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Abstract. Detecting the position of retinal structures, including the fovea center and macula, in retinal images plays a key role in diagnosing eye diseases such as optic nerve hypoplasia, amblyopia, diabetic retinopathy, and macular edema. However, current detection methods are unreliable for infants or certain ethnic populations. Thus, a methodology is proposed here that may be useful for infants and across ethnicities that automatically localizes the fovea center and segments the macula on digital fundus images. First, dark structures and bright artifacts are removed from the input image using preprocessing operations, and the resulting image is transformed to polar space. Second, the fovea center is identified, and the macula region is segmented using the proposed dynamic identification and classification of edges (DICE) model. The performance of the method was evaluated using 1200 fundus images obtained from the relatively large, diverse, and publicly available Messidor database. In 96.1% of these 1200 cases, the distance between the fovea center identified manually by ophthalmologists and automatically using the proposed method remained within 0 to 8 pixels. The dice similarity index comparing the manually obtained results with those of the model for macula segmentation was 96.12% for these 1200 cases. Thus, the proposed method displayed a high degree of accuracy. The methodology using the DICE model is unique and advantageous over previously reported methods because it simultaneously determines the fovea center and segments the macula region without using any structural information, such as optic disc or blood vessel location, and it may prove useful for all populations, including infants. © 2016 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.3.3.034002](https://doi.org/10.1117/1.JMI.3.3.034002)]

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1 Introduction

The statement that ethnicity appears to be associated with vision problems in children and adults was made by researchers participating in the Collaborative Longitudinal Evaluation of Ethnicity in Refractive Error study.¹ In a 2012 “Vision Problems in the U.S.” report, Prevent Blindness America identified a significant increase over the past decade in vision impairment and blindness among older Americans, including an 89% spike in diabetic eye disease. While this increase may result from a national diabetes epidemic in general, it is also connected to the nationwide increase in ethnic populations who are at higher risk for the disease.

The macula is circular, with a diameter of ~5.5 mm and a pigmented area near the center of the retina. The fovea is a small depression at the center of the retina and visible as a round dark area in retinal images. The locations of these retinal regions are particularly important in the development of automated diagnosis systems because they are diagnosis keys for disease classification. Several computer-aided diagnosis

models have been proposed to enhance diagnosing various eye problems. These models detect developmental changes in the optic disc and macula to diagnose eye diseases, such as optic nerve hypoplasia, amblyopia, diabetic retinopathy, and macular edema. From an anatomical point of view, approximate locations of the fovea center and the macula have already been established for healthy adults, with the fovea center located on average 2.5 optic disc diameters from the optic disc center following the horizontal raphe of the retina.² However, this localization method is unreliable in infants or across all ethnic groups.³ Therefore, a new methodology using an anatomical viewpoint is needed to localize the fovea center for different ethnic populations. However, owing to problems of retinal image quality, such as poor contrast and physicians’ subjective observations, the results obtained by manually identifying the fovea location can be unstable and uncertain. By contrast, computer analysis systems of retinal images offer efficient and stable localization assistance for this retinal region.

Various approaches using structural information have been proposed for identifying the fovea and macula in fundus images

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of adults. Sinthanayothin et al.² took advantage of the increased pigmentation around the fovea to detect its location using a template-matching technique and reported a performance accuracy of 80.4% on 100 images. Gagnon et al.⁴ used a similar approach to detect the fovea center. They first generated a coarse resolution image from the original image. They then selected the darkest pixel in the coarse resolution image following the above-described distance criterion. Finally, the fovea center was found by searching in that vicinity for the darkest pixel on the original fine resolution image. Li et al.⁵ presented a model-based approach in which an active shape model was used to extract the main course of the vasculature based on its optic disc location. This course and the distance criterion of the fovea were used to specify a region of interest (ROI). The fovea center was obtained by applying a thresholding scheme to the ROI. Niemeijer et al.⁶ presented an approach for detecting the location of the optic disc and fovea using an optimization method to fit a point distribution model to the fundus image. After fitting, the points of the model indicated the location of the normal anatomy. This method requires the vascular arch to be at least partially visible but is useful for images centered on the fovea as well as centered on the optic disc. Tobin et al.⁷ presented an automated method for detection of the optic disc and fovea. Their method begins by locating the optic disc and the vascular arch. Based on these two anatomical landmarks, the location of the fovea is inferred. This method requires that retinal images are approximately centered on the fovea and that the vascular arch is visible. A similar method for fovea-centered images has been presented by Fleming et al.⁸ After detection of the vascular arch, the optic disc is located using the Hough transform, and the fovea is detected by template matching, with the template derived from a set of training images. Sekhar et al.⁹ proposed a method for fovea localization based on the spatial relationship with the optic disc and from the spatial distribution of the macula lutea. A method based on the structure of blood vessels and information of the optic disc has been proposed by Li et al.⁵

Although many researchers have examined this problem, the resulting methods to date still have many restrictions. The main restriction lies in having to use location information about the optic disc and blood vessels to locate the fovea. However, this approach does not reliably work in infants or across all ethnic populations because their anatomical structures may differ. To the best of our knowledge, no method currently available for finding the location of the fovea center and macula region does so without using location information about other structures, such as the optic disc and blood vessels, in fundus images.

Therefore, the aim of this study is to address this limitation by developing an algorithm for the automated localization of the fovea center and segmentation of macula in fundus images so the optic disc-to-fovea distance may be reliably determined in infants and across all ethnic populations. We propose a new dynamic identification and classification of edges (DICE) model for this purpose. We also propose a unique image preprocessing step to prepare images for the DICE model.

The proposed DICE model is presented in Sec. 2. The experimental results, performance evaluation, and comparison with other commonly used methods are presented in Sec. 3. A discussion and our conclusions are included in Secs. 4 and 5, respectively.

2 Methodology

Because identifying the fovea center and segmenting the macula region in fundus images is time-consuming and subjective, an automated process is needed for marking the fovea center and extracting the macula region using these images. However, this is a nontrivial task due to signal noise, artifacts, and lack of contrast in the images.

Our proposed method comprises three main phases: image preprocessing, approximate localization of the ROIs, and segmentation.

2.1 Dataset Description

To evaluate the proposed method, the publicly available Messidor database was used.¹⁰ This database contains 1200 color images of the posterior pole of the eye fundus. Using a Topcon TRC NW6 nonmydriatic retinal camera with a 45-deg field of view (FOV), 800 of these images were captured with pupil dilation and 400 without dilation. The images were digitalized to 1440×960 , 2240×1488 , or 2304×1536 pixels, corresponding to retina diameters of ~ 910 , 1380 , and 1455 pixels, respectively, with 8 bits per color plane. All images were provided as TIFFs.

2.2 Image Preprocessing

The first phase of the DICE algorithm is the image preprocessing step, which handles the removal of noise and the detection of artifacts that might have occurred by reflections during image acquisition. The proposed preprocessing phase has two substeps for removing these spurious structures. In addition to the fovea and macula regions, other dark structures are present in the fundus images and may mislead the proposed algorithm. Therefore, all dark structures including blood vessels and dark lesions are removed first. The bright artifacts are then eliminated. A final clean image is gained after this two-step procedure to finalize the fovea and macula detection process.

This two-step procedure provides the main novelty in this portion of the method and is described in detail below. The dark structures, including vessels and dark lesions, are removed by morphological inpainting. Then, the bright structures, such as image artifacts, are eliminated by applying a Gaussian filter to the image that has the dark structures already removed and dividing that result by the maximum mean of the image data for the corresponding band.

2.2.1 Eliminating dark structures

This step for eliminating spurious structures is based on spatial calibrations and was inspired by the work of Zhang et al.¹¹ However, the method used in their study was fixed to the e-ophtha EX database.¹² The proposed method is independent of image datasets and functions for any image data. First, the FOV that includes the area of the retina is extracted from the color input image. Adaptive thresholding is used to find this FOV.¹³ The color image is converted to a grayscale image, which is subsequently converted to a binary image with a threshold value, which is the mean of the grayscale image.

As indicated by Zhang et al.,¹¹ the blood vessels and dark lesions introduce intensity variations. By examining the eye structures, it can be determined that the blood vessels represent the foreground of the image FOV. To eliminate this foreground

from the background, the morphological operations of closing and opening on the image are implemented, which helps to inpaint the image across the corresponding RGB bands of the image. Let I_{org} be the original image, I_{γ} the morphological opening operation, and I_{ϕ} the morphological closing operation. To eliminate the dark structures on the RGB bands of I_{org} , morphological operations with an eight-connectivity structuring element of a hexagon with size $N \times N$ are implemented. The size of the structuring element is fixed as 21 to preserve larger features.

I_{β} , the final image after dark structure removal, is defined as follows:

$$I_{\beta} = \gamma[\phi(I_{\text{org}})]. \quad (1)$$

2.2.2 Eliminating bright structures

Bright structures caused by reflection as well as blinking of the eye are eliminated with this step. An examination of the image data reveals that this information is close to the intensity of the optic disc, which is the brightest region in the image. To eliminate these bright structures, a histogram shrink process is used as follows. A Gaussian filter is applied for each band whose kernel size is defined based on the size of the mean for each band across the image with the dark structures eliminated. This helps remove the high-intensity pixels, as well as the noise, related to the image. In this manner, the most important data across the image will not be lost due to the filtering. In this study, we use a Gaussian kernel due to its computational efficiency and ability to control the degree of smoothing. A Gaussian kernel blurs the structures. However, the kernel size here is 3×3 pixels, so the blurring is minimal. Another advantage of Gaussian filtering is that it preserves the high frequency edges, which means the edge points can still be identified by the proposed DICE model. Let the corresponding image be I_{Gauss} . To reduce the intensity of pixels, the mean (μ) of the corresponding band is multiplied by the Gaussian-filtered image of the image with the dark structures removed, and that result is divided by the maximum mean of the image data for that corresponding band.

$$\text{Intensity of pixels} = \frac{\mu * I_{\text{Gauss}}}{\max(\mu)}. \quad (2)$$

This method helps not only to eliminate bright structures but also to reduce the intensity of optic disc pixels. It also intensifies the fovea region in the image, as shown in Fig. 1.

2.3 Detecting the Region of Interest

This step approximates the location of the fovea by exploiting the visual appearance of this retinal region in fundus images. The fovea is recognizable as a round region darker than its surrounding retinal tissue. First, the clean image is converted to a 16-bit grayscale image. Image enhancement is then achieved using adaptive histogram equalization immediately before adaptive thresholding to separate the darkest regions from the image. Small 9×9 pixel regions are combined using a bell-shaped histogram to eliminate artificially induced boundaries, as seen in Fig. 2(a). After image enhancement and thresholding, spatial filtering is applied to select the fovea region. The mathematical description of the spatial filtering operation to find the desired

Fig. 1 Elimination of dark and bright structures. (a) Original image, (b) output image after the dark structures have been removed, (c) bright artifacts in the original image (reflection), and (d) output image after removal of bright artifacts.

region F is shown below. R_m corresponds to the set of regions obtained after thresholding.

$F = (s_{\min} < s_{R_m} < s_{\max} \text{ and } 0.8 \leq \phi_{R_m} \leq 1)$, where s_{R_m} denotes the size of the m 'th region in set R , which was obtained in the previous step; $s_{\min}$ and $s_{\max}$ are the estimated minimum and maximum region sizes $[\text{round}_{\text{odd}}(D_{\text{FOV}}/14)]$ and $[\text{round}_{\text{odd}}(D_{\text{FOV}}/13)]$, respectively, where D_{FOV} is retina diameter. ϕ_{R_m} is the specified circularity number, which is set as 0.8 to 1. The circularity is defined as $4\pi(\text{Area}_{R_m}/\text{Perimeter}_{R_m})$, with a value of 1 indicating a perfect circle. After spatial filtering, a bounding box with the size of $M \times M$ that covers the entire fovea region is generated, as seen in Fig. 2(b). This bounding box is centered at the particle determined in the previous step, and the size of the box is set to a dynamic value of $[\text{round}_{\text{odd}}(3 \times s_{\max})]$. This procedure allows for evaluating the methodology with different image sizes and datasets.

Fig. 2 Illustration of the approximate localization of the fovea. (a) Image generated after adaptive thresholding. (b) Following spatial filtering, a bounding box is generated for the fovea with the size of $M \times M$ using size and shape constraints.

2.4 Marking the Fovea Center and Segmenting the Macula

2.4.1 Polar image transformation

The shapes of the fovea and macula are approximately circular. This circularity constraint can be implemented by conducting the calculations in polar space. A polar transform is a crucial step in the method because it converts a closed curve in image space to polar space. Thus, the original image is transformed to simple columnwise polar space. A polar transformation can be achieved as follows. Let (x_c, y_c) be the point specified as the pole. Mapping from the polar space (θ, r) to the image space (x, y) can be written as

$$(x = x_c + r \sin \theta) \quad \text{and} \quad (y = y_c + r \cos \theta), \quad (3)$$

where θ and r are the coordinates along the angular and radial directions, respectively.

Using image interpolation techniques, the original image coordinates $I(x, y)$ can be transformed to polar space coordinates $I_p(x, y)$. In practice, suppose $(r_{\min}, r_{\max})$ is the range of the radial coordinates of the ROI, and the size of I_p is assumed to be $(N_\theta \times N_r)$. The intervals along the angular and radial directions would be $\Delta_\theta = (360/N_\theta)$ and $\Delta_r = [(r_{\max} - r_{\min})/(N_r - 1)]$, respectively.

Those pixels with minimum values along the radial direction from each column can be identified as the boundary pixels. However, using information only along the radial directions would detect a false boundary owing to the complexity of retinal images. Hence, information along the angular direction is also taken into consideration. In the polar image, the x -axis represents the angle from $-\pi$ to π , and the y -axis represents the radius from 0 to R . Figure 3(b) shows the polar space image transformed from the region marked in Fig. 3(a).

The programming-based DICE model is applied to the ROI in polar space to find the optimal path from one of the pixels in the first column to one of the pixels in the last column.

2.4.2 Dynamic identification and classification of edges model

Identifying a set of points lying on an edge of a contour is a challenging problem. Active contour and curvature estimation were proposed in the late 1980s.¹⁴ Since then, several methods have been proposed, including dynamic programming,¹⁵ greedy algorithm,¹⁶ region-based energy criterion,¹⁷ and more recently,

Fig. 3 Illustration of the polar transformation. (a) Original image with the ROI outlined and (b) polar transformed image.

global minimization of the snake model.¹⁸ However, all of these methods require a set of points around or on an edge as input.

The DICE model developed here aims to automatically identify the edges of a contour without any intervention from domain experts. The DICE model includes three sequential but intertwined steps: (a) identifying potential edge points of a contour using moving range control charts,¹⁹ (b) extrapolating additional edge points of a contour through noise reduction, and (c) classifying potential points into different edges using a neighborhood gradient search. The pseudocode for the DICE model is described in Table 1.

Step (a1) of the DICE model calculates the second-order derivatives of pixels in an image. A challenge in identifying edges of a contour is that pixels change rather smoothly around an edge. These small differences between adjacent pixels are difficult to detect. The first-order derivatives, which indicate the slopes of the pixel changes, may be calculated and used to detect such subtle differences. In many situations, however, the slopes also vary gradually, and the first-order derivatives become inadequate. Thus, second-order derivatives may be calculated to detect small changes in slopes. For example, a polar image is an $m \times n$ matrix with m rows and n columns. A column may have one or more edge points or may not have any edge point. The edge points form edges that cross multiple columns. For each column, the difference between every pair of pixels in two adjacent rows is calculated, which is the first-order derivative. The difference between every pair of adjacent first-order derivatives is then calculated, and this is the second-order derivative.

Step (a2) detects relatively significant differences among the second-order derivatives. For a polar image, this process involves checking the second-order derivatives in each column and determining which pairs of adjacent second-order derivatives are significantly different. Moving range control charts¹⁹ are used to detect these differences. To construct a moving range control chart, the moving range of two successive second-order derivatives is calculated. Let MR_i represent the moving range of two successive second-order derivatives, where i is the index of moving ranges, and $\overline{MR}$ is the mean of MR_i . The lower control limit of a moving range control chart is 0, and the upper control limit is $[1 + c(d_3/d_2)]\overline{MR}$. Because each moving range is calculated for a sample size of 2, i.e., two successive second-order derivatives, the two factors are $d_2 = 1.128$ and $d_3 = 0.853$. The coefficient c indicates the size of the control limit. For example, if the typical three-sigma control limit is used, $c = 3$. The DICE model uses one-sigma control limits (i.e., $c = 1$), which help to detect smaller differences than do the two-sigma and three-sigma control limits. Anytime a moving range exceeds the upper control limit, a potential edge point is identified through step (a3).

Step (a) may identify multiple potential edge points in a column of a polar image, each of which may belong to either an edge of a contour or noise. It is also possible that no potential edge point is identified in step (a) for a column, indicating that pixels in the column are homogeneous. Different columns often have different numbers of potential edge points. Some edge points in a column are missing, whereas some columns have noise, i.e., points that do not belong to any edge. Both situations increase the difficulty of classifying points into different edges. Step (c) of the DICE model applies a neighborhood gradient search to address this issue. However, before moving to step (c), step (b) of the DICE model is used to remove noise and

Table 1 Pseudocode for the DICE model.**Step (a) Identify potential edge points**

- (a1) Calculate the second-order derivatives of the pixels in an image.
- (a2) Apply moving range control charts to the second-order derivatives, and identify those that exceed the upper control limit.
- (a3) Identify potential edge points (pixels) that correspond to the second-order derivatives exceeding the upper control limit.

Step (b) Extrapolate additional edge points through noise reduction

- (b1) Remove potential edge points identified in step (a) from the image.
- (b2) Repeat steps (a) and (b1) until all potential edge points are identified.

Step (c) Classify potential edge points into different edges through a neighborhood gradient search.

- (c1) Cluster adjacent potential edge points in a column into one group, and represent the group with one potential edge point.
- (c2) Determine the starting point of an edge, which is designated as the current point on the edge.
- (c3) Determine a set of Euclidean distances between the current edge point and its adjacent edge point.
- (c4) Determine a set of slopes (gradients) of the straight line that connects the current edge point and its adjacent edge point.
- (c5) Search the neighborhood of the current edge point from the closest to the farthest and from the smallest gradient to the largest gradient.
- (c6) Stop the neighborhood search if a potential edge point is identified or if no potential edge point is identified after searching the entire neighborhood.
- (c6.1) If a potential edge point is identified, mark it as the current point on the edge and go to step (c5).
- (c6.2) If no potential edge point in the neighborhood is identified, an edge is identified and the current edge point is the end point of the edge. If all edges are formed, stop; otherwise go to step (c2).

extrapolate additional edge points. A column may have additional edge points that are not identified due to the interference of points identified in step (a). In step (b1), all points identified in step (a) are removed from the image. These points may be edge points or noise. Step (b2) repeats steps (a) and (b1) to identify and remove additional points, which include edge points and noise. Step (b2) continues until no more points can be identified in the column, indicating that the remaining pixels are homogeneous.

At the conclusion of step (b), all potential edge points in the image are identified. Some of those are noise, and others belong to edges. Step (c) uses a neighborhood gradient search algorithm to classify points and form edges of a contour. Step (c1) applies a simple clustering method to group adjacent points in a column. Each group (cluster) is represented using one point. Steps (c2) to (c6) classify edge points and form all edges. In a polar image, step (c2) chooses a column (usually column 1) as the base column. Each point in the base column is the starting point of an edge. The top (first) point in the base column is the starting point of the top (first) edge. Step (c3) determines the minimum and maximum distances between two adjacent points on an edge. The minimum distance is 1, and the maximum distance is usually the distance between the two closest edge points in the base column. Step (c4) determines the minimum and maximum slopes of a straight line that connect two adjacent points on an edge. The minimum slope is 0, and the maximum slope is also the distance between the two closest edge points in the base column. Steps (c5) and (c6) iterate and form the first edge. Afterward, steps (c2) to (c6) are repeated until all edges are identified as seen in Fig. 4(a).

2.4.3 Curve fitting

Curve fitting is a critical step that fits edge pixels obtained in the previous step with appropriate curves. A Fourier curve descriptor is adapted to describe the curves analytically because this descriptor provides a more compact way to represent the curve than other curve fitting methods.²⁰

The initial curvature $[x(n), y(n)]$ can be expressed using a Fourier curve descriptor as follows:

$$x(n) = a_0 + \sum_{k=1}^H a_k \cos(wn) + b_n \sin(wn), \quad (4)$$

$$y(n) = c_0 + \sum_{k=1}^H c_k \cos(wn) + d_n \sin(wn), \quad (5)$$

Fig. 4 Illustration of DICE. (a) Polar image after application of the DICE model and (b) image space after DICE.

Fig. 5 Illustration of curve fitting. (a, c, e, g, and i) Polar images after curve fitting. (b, d, f, h, and j) Original image space after curve fitting.

where H is the number of harmonics, and $(a_0, \dots, a_M, b_1, \dots, b_M)$ and $(c_0, \dots, c_M, d_1, \dots, d_M)$ are two sets of Fourier descriptors for $x(n)$ and $y(n)$, respectively; w is the fundamental frequency of the signal.

To fit the set of pixels, two sets of Fourier descriptors can be estimated using the objective function defined as

$$\min \sum_{i=1}^N \|x_i - s(n_i)\|^2 \quad \text{and} \quad \sum_{i=1}^N \|y_i - s(n_i)\|^2, \quad (6)$$

where n_i , for $\forall i \in Z_N$, is computed as the cumulative sum of the curve lengths along the curve, starting from (x_1, y_1) and ending at (x_i, y_i) , divided by the total cord length of the whole boundary. The solution of each of these least squares problems can be derived analytically by solving a set of linear equations in terms of the associated Fourier descriptors. If the distance between starting and ending points is less than 5 pixels, the contour is accepted as a closed contour. However, for some cases, the gap is greater than 5 pixels. Here, an additional step of accepting the starting and ending points as the same during the curve fitting process is necessary to close this gap. Figures 5(a), 5(c), 5(e), 5(g), and 5(i) illustrate this curve fitting procedure, providing five examples of the final results for the fovea center and macula location using the DICE model on polar space, while Fig. 5(b), 5(d), 5(f), 5(h), and 5(j) provide examples of the final segmentation result of the fovea center and macula on original image space.

3 Results

3.1 Fovea Center Localization Accuracy

The locations of the fovea centers and macula borders for the 1200 images were manually identified by two ophthalmologists expertly trained in this procedure. The minimum and maximum standard deviations (in mm) for the reference points of the fovea centers manually determined by these two experts were 1.51 to 7.52 for the x -axis and 2.42 to 9.37 for the y -axis. The intraclass correlation coefficient (ICC) value, which is a measure of the reliability of two measurements, of the performance by the two experts was also determined. An ICC value $\geq 90\%$ indicates excellent agreement among subjects, 89% to 80% represents good agreement, and 79% to 70% indicates poor agreement.²¹ We found an ICC value of 71% (95% confidence interval, 0.32 to 0.91), indicating poor agreement for the manual measurements obtained by two experts and a need for an automated model to identify the fovea center.

The accuracy of locating the fovea center was measured by comparing the center location derived by the DICE model with a ground truth set of fovea centers that was built by averaging the locations established by two ophthalmologists expertly trained in this procedure. This measurement is based on determining the number of cases within a specified range. Because the Messidor dataset has three different image sizes, the distances were normalized as $d = \sqrt{D_{\text{FOV}}^2}$, where $i = 1, 2, \dots, n$ (for n different retina sizes). This is measured by number_j / T , where number_j is the number of cases where the points are within the distance range j , and T is the total number of cases in the test set. The results are presented in Table 2 and indicate high accuracy.

We also compared the fovea locations determined manually and with the model by using the mean distance and the

Table 2 Performance accuracy overview of the proposed method as determined using the percentage of the 1200 images that belong to the specified distances.

Image size	Distance scales		
	$0 < x \leq d/6$	$0 < x \leq d/4$	$0 < x \leq d/2$
D_{FOV}^1	77.7%	96.1%	100%
D_{FOV}^2	68.4%	93.0%	99.2%
D_{FOV}^3	65.3%	88.4%	98.7%

Hausdorff distance, d_{HDF} , which is obtained by finding for each point in A the minimum distance to all points in B . Then, d_{HDF} is the maximum of this set of minimum distances.

$$d_{HDF}(A, B) = \max_{a \in A} \{ \min_{b \in B} [d(a, b)] \}, \quad (7)$$

where a and b are points of sets A and B , respectively, and $d(a, b)$ is the Euclidean distance between points a and b .

The Hausdorff distance and mean distance between the locations of the fovea centers identified by the proposed method and by the ophthalmologists was 5.27 and 2.35, respectively.

The robustness of the proposed method was evaluated by comparing it with previously reported algorithms. For this purpose, the sensitivity, specificity, and accuracy of the proposed method were determined as follows:

$$\text{Sensitivity} = \frac{Tp}{Tp + Fn}, \quad \text{Specificity} = \frac{Tn}{Tn + Fp}, \quad (8)$$

$$\text{Accuracy} = \frac{Tp + Tn}{Tp + Fp + Fp + Tn}. \quad (9)$$

The proposed method achieved an average performance accuracy of 97.4%. The performance of our method compared with those of four other reported methods for fovea localization is summarized in Table 3. Benchmark algorithms are not publicly available. Therefore, the proposed algorithm could not be tested against them. However, an overview of the values presented in Table 3 shows that our proposed method achieved better performance than the other fovea center detection techniques, although comparisons could not be conducted under identical conditions, and thus no solid conclusions can be drawn.

Table 3 Comparison of the performance of different methodologies for localizing the fovea center. The methods were tested using different image datasets.

Method	Sensitivity	Specificity	Accuracy
Our method	81.6%	98.8%	97.4%
Sinthanayothin	80.4%	99.1%	—
Fleming et al.	—	—	96.5%
Tobin et al.	—	—	92.5%
Niemeijer	—	—	94.4%

3.2 Macula Contour Detection Accuracy

The performance of the proposed macula segmentation method using the DICE model was also measured by quantifying the region overlap between the manual and automated segmentations using the dice similarity index (DSI), where

$$\text{DSI} = 2 \frac{|A_{\text{ref}} \cap A|}{|A_{\text{ref}}| + |A|}, \quad (10)$$

A_{ref} and A indicate the manual and automatic segmented region, respectively.

In addition to the DSI, we used an area error measure (AEM), which is defined as the percentage of area error for the evaluated segmented area as follows:

$$\text{AEM} = |A_{\text{ref}} - A| / |A_{\text{ref}}|. \quad (11)$$

For perfect segmentation, AEM would equal 0. We determined that for the 1200 images in the Messidor database, the proposed macula segmentation DICE model provided an average DSI value of 96.12% and an average AEM of 3.03%, indicating that the DICE model segmented the macula regions with high accuracy.

4 Discussion

Our proposed methodology, including the DICE model, for locating the fovea center and segmenting the macula region in retinal digital images is presented in this paper. Compared with those determined manually, our results demonstrated that the proposed model accurately localizes the fovea center and segments the macula region. By contrast, the intraobserver reliability as determined using the ICC value comparing the results of two ophthalmologists to localize the fovea center in 1200 images obtained from the Messidor dataset showed only poor agreement (ICC value of 0.71), indicating subjectivity and some disagreement between the two experts.

The proposed method begins with a two-level preprocessing step to remove spurious structures. First, the method removes all dark structures, including vessels and dark lesions, using morphological inpainting. The bright artifacts are then eliminated by applying a Gaussian filter to the resulting image (without the dark structures) and dividing that result by the maximum mean of the image data for the corresponding band.

After this preprocessing step, the cleaned image is transformed to polar space. The DICE model is applied to the polar space image to automatically identify the contour edges, without any intervention from domain experts. The DICE model includes three sequential but intertwined steps: (a) identifying potential edge points of a contour using moving range control charts, (b) extrapolating additional edge points of a contour through noise reduction, and (c) classifying points into different edges using a neighborhood gradient search.

The proposed methodology was tested on 1200 fundus images obtained from the Messidor database. This database was selected because not only is it publically accessible, but also, it is composed of a large number of images, although the ethnic diversity and ages of the participants from whom the images were obtained are unknown. To evaluate the accuracy of the proposed method, the distance between the fovea centers as identified automatically by the model and manually by two ophthalmologists was measured for each fundus image. We found that 96.1%, 93%, and 88.3% of those images with

retina diameters of 910, 1380, and 1455 pixels, respectively, fell within the distance scale of $0 < x \leq d/4$, indicating high accuracy for the DICE model. As evaluated using the DSI for the region overlap between the manual and automated segmentations and AEM values, the DICE model macula region segmentation was highly accurate in these 1200 cases.

The uniqueness and advantages of using the proposed methodology with the DICE model are that the fovea center can be localized and the macula region segmented simultaneously, with no additional steps or postprocessing operations required. We are currently obtaining images from participants in which the ethnicities and ages are known to further test our model.

5 Conclusion

A new methodology is presented and evaluated for the automated localization of the fovea center and segmentation of the macula region based on dynamic programming. The proposed method with the DICE model overcomes current limitations by performing these two operations simultaneously and without the need for first extracting information about other nearby anatomical structures, such as the optic disc and blood vessels, enabling high-throughput image analysis. The proposed method was found to accurately localize the fovea center, and the DICE segmentation algorithm was shown to be robust and accurate, displaying a strong overlap (96.12%) with the results of manual segmentation performed by ophthalmologists for a relatively large number of cases (1200).

In the future, we plan to further test the model using an ethnically and age-diverse population, and then extend the DICE model by adding an additional feature that will localize multiple regions simultaneously. The current algorithm is capable of identifying ROIs located within a single selected window. However, identifying multiple structures, such as exudates or lesions, in a given image will require the use of the multiple windows.

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