetic retinopathy feature. The Cup-to-Disc Ratio (CDR) is an important clinical parameter which has been used by the ophthalmologists worldwide in deciding a fundus image is healthy or unhealthy with Glaucoma.

A method of blood vessels segmentation for detection of glaucoma is introduced by L. Shyam and G. S. Kumar [81].

This algorithm requires two images for processing. The blood vessels are extracted using median filter to the green plane and red regions are extracted from enhanced image. The top-hat reconstruction of image is performed through rotating the structuring elements at 15 degree. This produces a bank of 12 filters and second pre-processed image is reconstructed by taking mean image of 12 images. Both images are binaired by a thresholding technique and common regions are marked as blood vessels. For glaucoma detection, the ISNT ratio is defined. The area of blood vessels in four quadrants, have the relation Inferior > Superior > Nasal > Temporal. First of all, blood vessels are segmented and then area of blood vessels in four regions are calculated and nasal and temporal regions of optic disc contain most of blood vessels. The ratio of the blood vessel area covered by inferior and superior regions to area covered by nasal and temporal regions is taken. The ratio is lower for glaucomatous case and higher for normal case. Julian Zilly et al. [106] presented a method for glaucoma detection. Optic disc is located by hough transformation and image is cropped into tiles using envelop of the optic disc. This cropping approach helps the training procedure to capture image features and more focus will be on region of interest. Image enhancement is performed in *lab* color space and image is normalized by subtracting mean value from the pixel values and divided by standard deviation. The pixel values are re-scaled and entropy based informative pixels are selected out of a patch. These informative pixels lie on edges, blood vessels etc. The convolutional network is an ensemble learning technique and convolutional filters are trained for five scales. The filter weights are updated by implementing gentle Ada Boost classifiers. Two 37 dimensional feature vectors are used for optic disc and cup segmentation. The segmentation is a energy minimization problem. This function is optimized by implementing graph cut algorithm. After that a convex hull transformation is applied to output of graph cut algorithm. Then optic cup to disc ratio is defined in terms of two perimeters.

An algorithm for detection of glaucoma is proposed by Soorya M. et al.[60]. In this method, Red lesion and optic disc are separated using statistical features such as solidity, eccentricity, circularity, area, perimeter, border, etc. The OD boundary is detected using iterative process in red and blue channel and final image is subject to intensity based threshold. The false candidates are removed by applying binary image transformation. The Gaussian filter and polynomial interpolation are used for image smoothing and shade removing. Image contrast is improved by dividing the pixel intensity in green image plane by pixel intensity in shade corrected image. At next step, the seed points are detected and blood vessels are tracked using these seed points and inverted gaussian profile is drawn for blood vessels. The tracking should happen towards centroid. Considering a single pair of seed point, a dynamic elliptical searching window is created using the major and minor axis and the size of blood vessel is dynamically adjusted. The angle is defined by ellipse and inverted gaussian profile is plotted for all these points. The points with distinct intensities are filtered out and degeneracy is handled by choosing only one point and next points are determined using these points. The points where seed point changes are called the bend points. Joining these bend points with each other gives the contour for optic cup. Finally, all the bend points are joined with each other to form a cluster like structure, then a convex hull is formed which creates the contour of optic cup. The normal and unhealthy images are defined as ratios between the cup and disc.

4.3. Algorithms for blood vessels detection and segmentation

In this section, methods for detection and segmentation of blood vessel summarized in Table (3). These methods are discussed above. Method performance is measured in terms of accuracy (acc.), sensitivity sen. and specifity sp. . These measures are described in last column of the table.

5. Clinical, geometrical & haemodynamics features

The DR is detected and classified by multiple features. These features aee divided into categories as

1 Clinical features
2 Geometrical & haemodynamic features

In the following subsections, the algorithms for determining these features are described.

5.1. Clinical features

The DR detection and classification depends upon sort and type of lesion which exist in retina. These lesions are called clinical features, these features are named as:

1 Red and White Lesion: Microaneurysms (MAs), appears as Red dots and circular in shape. Hemorrhages (HMAs) appears in red colored flag shape. White lesion in retina images are called cotton wool spots.
2 Exudate: The formation of yellowish or white objects in retina is called Exudates.
3 vascular proliferation is the sign of PDR, so this feature is considered as classification of DR and algorithms that deal with PDR are discussed in Section 6.

Now these algorithms are described in detail:

5.1.1. Red lesion

The MAs and HMAs are reddish in color, these are known as red lesion. These lesions differ in shape. The MAs are balloon shaped and HMAs are dotted shape. These are early sign of diabetic retinopathy and it is hard to differentiate these two lesions in color fundus images. These are proximate to blood vessels. The blood vessels and OD must be excluded from image for detection of all sort of lesions.

G. Quellec et al. [74] proposed a filter framework for the detection of red lesion. An optimal feature space is generated by the set of optimal filters. Initially a risk is generated then this risk is used for the estimation of lesion. This risk is computed with a classifier. A threshold method for segmentation of lesion is defined and foreground samples are identified with the application of morphological operators. A maximal risk is present in every sample then this is called the risk of disease. Ruchir Srivastava et al. [83] presented a method for detecting retinal microaneurysms and hemorrhages. An inverted green plane is divided into tiles of equal size. These tiles are called patches. The bright objects are detected by applying filters. A feature vector is generated from features extracted from patches and a kernel is formulated by this feature vector and SVM classifier is implemented for prediction of lesion.

Bo Wu et al. [98] proposed a method for automatic detection of microaneurysms. The mean filter is applied to green image plan for estimation of illumination and illumination equalization is performed. This image is subtracted from original image for shade correction. The CLAHE is used for image enhancement step on inverted green image plane. The circular region of interest is considered with fixed diameter. The MAs candidates become more visible and identified with the help of peak identification and region growing algorithms in preprocessing step. The gaussian smoothing is performed. The MAs are bright structures and contain at least one maximum thus local maximum is considered as MAs. A 27 dimensional feature vector is constructing using Hessian matrix based features, mean, max, standard deviation, shape features, aspect ratio etc. For classification, Three supervised classifiers, K-Nearest Neighbor (KNN), Naï ve Bayes (NB) and Adaboost are implemented.

Pereira [71] introduced the model for MAs detection. The median filter is used for separation of background and foreground images from green image plane and gaussian filter is used for image enhancement. The agents are designed for segmentation process and RA then segments and analyzes its region and attempt for fusion of regions. Finally the MAs features are extracted by agents. An other method proposed by Niladri Sekhar Datta et al. [20], for microaneurysms detection of non-dilated retinal fundus image. Image is divided into tiles and median filters are implemented for smoothing. The normal and diabetic eye images are classified by an exiting classification technique. The CLAHE and canny edge detector are used for image smoothing and edge detection respectively on green image plane. The morphological and logical operators are used for detection and segmentation of blood vessels and exudates. A mask is created to segment the optic disc. Then, created mask is subtracted from segmented retinal image and obtained an image without optic disk. The MAs area is obtained after removing other existing elements. A method for identification and classification of MAs for early detection of diabetic retinopathy was introduced by M. Usman Akram et al. [4]. In this method, image contrast enhancement is performed using mathematical morphological operators on green image plane. First of all, morphological opening operator is used to smooth OD and other bright lesions. This gives us a smooth fundus region containing dark lesions and blood vessels with low contrast. Contrast enhancement using sigmoid function, is performed to improve the contrast of lesions for easy detection. This contrast enhanced image is taken as input to the gabor filter for enhancement of red lesion. Binary candidate regions for MAs and HMAs are extracted by applying a threshold value. The blood vessels are subtracted by any blood vessel segmentation algorithm. The MAs regions appear with distinguishable properties such as color, size and shape and they are small in size, dark red colored and circular in shape. A feature vector is formed for each candidate region. These features are,shape based, gray level, color and statistical features. Shape based features are area, eccentricity, perimeter, compactness, and aspect ratio of candidate region. Gray level features are mean and standard deviation, Mean gradient magnitude value for boundary pixels. Color features are hue, saturation and value. The statistical features consist of entropy, energy, homogeneity and moments. Then binary classification is performed using the multi model m-mediods classifier.

5.1.2. Detection of exudate

The yellowish or white objects in retina image are called hard exudates. Leaky blood vessels are main cause for formation of hard exudates. The following is the summary of algorithms for detection of exudates.

Table 3
Algorithms for detection and segmentation of blood vessels during the survey period.

Year	Authors &Title	Preprocessing	OD and bllod vessel seg.	Classifier &Databases	Evaluation Measure
2010	Lili Xu and Shuqian Luo [56], A novel method for blood vessel detection from retinal images	Median filter, curvelet for thin vessels	Sobel filter for OD, Adaptive threshold,	Large and small blood vessels, SVM, DERIVE	acc. = 93.36% sen. = 85.57%
2017	Mehdi Hassan et al. [38], Robust Hidden Markov Model based intelligent blood vessel detection of fundus images	Green image, median filter, binary threshold Mathematical morphology	HMM, OR	Blood vessels, DERIVE	acc. = 95.7% sen. = 81.0% sp. = 97.0%
2017	Jyotiprava Dash and Nilamani Bhoi [19], A thresholding based technique to extract retinal blood vessels from fundus images	CLAHE, median filter, c-mean clustering	difference of binary and enhanced image	Blood vessels, DERIVE, CHASEDB1	acc. = 95.5%, sen. &sp. not mentioned
2013	Uyen T.V. Nguyen et al. [65], An effective retinal blood vessel segmentation method using multi-scale line detection	Green image, vessel lines, Gaussian filter	linear combination of line responses	Blood vessels, SVM, STARE, DERIVE, REVIEW	acc. = 93.24%, 94.07%, sen. & sp. not mentioned
2016	R. GeethaRamani and Lakshmi Balasubramanian [32] Retinal blood vessel segmentation employing image processing and data mining techniques for computerized retinal image analysis	Green, G_1, y, L color planes are chosen from RGB, Lab, Gaussian, yc_bc_r color spaces respectively, CLAHE	Gabour filters, PCA	Blood vessels, Root guided tree, DERIVE	acc. = 95.36% sen. = 70.79% sp. = 97.78%
2017	Zhun Fan, Jiewei Lu and Wenji Li [24],Automated Blood Vessel Segmentation of Fundus Images Based on Region Features and Hierarchical Growth Algorithm	Regional features such as area, Extent, Convex hull etc.	hierarchical	Blood vessels, ROC, DRIVE, STARE, CHASE DB1,	acc. = 96.0% sen. = 73.6% sp. = 98.10%
2012	M.M. Fraz et al. [29]An approach to localize the retinal blood vessels using bit planes and centerline detection	RGB, HIS, NTSC(YIQ) and Lab color space, Matching and mean filter, max. principal curvature and decoder method, gaussian filter	Mathematical morphology, aggregation operators	Large and thin blood vessels, DRIVE, STARE MESSIDOR	acc. = 95.52% Sp. = 97.23%
2012	M. Usman Akram and Shoab Ahmad Khan [6], Multilayered thresholding-based blood vessel segmentation for screening of diabetic retinopathy	inverted green image plane, 2D gabour wavelet,	binary threshold	Blood vessels, DERIVE, STARE,	acc. = 94.69%
2011	D. Marin et al. [61] A New Supervised Method for Blood Vessel Segmentation in Retinal Images by Using Gray-Level and Moment Invariants-Based Features	Green image plane, Mathematical morphology, mean and gaussian filter	grey level features	ANN, DERIVE, STARE	acc. = 95.26%, sen. = 69. 44 %sp. = 98.19%
2016	Shahab Aslani and Haldun Sarnel [11], A new supervised retinal vessel segmentation method based on robust hybrid features	Green Image plane, Mathematical morphology, CLAHE	Hybrid features	Blood vessels, Cosifire, DERIVE, STARE	acc. = 95.13%, sen. = 77. 96% sp. =97.17%
2017	Luiz Carlos Rodrigues et al.[76] Segmentation of optic disc and blood vessels in retinal images using wavelets, mathematical morphology and Hessian-based multi-scale filtering	Mathematical morphology,	histogram analysis, Wavelet hessian based and gaussian filter,	Blood vessels, DRIVE, HRF,	acc. = 94.65%, sen. = &sp. not mentioned
2010	C. A. Lupascu and D. Tegolo and E. Trucco [59], FABC: Retinal Vessel Segmentation Using AdaBoost	Hessian and gabour filter	Adaboost classifier	Blood vessels, adaboost, DERIVE	acc. = 95.69% sen. = 55.74% sp. = 99.36%
2014	S. Wilfred Franklin and S. Edward Rajan [27], Retinal vessel segmentation employing ANN technique by Gabor and moment invariants-based features	Gabour filters, multiscale gabour filters	SIFT	Blood vessels, ANN, DERIVE	not reported
2015	Lei Zhang et al.[102],Retinal vessel segmentation using multi-scale textons derived from keypoints	gabour filters, scale invariant transformation	KNN	Blood vessels, DERIVE	acc. = 95.05% sen. = 78.12% sp. = 96.62%
2017	Chengzhang Zhu et al. [105],Retinal vessel segmentation in colour fundus images using Extreme Learning Machine	Green image plane,	boold vessel profile, gaussian filter, Mathematical morphology	Blood vessels, ELM, DERIVE, RIS	acc. = 96.07, Sen. = 60.18, Sp. = 98.68%
2017	Luiz Câmara Neto et al. [64], An unsupervised coarse-to-fine algorithm for blood vessel segmentation in fundus images	Green image plane, gaussian smoothing, mathematical morphology	Binary morphological reconstruction algo.	Blood vessels, DERIVE, STARE	acc. = 86.16%, 87.87% Sen. = 79.42, 76.96% Sp. = 95.37%, 96.31%
2015	Roberto Vega et al. [89] Retinal vessel extraction using Lattice Neural Networks with dendritic processing	Mathematical Morphology, mean filter	lattice neural network with dendritic processing	Blood vessels,, ANN	acc. = 94.83%, Sen. = 96.71%, Sp. = 70.19%
2015	Amna Waheed et al. [94], Hybrid Features and Mediods Classification Based Robust Segmentation of Blood Vessels	inverted green image plane, 2D gabour wavelet,	Connected component Analysis, Binary threshold,	Blood vessels, Localized Fisher Discriminant Analysis, DERIVE, STARE, AFIO	acc. = 95.81%, 96.16%, sen. & sp. not mentioned
2014	S. Wilfred Franklin and S. Edward Rajan [26],Computerized screening of diabetic retinopathy employing blood vessel segmentation in retinal images	RGB, HSL color spaces, mean filter,	gabour filters,	Blood vessels, ANN, DERIVE	acc. = 95.03% Sen. = 77.68% Sp. = 98.10%

(continued on next page)

Table 3 (*continued*)

Year	Authors &Title	Preprocessing	OD and bllod vessel seg.	Classifier &Databases	Evaluation Measure
2016	L. Shyam and G. S. Kumar [81], Blood vessel segmentation in fundus images and detection of Glaucoma	Green plane, Median filter, Mathematical morphology	difference of mean and processed image, ISND ratio	Glaucoma, STARE, DERIVE, HRF	acc. = 93.10% sen. = 74.20% sp. = 94.30%
2017	Julian Zilly et al. [106] Glaucoma detection using entropy sampling and ensemble learning for automatic optic cup and disc segmentation	Lab color space, hough transformation, graph optimization method	Ada Boost classifiers	Glaucoma, MESSIDOR, DRISHTI-GS	not reported
2018	Soorya M. et al. [60], An automated and robust image processing algorithm for glaucoma diagnosis from fundus images using novel blood vessel tracking and bend point detection	RGB color space is used, gaussian filter, polynomial interpolation	Iterative process, bend points detection as countour of OD	Glaucoma, VIER	acc. = 97.01%, sen. = &sp. not mentioned

C. JayaKumari and R. Maruthi [41] proposed a method for segmentation of exudates. The image enhancement is performed by CLAHE and foreground is separated from background by contextual clustering. Exudates and non-exudates are separated by bottom up approach and statistical features are used as input into the network. Doaa Youssef and Nahed H. Solouma [101] developed a method for exudate detection. In this method, The dilation and erosion are applied for detecting dark regions with two linear structured elements and blood vessels are the difference of these two images. The hough transformation is used to detect OD and canny edge detector was used for detection of pixels of exudates. The initial estimate of exudates are detected after segmentation of blood vessels and OD and final estimate of exudates is obtained by implementing mathematical morphological reconstruction algorithm. The authors report 100 % sensitivity of the method.

Jaskirat Kaur and Deepti Mittal [46] introduced a method for exudates segmentation. Two pass filters and calculus are used for determining high frequency components and image enhancement respectively. The basic structure such as lesion, optic disc and blood vessels are segmented by high pass filter. Low frequency components are removed by applying the Laplacian filter. Blood vessels are detected by matching filters and circular disc is approximated by a mask and this mask is subtracted from normalized vesicular image and blood vessels and OD is subtracted. At this stage, image have only lesion details and exudates have the highest density among other lesion types.

A deep learning method is introduced by José Ignacio Orlando et al. [68]. The candidate regions are detected in green image plane. The image is enhanced by implementing cubic interpolation polynomial and noise is removed by gaussian filter. The mathematical morphological closing operator with linear structuring element is used for image reconstruction with 15 degree angle rotation. Small sized red lesion is removed by closing operator and remaining will appear in image structure. A score map is then obtained and a threshold is applied to new candidate image and a dedicated CNN is trained for red lesion. Equalization is performed for each color band. A training set of square patches around the center of lesion candidates are chosen and patch size is always about double of lesion candidate region. This choice allows CNN to capture the internal features and information about its shape, borders and context. Square windows doesn't affect the appearance of lesion candidate. Samples are centered by subtracting training set mean image. The CNN consists of 4 convolution layer and a fully connected layer. The optimization is performed using the stochastic gradient method.

Xiwei Zhang et al. [104] exudate detection in color retinal images for mass screening of diabetic retinopathy. After the noise removal and reflection zone determination, all dark structures such as blood vessels and dark lesions are removed by applying morphological inpainting along with the isotrophic structure elements respectively. Bright structures are removed by template matching and profile of remaining parts is restored by morphological reconstruction. All maxima are obtained and maxima touching restricted regions are removed and remaining maxima are used to reconstruct exudates. Another method for automatic segmentation of exudates is introduced by Qing Liu et al. [57]. In this method, the contour of field of view is obtained by taking gradient then field of view is segmented by threshold method. Gaussian filter is used for blood vessels localization for green channel and Optic disc is segmented using frequency tuned salient region detection method (FT) introduced by R. Achanta et al. [2]. The whole image is divided into small regions and CLBP histogram for each region is computed. Its local difference is decomposed into two complementary components via a sign-magnitude transform (LDSMT). The joint histograms are computed from CLBP histogram and feature vector is computed for each patch. Classification of exudates patch is achieved by random forest classifier.

Statistical based exudate segmentation method is presented by Sharib Ali et al. [8]. In atlas system, retinal features such as vessels, optic disc, fovea and eye pigmentation are represented. The reference coordinate system is identified by rigid alignment of detected optic nerves center and mean shape of tracked vessels. All training images are warped onto a reference coordinate system giving the mean image representing retinal atlas. The paired images are first registered using a feature based registration method. Feature vector is extracted from the intensity image. A 64 dimensional feature vector is generated by implementing SURF algorithm by Herbert Bay et al. [13]. The Euclidean distance is used for comparing the interest points of test and target images. A pair is considered matching if the distance between them is less than 0.7, it is used to eliminate the ambiguous features. Then feature vector is further refined by eliminating the outliers and optic center is determined by circular Hough transformation. Optic disc center and macula center defines the two land mark positions in atlas co-ordinate system. Large vessels are considered as seed points. large vessels are detected by Hessian matrix features with rotated kernel by 22.5 degree and templates are correlated with seed points and 60 weights are used in this computation. The major vessels are obtained by implementing the PCA and thin plate spline are used for warping training images. This is followed by mean image normalization. Bright lesion is segmented by retinal atlas. Chromatic differences between mean atlas image with fundus image of a diseased eye are main features and post-processing schemes like edge detectors are applied for segmentation of exudates.

Elaheh Imani and Hamid-Reza Pourreza [40] presented a method for exudate segmentation. In this method, Otsu thresholding algorithm [69] is used to determined the region of interest in green image plane. Then image noise is removed by implementing the morphological opening and closing operators. A bounding box is created around the Field of View and image is cropped. The shearlet transform introduced by Gitta Kutyniok et al. [51] are used in this method and image is decomposed in 8 directions with four levels. The lesion spots are detected by Non Subsampled Contourlet Transform (NSCT). This separates vessels from lesion. It is a threshold method and first threshold is the maximum coefficient. Abnormal blood vessels and exudates are separated by median operator and thresholding. The optic disc is segmented by implementing using algorithm proposed by S. Lu [58] and lesion is segmented by thresholding. A multiscale segmentation of exudates is introduced by M. Moazam Fraz et al. [28]. The contrast, luminosity and contrast correction was corrected in green image plan. Mean kernel is used for background approximation and this background is subtracted from green image plan for image normalization. Image correction is performed by linear transformation. The optic disc and blood vessels are detected and removed using algorithm [12,87]. The dark lesion is removed by implementing the morphological closing. A nine dimensional feature vector is constructed by using the local features. These features are feed into a classifier for classification. Javeria Amin et al. [10] A method for the detection and classification of diabetic retinopathy using structural predictors of bright lesions. The image enhancement is achieved by gabour filters and region of interest is determined by feature vector composed of area, perimeter, circularity, and diameter. The other dimensions are geometric and statistical features. Lastly a combinations of different classifiers are applied to classify an image with and without exudates.

5.2. Geometric & haemodynamic features:

G. Leontidis et al. [53] introduced the concept of geometric features such as significance of vessel widths, angles, branching coefficient (BC), angle-to-BC ratio, standard deviations, means and medians of widths and angles, fractal dimension (FD), lacunarity and FD-to-lacunarity ratio. These features are measured by analysis of variance (ANOVA) design.

Francesco Calivá et al. [17] proposed the method for haemodynamics in the retinal vasculature during the progression of diabetic retinopathy. The parent and child venous and arterial vascular bifurcation are used in zero dimensional modal and fluid dynamic conditions such as volumetric blood flow, blood flow velocity, nodal pressure, wall shear stress, and Reynolds number are estimated. These features are used to analyze the dieses development.

Maged S Habib et al. [35] studied the changes in retinal vascular geometry due to DR and its role in prediction of progression. The RVG structure is exploited and the changes are measured for progression of No. Dr to DR and grading from NPDR and PDR.

5.2.1. Clinical, geometric & haemodynamic features of DR

This subsection covers methods for detection of different features of diabetic retinopathy. These are represented in Table 4. The features are discussed in third column of table and last column describes the classifier and test databases.

6. Diabetic retinopathy detection & classification

The algorithms which are implemented for deciding either the fundus image is effected by DR or No DR and the algorithms which can further classify the DR grads are called the classification algorithms. These algorithms are analyzed in this section. These algorithms are further classified into two sub classes.

1 Diabetic Retinopathy Detection Algorithms
2 Classification of DR

The algorithms which are used for deciding that the fundus image is effected by DR or not are named as DR detection algorithms. The algorithms whose output is more than two classes can also be used classification of DR. These algorithms are analyzed in following subsections.

6.1. Diabetic retinopathy detection algorithms

The algorithms which are used to detect the DR. The output of these algorithms are commonly two classes, which are NoDR and DR, in some case, further classes are also developed such as mild, moderate and severe DR. The methodology of

After screening methods, the DR can be classified into proliferation and non proliferation.

The ANN are used in methods introduced by GG. Gardner et al. [33], Jen Hong Tan et al. [84] and deep learning technique Varun Gulshan et al. [88]. In first method, the back propagation neural network is used for training of the algorithm. The OD is removed using mask in green image plane and manual segmentation is performed. The whole image is divided into sub images as normal retina with or without blood vessels, retina with exudates, haemorrhages or microaneurysm. These sub-images are divided into training and test data sets. The training data set is used to train the network for the given set of features. The accuracy of the method is mentioned as DR screening, Blood vessels, Exudates, haemorrhages, 91.7%, 93.1%,73.1% respectively, sensitivity is 88.4% and specifity is 83.5%. A two stage network method is introduced by Yang et al. [100], where images are resized by the overlapped grid map. This is implemented by a sliding window. The small lesions are located at more conspicuous place in the yellow grid. The whole image is divided into a square sized image and the network is trained in four layers. These are, convolutional layer, max-pooling layer, fully connected layer. The soft max regression function at fourth layer, generates the labels of the input patches. Two maps, label map and probabilistic map, are generated after the classification of patches. These maps are used for constructing the weighted matrix for input image. The probability of lesions in local patches are represented in entities of the weighted matrix. These weights are feed into the grading network. The global network grades the DR according to international scale of retinopathy. The network is trained with weighted lesion map and output layer grades the severity of the fundus image. In algorithm proposed by Varun Gulshan et al. [88], lesions are recognized by using

Table 4
Algorithms for detection of DR features. The features are described in third column.

Year	Authors &Title	Preprocessing	Features	Classifier &databases
2011	G. Quellec et al. [74], Optimal Filter Framework for Automated, Instantaneous Detection of Lesions in Retinal Images	Treshold method, mathematical morphology	MAs	Not reported
2017	Ruchir Srivastava et al. [83], Detecting retinal microaneurysms and hemorrhages with robustness to the presence of blood vessels	Filters for feature extraction	MAs, HMAs	SVM, DIARETDB1, MESSIDOR
2017	Bo Wu et al. [98], Automatic detection of microaneurysms in retinal fundus images	Mean filter, CLAHE, gaussian smoothing	MAs, KNN, Naive and Bayesian classifier	E OPHTHA, (ROC)
2014	Carla Pereira et al. [71], Using a multi-agent system approach for microaneurysm detection in fundus images	Median, gaussian filter,	MAs	Not reported
2012	M. Usman Akram et al. [4], Identification and Classification of Microaneurysms for Early Detection of Diabetic Retinopathy	Mathematical morphology, gabour filter, geometrical and statistical features	MAs, HMAS	hyberid m-mediod, DIARETDB0,DIARETDB1
2013	Niladri Sekhar Datta et al. [20], An Effective Approach: Image Quality Enhancement for Microaneurysms Detection of Non-dilated Retinal Fundus Image	Median, CLAHE and canny edge detection, Morphological and logical operators	MAs	not reported
2012	C. JayaKumari and R. Maruthi [41], Detection of Hard Exudates in Color Fundus Images of the Human Retina	CLAHE, Contextual clustering, bottom up approach and statistical features	Hard exudes,	ESNN,
2012	Doaa Youssef and Nahed H. Solouma [101], Accurate detection of blood vessels improves the detection of exudates in color fundus images	Mathematical morphology and hough tranformation	Exudates	Not mentioned
2018	Jaskirat Kaur and Deepti Mittal [46], A generalized method for the segmentation of exudates from pathological retinal fundus images	Two pass filter, calculus, Laplace filter and high pass filter, matching filter	Exudates	STARE, MESSIDOR, DIARETDB1
2018	José Ignacio Orlando et al. [68], An ensemble deep learning based approach for red lesion detection in fundus images	interpolation, gaussian filter, Mathematical morphology	Red lesion,	Deep learning, Random forest classifier,CNN, E OPHTHA, DIARETDB1, MESSIDOR
2014	Xiwei Zhang et al. [104] Exudate detection in color retinal images for mass screening of diabetic retinopathy	Morphological inpainting, template matching, mathematical morphology	Exudates	Exudates, E OPHTHA, DIARETDBI
2017	Qing Liu et al. [57], A location-to-segmentation strategy for automatic exudate segmentation in colour retinal fundus images	Gaussian filter, region detection method CLBP histogram	Exudates	RFC, ROC
2013	Sharib Ali et al. [8],Statistical atlas based exudate segmentation	Blood vessel atlas system, hough transformation	Hard exudates	HEI-MED
2016	Elaheh Imani and Hamid-Reza Pourreza [40],A novel method for retinal exudate segmentation using signal separation algorithm	Mathematical morphology, shearlet transformation, non subsampled contourlet transformation	Exudates	DiaretDB, HEI-MED, E OPHTHA
2017	M. Moazam Fraz et al.[28] Multiscale segmentation of exudates in retinal images using contextual cues and ensemble classification	Mean filter, Mathematical morphology	Exudates	DIARETDB1, HEI-MED, E-OPTHIA
2017	Javeria Amin et al.[10] A method for the detection and classification of diabetic retinopathy using structural predictors of bright lesions	Gabour filter, geometric features	Exudates, HRIS,DERIVE, VDIS, HRF, MESSIDOR, DIARTDB1	acc. 98%
2015	G. Leontidis et al. [53] Evaluation of geometric features as biomarkers of diabetic retinopathy for characterizing the retinal vascular changes during the progression of diabetes	widths, angles, branching coefficient (BC), angle-to-BC ratio and statistical features	Biomarkers for DR	Applied on real data
2017	Francesco Calivá et al. [17], haemodynamics in the retinal vasculature during the progression of diabetic retinopathy.	volumetric blood flow, blood flow velocity, nodal pressure, wall shear stress, and Reynolds number	fluid conditions	Applied on real data
2014	Maged S Habib et al. [35] The association between retinal vascular geometry changes and diabetic retinopathy and their role in prediction of progression an exploratory study	Retinal vascular geometry	retinal vascular geometry (RVG	Real data

the local features. A single network was trained to make multiple binary predictions and the image is classified into diabetic and non-diabetic retinopathy class. The authors report 97% sensitivity of method.

Joel E.W. Koh [48] presented diabetic screening in digital fundus images. The fundus images are preprocessed and then subjected to 2D-CWT. The whole image is divided into tiles then CLAHE is used for image enhancement. The Morlet wavelet is used for detection of angular profile of blood vessels. A scalogram is used for expressing the translation, dilation and coefficients of the pixel values of a wavelet and entropy is computed and classes are balanced. A 15 dimensional feature vector is selected by Particle Swarm Optimization (PSO). These features are fed into the random forest classifier for classification. This method divides the image into Normal, DR and NPDR images.

Cemal KöSe et al. [49] presented a method for the measurement of diabetic retinopathy lesion. High and low level intensity areas are separated by inverse segmentation method proposed by Cemal Köse et al [44]. The vessels and dark lesion have low intensities and blood vessels are removed, then only dark lesion remains. This lesion can be classified as MAs and HMAs. The changes in retinal image is measured. Modified sobel filters are implemented for OD detection and at next step, OD is eliminated from image. The vessel structures consist of short, narrow, large and long vessels and bleeding areas. The blood vessels, MAs and HMAs are eliminated for detection of hard exudates and cotton wool spots. The adaptive region growing algorithm is used for the segmentation of DR lesion.

S. Saranya Rubini and A. Kunthavai [77] proposed an eigenvalue based method for detection of diabetic retinopathy. The second order partial derivatives describe second order variation in images and eigen values are computed. The circular dark regions are extracted from image. Noise is removed by using Fourier transformation. Then MAs candidates are classified as red lesion by using the adaptive threshold. These features are feed into the SVM classifier for MAs and HMAs classification.

6.2. Classification of diabetic retinopathy

The diabetic retinopathy is classified as non-proliferate diabetic retinopathy(NPDR) and proliferate diabetic retinopathy (PDR). Microaneurysm (MA) and neovascularization (NV) are two important signs of DR. The appearance of MAs is classified as NPDR. On the other hand, neovascularization (NV) is the symptom of PDR, which is formation of new blood vessels.

6.2.1. Non-proliferate diabetic retinopathy

Dilip Sisodia et al. [82] introduced the method for early detection of DR in fundus images. The image is segmented between normal and abnormal objects using the green plan. The circular image is chopped into a square image containing the Field of view (FOV) after the enhancement by CLAHE. A morphological closing operator with a circular structure element is used to remove the blood vessels which lies inside the optic disc. A 14 directional feature vector such as exudates area blood vessel area, Bifurcation point count, Shannon entropy etc are used for the hemorrhages and microaneurysms classification. The SVM is implemented for the classification of MAs and HMAs. The color corrlograms features for the detection of blood vessels are used by Ragav Venkatesan et al. [92]. A priori knowledge of DR images is used for feature computation and images are labeled with or without MA or NV. The multi-class, multiple-instance learning (MIL) framework is implemented for classification task using the color correlogram features. The dimensions of feature vector is equal to the number of bins in histogram

6.2.2. Proliferate diabetic retinopathy

The neovascularization is the process where new blood vessels emerges in the retina. This class DR is called the proliferate diabetic retinopathy.

M. Usman Akram et al. [5] Presented the method for grading of PDR. In NVD, some new abnormal blood vessels emerge in optic disc area. The fundus image is a semi circular region with dark background. First of all, foreground and background image parts are separated and back grond image is removed. The mean filter and hough transformation are used for optic disc segmentation then histogram smoothing is performed. The vascular patterns are important in diabetic retinopathy. Blood vessels are enhanced by Gabor wavelet filters. New blood vessels are thin and separated by Gabor filters. A multilayered thresholding algorithm is applied for vascular segmentation and morphological operators are applied for vessel thinning. Area, energy, mean gradient, intensity mean and variation, vessel segments, blood vessel density, blood vessel width and vascular direction variation are the points of feature vector. The abnormal and normal vessels are compared. The local Fisher discriminant analysis (LFDA) is implemented and feature space is generated by eigenvalue decomposition. These features are used to generate models of different vascular patterns and classification. Then multimodal m-Mediods classification is used for diabetic classification.

An ANN technique for detection of PDR is introduced by Harry Pratt et al. [73]. The diabetic retinopathy features are determined at last layer of the network and convolution operators are used as activation functions at the first layer. The soft max and leaky rectified linear unit functions are used for node layers activation and classification task respectively. In this method, stochastic gradient descent with Nestrov momentum is used for network training. After training, network is implemented for the classification. The over fitting problem arises in images without retinopathy. This issue is handled with real time class weights.

A blood vessels extraction method is proposed by K. Verma et al. [93]. These blood vessels have measurable abnormalities in diameter, color and tortuosity for DR measure. Blood vessels profile approximation and segmentation are performed by Gaussian and matching filters respectively in green image plan. A binary image is obtained by adaptive threshold on the noise free image and discontinuities are removed by binarisation. An enhancement is performed to enhance the pixel values. A gamma correction is performed in RGB space for hemorrhages detection. At the next step, histogram smoothing is implemented for each R, G and B image. A histogram density analysis is performed for hemorrhage candidate detection. The blood vessels and hemorrhage are detected by the difference between two smoothed images. The bounding box technique is used for removing false positives and RFC is used for classifying hemorrhages.

P.N. Sharath Kumar et al. [50] presented a method for Diabetic Retinopathy. At preprocessing step, images were resized by implementing bi-cubic interpolation method. Priori information about center of fundus image are used to approximate OD. At the next step, an optic disc segmentation algorithm presented by Lalonde et al. [52] is implemented. A gamma correction is performed to enhancement the exudate. A shade correction was performed on bake ground green image plane to separate retinal features. This shade corrected image contains red and white lesions, which comprised of pixels with negative and positive values respectively. The white lesion is removed by setting positive pixel values to zero. Red lesion and blood vessels are differentiated by top-hat transformation. This vascular image is then subtracted from preprocessed image to obtain an image containing actual red lesions and red lesion like objects. The image foreground is obtained containing red lesion. The blood vessels are extracted by implementing matching filters. Blood vessels and optic disc detection and segmentation is employed. Flame hemorrhages appear as brighter than MAs and elongated in shape compared to dot and blot hemorrhages. The flame hemorrhages are extracted by implementing the CLAHE and binary thresholding.

Garima Gupta et al. [34] introduced a method for identification of neovascularization. In AM-FM multi scale analysis method, green image plane is used. First of all, patches are defined and OD is considered as

Table 5
The methods for diabetic retinopathy screening and classification. The efficiency of method is mentioned in last column of table.

Year	Authors &Title	No. of classes	Methodology, classifier &databases	Evaluation Measure
2017	R. Venkatesan et al. [92], Classification of diabetic retinopathy images using multi-class multiple-instance learning based on color correlogram features,	3	Color autocorrelogram features, MA, Neovascularization, MIML, STARE, DIARETD0, DIARETD1	acc. = 87.61
1996	GG. Gardner et al. [33], Automatic detection of diabetic retinopathy using an artificial neural network: a screening tool	3	DR screening, Blood vessels, Exudates, haemorhages, ANN	acc. = 91.7%, 93.1%,73.1% Sen. = 88.4% Sp. = 83.5%
2013	M. Usman Akram et al. [5], Detection of neovascularization in retinal images using multivariate m-Mediods based classifier	2	Blood vessels, Neovascularization, m mediod classifier, STARE, DERIVE,DIARETDB1, MESSIDOR	acc. = 95% Sen. = 97% Sp. = 92%
2017	Joel E.W. Koh [48],Diagnosis of retinal health in digital fundus images using continuous wavelet transform (CWT) and entropies	3	Glucoma, DR, AMD, ANN, KMC	acc. = 92.48%, Sen. = 89.37%, Sp. = 95.58%
2012	Cemal KöSe et al. [49], Simple Methods for Segmentation and Measurement of Diabetic Retinopathy Lesions in Retinal Fundus Images	2	Hard exudates, cotton wool,MAs	acc. = 96.4%
2017	Dilip Sisodia et al. [82], Diabetic Retinal Fundus Images: Preprocessing and Feature Extraction For Early Detection of Diabetic Retinopathy	5	ANN,Kaggle	acc. = 95.03%
2016	P.N. Sharath Kumar et al. [50], Automated Detection System for Diabetic Retinopathy Using Two Field Fundus Photography	10,	Tested on Reel images	acc. = not mentioned, Sen. = 80%, sp. = 50%
2011	K. Verma et al. [93], Detection and classification of diabetic retinopathy using retinal images	3	Blood vessels, Hemorrhages	acc. = 90%, Sen. = 87.5%, sp = 100%
2015	S. Saranya Rubini and A. Kunthavai [77], Diabetic Retinopathy Detection Based on Eigenvalues of the Hessian Matrix	2	MAs, hemorrhages, red lision, SVM	acc. not mentioned
2016	Gulshan V et al. [88],Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs	2	Detection and grading DR, Deep learning, EyePACS, MESSIDOR,	AUC = 0.991 and 0.990, sen. = 90.3,87,97.5 and 93.4% sp. = 98.1, 98.5,93.9 and 93.9%
2016	Harry Pratt et al.[73],Convolutional Neural Networks for Diabetic Retinopathy	5	MAs, exudate and haemorrhages, SVM, DIARETDB0, DIARETDB1	acc. = 75% Sp. = 30% Sen. = 95%
2017	Jen Hong Tan et al. [84],Segmentation of optic disc, fovea and retinal vasculature using a single convolutional neural network	2	DERIVE	acc. = 92.68%
2017	Yang et al. [100], Lesion Detection and Grading of Diabetic Retinopathy via Two-Stages Deep Convolutional Neural Networks	3	MAs, HMAs, Exudates, ANN, Kaggle	acc. = 96.87%, Sp. = 97.3%, Sen. = 95.5%
2014	Garima Gupta et al. [34],Local characterization of neovascularization and identification of proliferative diabetic retinopathy in retinal fundus images	3	ROC, DRIVE, MESSIDOR, STARE, HRF	acc. not mentioned, Sen. = 92.4%, sp. = 92.6%
2017	Sudeshna Sil Kar and Santi P. Maity [45],Detection of neovascularization in retinal images using mutual information maximization	2	neovascularization, DERIVE, STARE, HRF, MESSIDOR, DIARTDB1	acc. = 97.49%, sen = 97.45%, 96.03%
2017	Georgios Leontidis [54] A new unified framework for the early detection of the progression to diabetic retinopathy from fundus images	2	Real images	acc. = 0.963

central patch, patch size depends upon OD in an image. A 360 dimensional feature vector for each patch is developed. This feature vector consist of gabour, statistical and blood vessel based features. Statistical features are 1^{st}, 2^{nd}, 3^{rd} and 4^{th} statistical moments. The features such as ridge, hessian matrix, eigen values, coherence enhancing diffusion are called vessel based features. The DR classes are defined using the rule based analysis and five classes are defined for the multi scale AM-FM analysis and 9 combinations are used for estimation of normal, NPDR and PDR. Another method for neovascularization detection is introduced by Sudeshna Sil Kar and Santi P. Maity [45]. The blood vessels are segmented by implementing method proposed in [89] in green plan. The optic disc is removed using the morphological opening operator with disk structured element on the enhanced image by CLAHE. Matching filters are used for blood vessels detection and blood vessels on edges of OD are enhanced by curvelet transformation. The fuzzy functions are used for modeling thin and thick blood vessels. Fuzzy classification is used for blood vessels classification. The objects with area less than a certain threshold are then removed to obtain final neovascularization structure. The morphological bridging is used to remove discontinuities in vessel segments.

Georgios Leontidis [54] introduced the method for early detection of progression to DR. In this method, author used the geometric features on real images for detection of no DR to DR progression in fundus eye images in the successive years.

6.3. Diabetic retinopathy detection & classification algorithms

The summary of all the above discussed methods for screening and classification of diabetic retinopathy is presented in the following Table 5. The reported accuracy of these algorithms is described in the last column of table. Last column of the table describes the method efficiency in terms of accuracy, sensitivity and specifity.

The methods mentioned in Table 5 are used for screening and classification of DR. The methods with just two classes are used only for screening of DR or these methods are used for DR affected images for classification of DR into NPDR and PDR. These methods can further enhanced for the classification purposes. The methods with more than two classes are the capability for classification and grading of the DR.The accuracy of these methods can be enhanced by adding new DR features as decision variables.

7. Conclusions

In this review, we studied 77 research algorithms for different levels of CAD system for diabetic retinopathy. This study shows that much importance is given to the feature extraction, development of the detection and classification algorithms. The results of these algorithms are performed on numerous well-standard databases while some algorithms are tested on a small local database. The field of image preprocessing on medical images need much more attention, due to its importance for accurate detection of diabetic features in diabetic screening algorithms.

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