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Additional Information

Evaluation of Fractal Dimension effectiveness for damage detection in retinal background

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Abstract

This work investigates the characterization of bright lesions in retinal fundus images using texture analysis techniques. Exudates and drusen are evidences of retinal damage in diabetic retinopathy (DR) and age-related macular degeneration (AMD) respectively. An automatic detection of pathological tissues could make possible an early detection of these diseases. In this work, fractal analysis is explored in order to discriminate between pathological and healthy retinal texture. After a deep preprocessing step, in which a spatial and colour normalization are performed, the fractal dimension is extracted locally by computing the Hurst exponent (H) along different directions. The grayscale image is described by the increments of the fractional Brownian motion model and the H parameter is computed by linear regression in the frequency domain. The ability of fractal dimension to detect pathological tissues is demonstrated using a home-made system, based on fractal analysis and Support Vector Machine, able to achieve around a 70% and 83% of accuracy in E-OPHTHA and DIARETDB1 public databases respectively. In a second experiment, the fractal descriptor is

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combined with texture information, extracted by the Local Binary Patterns, improving the bright lesion detection. Accuracy, sensitivity and specificity values higher than 89%, 80% and 90% respectively suggest that the method presented in this paper is a robust algorithm for describing retina texture and can be useful in the automatic detection of DR and AMD.

Keywords: Retinal fundus image, Fractal analysis, Diabetic retinopathy, Age-related macular degeneration, Local Binary Patterns.

1. Introduction

Diabetic retinopathy (DR) and age-related macular degeneration (AMD) are two of the most common pathologies in the current society that provoke retinal damage and can be directly related to blindness and vision impairment. Although in recent years the number of cases has been significantly reduced, it is estimated that the 80% of cases of visual impairment is preventable or treatable. The early diagnosis of these pathologies allows to reduce costs generated when they are in advanced states and may become into chronic. Due to the large of population at risk, a potential automatic screening would highly benefit to clinicians reducing the workload of trained experts in the analysis of anomalous patterns of each disease.

Retinal fundus images are the most non-invasive acquisition modality in which different lesions are manifested; these lesions are the basis to identify the pathologies and their stage of proliferation. Figure 1 shows the distinctive lesions evidenced in pathological fundus images. This work is focused on the automatic detection of the bright lesions that characterize DR and AMD, exudates and drusen respectively.

In the literature, the most common procedure is to segment these lesions using different methods [1–3] but in this work the characterization of the healthy and the pathological retina is studied applying texture analysis techniques, in particular, fractal descriptors, avoiding the segmentation step.

Fractal objects are characterized by a high degree of complexity but also by

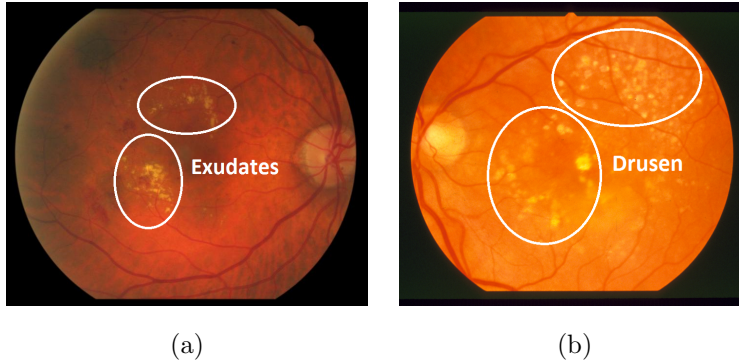


Figure 1: (a) Lesions of Diabetic Retinopathy and (b) signs of age-related macular degeneration.

self-similarity represented by a repetition of patterns or statistical properties over different scales. Based on this property of self-similarity it is possible to describe an image by means of a fractal dimension (FD) parameter. The characterization of gray level images is described using the potential usefulness of the fractional Brownian motion (fBm) model [4].

Fractals have been recognized as an effective descriptor of complex structures in biology and medicine [5]. In the literature, fractal analysis have been proposed for characterizing biomedical signals and images [6–10]. Regarding to retinal fundus images, fractals have only been applied to the retinal blood vessels characterization. In [11], a fractal analysis approach based on the box-counting method was used to quantify vascular patterns in normal and abnormal cases showing neovascularization (caused by proliferative diabetic retinopathy in advanced stages of the disease). The algorithm was validated in ten images. In [12], a blood vessel segmentation method based on fractal analysis was proposed and a comparison of the fractal dimension (extracted from the blood vessels) between hypertension and non-hypertension groups was carried out without significant evidences of discrimination ability. The authors of [13] proposed a semi-automatic method to compute the fractal dimension of fundus images. They established a comparison between their method and the box-counting method. Finally, the authors applied the proposed algorithm with the

aim of testing the impact in the variation of blood vessels due to the angle between the acquisition camera and the optical axis. To the best of the authors' knowledge, fractal analysis has not been used previously in the characterization of retinal lesions and it could be a key factor because exudates and drusen are the first recognizable signs of the diseases under study.

The main objective of this work is to demonstrate that the fBm model suits well for the characterization of pathological texture in retinal images and as novelty we demonstrate how it is possible to detect bright lesions by means of the fractal dimension. In addition, fractal dimension will be combined with another texture descriptor in order to enhance the yield of a computer-aided diagnosis system developed by the authors.

The rest of the paper is organized as follows: in Section 2, the fractional Brownian motion model able to describe the fractal dimension in grayscale images is explained. In addition, an explanation about how the fractal descriptor is extracted from the retinal texture is detailed. Section 3 shows, on the one hand, a statistical analysis of the fractal dimension according to the healthy and pathological retinal texture. On the other hand, the results of the automatic detection of bright lesions on two public fundus databases, using the home-made system, are presented. Finally, section 4 provides conclusions and some areas for future work.

2. Material and methods

2.1. Material

The validation of the proposed method was carried out on two public public databases. E-OPHTHA database [14] is divided in two subsets depending on the lesion type: exudates and microaneurysms. These lesions are manually annotated by experts and the ground-truth is provided. The exudates subset (E-OPHTHA_EX) used in this work is composed by forty seven retinal images of different spatial resolutions (see Table 1) acquired with the same field of view

angle, i.e. 40. Due to this resolution variety, a stage of spatial normalization is essential.

Image resolution (pix.)	1440 × 960	1504 × 1000	2048 × 1360	2544 × 1696
Number of images	13	2	9	23

Table 1: Distribution of the E-OPHTHA_EX images with exudates according to their resolution.

DIARETDB1 public database [15] consists of 89 colour fundus images, of which 47 contain exudates. Images were captured using the same 50 degree field-
of-view digital fundus camera and all images present a resolution of 1500 × 1152
pixels. The 89 images of this database were marked by four experts. These
annotations are provided as a probability map. The procedure proposed by
the authors of DIARETDB1 to generate the ground truth images from the
probability map, is follow in this work. Each pixel marked as exudate by 3 of
the 4 experts is considered as exudate pixel in the binary mask.

Note that a list with the original images used as well as the resulting source code implemented of this work is publicly available in https://github.com/adcogra/Fractal_Analysis_JCAM to reproduce and verify the obtained results facilitating future fair comparisons.

2.2. Fractals

The minimum number of independent variables to describe an object is defined by the Euclidean dimension (E). A point is a 0-dimensional object; a line is 1-dimensional while a plane is 2-dimensional. However, this approach does not extract information about the “roughness” of the object, in other words,
Euclidean dimension of a line will always remain constant (E=1) whatever it is
straight or crooked.

Two centuries ago different mathematicians such as Koch, Sierpinski and Hausdorff established a geometric definition of fractals demonstrating that shapes and objects have fractional dimension. Fractals objects are built based on a

95 pattern repeated at different scales and can therefore be described as a part of themselves. This property illustrated in Figure 2 is known as “self-similarity”.

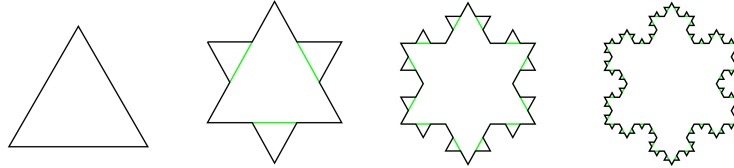


Figure 2: The first four iterations of the Koch snowflake.

To characterize such objects, a non-integer dimension is used: the fractal dimension (FD). However, this term does not reflect a single descriptor, as several definitions coexist. The simplest way to apprehend the FD is using the
 100 homothety a.k.a. similarity dimension (D_H):

$$D_H = \frac{\ln(N)}{\ln(r^{-1})} \quad (1)$$

where N is the number of elementary patterns included in the object and r is their reduction factor. This computation is valid only for a geometrical set with internal homotheties, and can be extended to any set using the box-counting a.k.a. Minkowski-Bouligand dimension (D_B):

$$D_B = \lim_{\epsilon \rightarrow 0} \frac{\log(N_\epsilon)}{\log(\epsilon^{-1})} \quad (2)$$

105 where N_ϵ is the minimal number of subsets with a size ϵ required to cover the object. This FD reflects the complexity of the object and its construction. In particular, a signal with higher FD is more complex or rough than a signal with lower FD.

Another popular way to define the fractal dimension concept is the so-called
 110 *capacity* (D_C). This definition makes reference to the characterization of fractal patterns or sets by quantifying their complexity as a ratio of the change in detail to the change in scale [16]. The relation between the length of an object and its

roughness is given by:

$$L_\delta = K \cdot \delta^{(1-D_C)} \quad (3)$$

where L_δ is the length of the object, δ the measuring scale, K a constant and
 115 D_C the object fractal dimension (FD).

2.3. Fractional Brownian motion model

In the work presented by Mandelbrot and Van Ness [17], fractional Brownian motion is defined by its stochastic representation based on the long-range dependence and self-similar behaviours. This representation is governed by a
 120 single parameter called the Hurst exponent (H) [18] which is linked to the fractal dimension by $H = E + 1 - FD$, where E is the Euclidean dimension. Due to the random nature of fundus lesions in terms of location, shape and size (see Section 1), the fractal model based on fBm is used to describe these random phenomena [19]. In the following lines, the fractional Brownian motion model
 125 is formulated to be applied in grayscale images.

The spectral representation of fBm, $B_H(t)$, is given by [20]:

$$B_H(t) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} \frac{1}{(i\omega)^{H+1/2}} (e^{it\omega} - 1) dB(\omega) \quad (4)$$

where $B_H(t)$ is a Gaussian, continuous, centered and non-stationary second-order process, ω designates the set of all values of a random function (where ω belongs to a sample space Ω), $dB(\omega)$ is the white noise integration corresponding
 130 to the Gaussian process and t refers time and it ranges in the interval $(-\infty, +\infty)$.

Applying the initial condition $B_H(0) = 0$, its covariance function (ρ) is given by:

$$\rho(s, t) = E[B_H(s)B_H(t)] = \frac{a^2 V_H}{2} (|t|^{2H} + |s|^{2H} - (t-s)^{2H}) \quad (5)$$

for $0 < s \leq t$ where $E[\cdot]$ is the mathematical expectation, a is a constant and

V_H a function of H defined as [21]:

$$V_H = \Gamma(1 - 2H) \frac{\cos(\pi H)}{\pi H} \quad (6)$$

135 where Γ is the gamma function.

The self-similarity property of the fBm can be expressed as:

$$B_H(km) \equiv k^H B_H(m); \quad \forall k \text{ and } m > 0 \quad (7)$$

As fBm is a non-stationary process, it is more convenient to study its incremental process called fractional Gaussian noise (fGn), defined as the derivative of fBm at a resolution m :

$$G_m(k) = B_H(k) - B_H(k - m) \quad (8)$$

140 The corresponding autocovariance function $\gamma(\cdot)$ is given by:

$$\gamma(\tau) = E[G_m(k)G_m(k + \tau)] = \frac{\sigma_m^2}{2|m|^{2H}} (|\tau + m|^{2H} + 2|\tau|^{2H} + |\tau - m|^{2H}) \quad (9)$$

where $\sigma_m^2 = a^2 V_H |m|^{2H}$ is the variance of G_m .

For fGn class signals, the probability distribution of a segment of the signal is independent of the segment size and its temporal position in the signal [22]. This property plays an important role in this work due to a local computation
145 of the fractal dimension is performed as detailed in the following subsection.

The Power Spectra Density (PSD) of the fGn can be calculated from (9), and when m tends to infinity, a normalized spectrum of the fBm increments can be defined as [23]:

$$PSD_{G_m}(f) \propto |f|^{1-2H} \quad (10)$$

In this work, the fGn-based Spectral Estimator (GSE) is used in order to
150 compute the parameter H from the PSD of the fBm increments. Equation (10) shows that the PSD follows a law in $|f|^{1-2H}$. In a log-log scale, the PSD

function of the fBm increments is a line of slope $1 - 2H$. The H parameter can be estimated by linear regression. Regarding to the GSE implementation, the average spectrum of the fGn is estimated for each patch by the square of the modulus of the Fourier transform computed by the Fast Fourier Transform (FFT) algorithm.

2.4. Application to retinal images

As we introduced in section 1, the main novelty of this work is to apply fractal analysis in order to model the healthy retinal texture and the bright retinal lesions produced by DR and AMD. With the aim of reliably obtaining the fractal description of both tissues reliably, an image preprocessing step is essential before the local fBm computation and the Hurst exponent estimation.

2.4.1. Retinal fundus image preprocessing

Public fundus images belonging to a specific database can present different resolutions due to the configuration of the retinal camera. This fact can hinder the comparison of the lesions and anatomical structures. E-OPHTHA_EX database is composed by images with four different resolutions as we mentioned in section 2.1. For this reason, the first preprocessing step is a spatial normalization. The images are resized to the dimensions of the smallest image (1440×960) after a local maximum filter applied in order to preserve the small bright lesions.

Another uncalibrated factor in fundus images is the background colour due to the retina variability. Retinal fundus colour depends on age, ethnicity, differences in retina pigmentation and other anatomical human factors. In order to avoid problems in the fractal description due to these factors, a colour normalization of the images is performed (Figure 3(b)). In particular, a colour normalization based on geometric transformations applied to the chromatic histogram of the image [24] is performed.

Blood vessels cover a high percentage of the fundus image and are considered as noise or artefacts that hamper the classification of pathologies based on

background textures. For this reason it is necessary to remove the contribution of this structure to the fractal analysis. Retinal vessels are detected using the algorithm proposed by Morales et al. [25]. This method is based on mathematical morphology and curvature evaluation for the detection of retinal vascular tree
 185 (Figure 3(d)). A possible procedure to avoid blood vessels is to consider these structures as missing pixels and trying to restore them using the background. This technique is known as image inpainting and different kind of methods exist in the literature. In this paper, the diffusion-based inpainting method by means of the simplest isotropic diffusion model is used with the implementation
 190 proposed in [26]. Figure 3(e) shows a retinal inpainted image, the input to the fractal analysis stage.

In fundus images, the green component of the RGB-representation shows the maximum contrast between lesions and background, the red channel is often saturated and has low contrast, and the blue channel is very noisy and suffers
 195 poor dynamic range. For these reasons, the green component is commonly used to segment the lesions [1, 27, 28] and it is used in this work (Figure 3(f)).

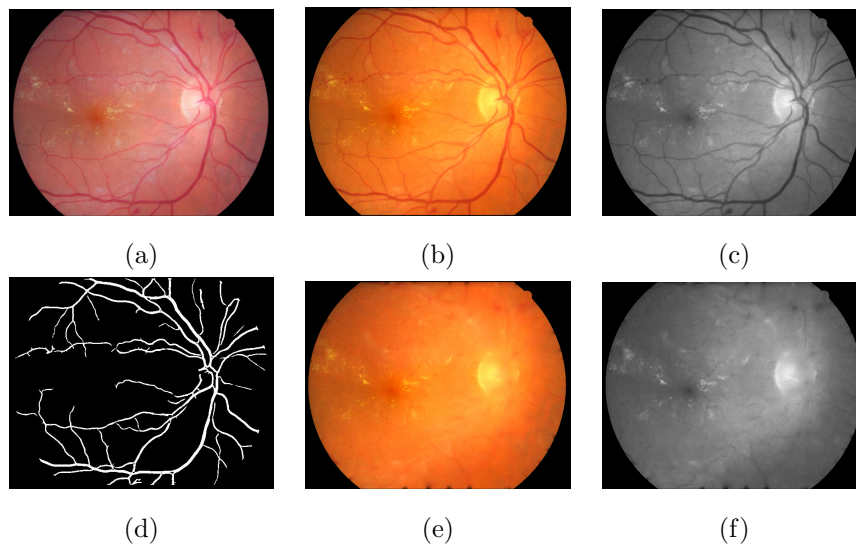


Figure 3: Retinal fundus image preprocessing. (a) Original image, (b) colour-normalized image, (c) green component of the normalized image, (d) vessel mask extracted using [25], (e) inpainted image without blood vessels and (f) input image to the fractal analysis stage.

2.4.2. Local computation of the fractal dimension

The lesions induced by macular degeneration or diabetic retinopathy present different sizes according to the stage of the disease. In most cases, lesions
 200 represent less than one percent of the total number of pixels that compose the retinal image. For this reason, in the feature extraction stage, fractal dimension is performed locally, in other words, the image is divided in patches using a sliding window (Figure 4(a)) and the texture descriptor is computed for each patch. The window used is a square of canonical size (N_w) with overlap of
 205 $(\Delta x, \Delta y)$. Note that patches containing optic disk pixels [29] are not considered in the process. Patches should also be completely contained within the field of view of the retinal image (Figure 4(b)).

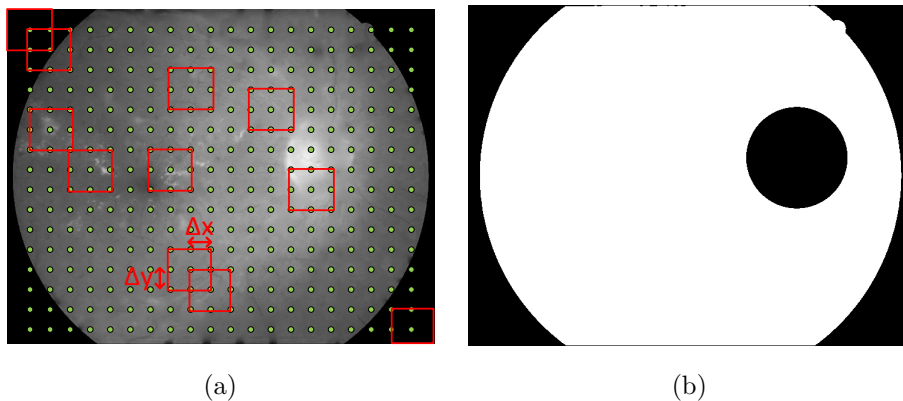


Figure 4: (a) Image grid indicating the positions of the sliding windows ($N_w = 64$) using $(\Delta x, \Delta y) = (32, 32)$ and (b) binary mask used in order to exclude the patches containing optic disk pixels or the patches located out of the field of view.

In this work fractal dimension of 2D image patches is extracted. With the aim of reducing the loss of information, a multi-dimensional extension of the
 210 fBm is used by means of the multiparameter Wiener process, or Brownian sheet presented in [30]. An anisotropic extension of the fGn allows the extraction of different Hurst exponents, one parameter in each of the L directions, gathered in the vector parameter $H = (H_1, H_2, \dots, H_L)$. In particular, the Hurst parameter in $L = 2$ directions (0 and 90 degrees) is computed from the average PSD (in

215 each direction) and stacked as a vector $H = [H^{0^\circ}, H^{90^\circ}]$.

Let X be an image patch of dimensions $M \times N$, for each row m we obtain the 1D signal $d[n] = X[m, n + 1] - X[m, n]$ and compute the discrete Fourier transform given by:

$$D[k] = \sum_{n=0}^{N-1} d[n] e^{-j \frac{2\pi k n}{N}} \quad (11)$$

220 These 1D spectra compound the M rows of a 2D matrix $D'[k, l]$. Finally, the PSD is computed by a pointwise averaging in each column as:

$$PSD[k] = \frac{1}{M} \sum_{l=0}^{M-1} D'[k, l] \quad (12)$$

Figure 5(a) shows a patch extracted from the retina background of the image displayed in Figure 4; the white arrow defines a specific patch row in which the intensity is studied. We can notice the non-stationarity of this intensity signal (Figure 5(b)) along the patch width. As recalled above, the increments of the intensity are easier to study due to their stationarity (Figure 5(c)). In Figure 5d it is possible to observe the \overline{PSD}^{0° extracted from the patch under study by means of equation (12).

230 Finally, in order to extract the H parameter of the patch, a linear regression in log-log scale for the PSD curve (Figure 5(d)) is performed and the Hurst exponent is estimated using equation (10). Linear regression is performed in the frequency interval $f \in [f_{ini}, f_{end}]$ in which the PSD curve, plotted in a log-log scale, is linear. This linear behaviour shows the fractal nature of the tissue under study. The intergroup roughness of image patches is quite different, in other words, the linear segment in the log-PSD curve for patches labelled as healthy and pathological is located in a different frequency interval. However, 235 this range of frequencies is quite similar between patch images of the same class (i.e. low intragroup deviation). These facts allow the automatic computation of the optimal frequency range for each category. Two representative subsets of image patches containing N_h healthy patches and N_p pathological patches 240 respectively are extracted from the training set. For each patch of both subsets,

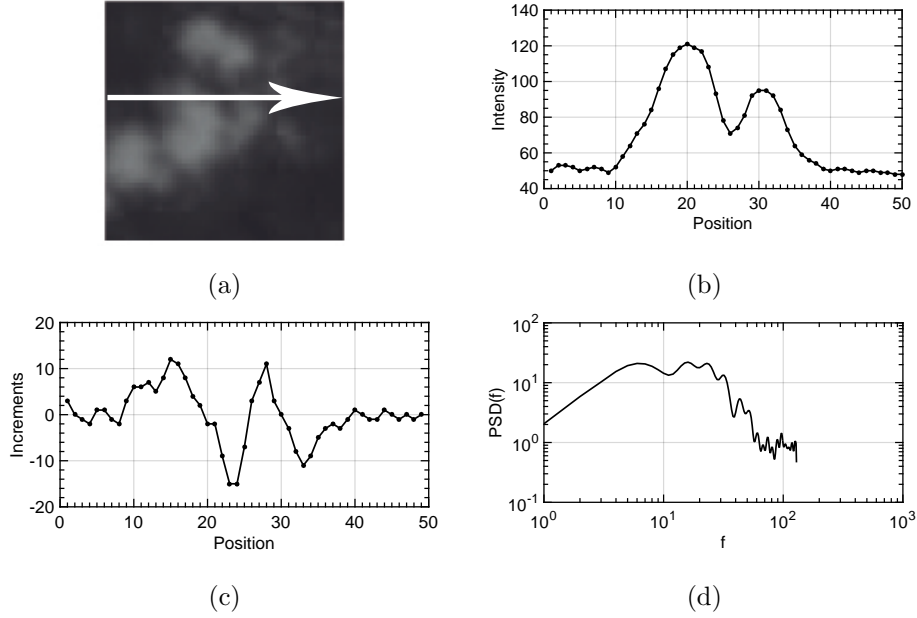


Figure 5: (a) A pathological ROI extracted from a retinal image, (b) the intensity of each pixel extracted from the ROI according to the arrow, (c) the increments of the line presented and (d) the periodogram of the increments of all lines of the ROI.

the optimal frequency range is manually selected $f_i = [f_{ini_i}, f_{end_i}]$ where i ranges between 1 and N_p or N_h depending on the subset. Thanks to the low intragroup deviation, two frequency ranges of reference $f'_h = [f_{h_{ini}}, f_{h_{end}}]$ and $f'_p = [f_{p_{ini}}, f_{p_{end}}]$ can be computed from each subset of the selected frequencies
245 $\Omega_h = \{f_1, f_2, \dots, f_{N_h}\}$ and $\Omega_p = \{f_1, f_2, \dots, f_{N_p}\}$ as the minimum f_{ini_i} and maximum f_{end_i} respectively. These frequency ranges of reference are used in the automatic computation of the fractal dimension. For each image patch, the curvature inside both frequency ranges is calculated. The frequency range in which the log-PSD curvature is minimum is the frequency range selected to
250 carry out the linear regression.

Algorithm 1 describes the complete process to locally estimate the fractal dimension in $L = 2$ directions from grayscale fundus images.

Algorithm 1: Local fractal analysis computation

Data: RGB fundus image $\mathbf{f} = (f_r, f_g, f_b)$ is the pre-processed retinal image as it was detailed in Section 2.4.1, optic disc mask \mathbf{M}_{od} , external mask \mathbf{M}_{ext} , size of the sliding window \mathbf{N}_w , vectors \mathbf{r} and \mathbf{c} containing the y and x coordinates of the centres of the patches in which the local analysis is performed.

Result: Hurst exponent matrix \mathbf{H} containing the fractal dimension in two directions per patch.

Initialization:

$ind \leftarrow 1$;

Green channel selection:

$f_{in} \leftarrow f_g$;

Mask computing:

$M \leftarrow and(M_{od}, M_{ext})$

Local fractal analysis:

```
for  $i \leftarrow 1$  to  $length(\mathbf{r})$  do
    for  $j \leftarrow 1$  to  $length(\mathbf{c})$  do
         $M^\diamond \leftarrow M^{N_w}(r_i, c_j)$ ;
         $f_{in}^\diamond \leftarrow f_{in}^{N_w}(r_i, c_j)$ ;
        if  $\sum_x \sum_y M^\diamond > 0$  then
             $PSD^{0^\circ} \leftarrow PSD(f_{in}^\diamond)$ ;
             $PSD^{90^\circ} \leftarrow PSD(rotate(f_{in}^\diamond, 90))$ ;
             $\overline{PSD}^{0^\circ} \leftarrow mean(PSD^{0^\circ})$ ;
             $\overline{PSD}^{90^\circ} \leftarrow mean(PSD^{90^\circ})$ ;
             $\widehat{PSD}^{0^\circ} \leftarrow polyfit(\log_{10}(\overline{PSD}^{0^\circ}))$ ;
             $\widehat{PSD}^{90^\circ} \leftarrow polyfit(\log_{10}(\overline{PSD}^{90^\circ}))$ ;
             $H^{0^\circ} \leftarrow [-0.5(slope(\widehat{PSD}^{0^\circ}) - 1)]$ ;
             $H^{90^\circ} \leftarrow [-0.5(slope(\widehat{PSD}^{90^\circ}) - 1)]$ ;
             $H_{ind} \leftarrow [H^{0^\circ}, H^{90^\circ}]$ ;
             $ind \leftarrow ind + 1$ ;
        end
    end
end
```

2.4.3. Classification process

After the feature extraction stage, the Support Vector Machine (SVM) classifier [31] using the Bootstrap Aggregating (Bagging) technique [32] is used to

classify each patch, extracted from an image, in healthy or pathological according to its fractal dimension. SVM maximises the distance between the hyperplanes defined by specific samples, called support vectors, with the aim of finding the optimal separation between classes. It is important to note that SVM algorithm is applied using the kernel trick technique [33]. In this technique, a specific non-linear function (Φ) is used for mapping non-linear separable data points ($\Omega = \{x_1, x_2, \dots, x_n\}$; points $x_i \in \mathfrak{R}^d$) in the original space Σ , into a higher dimensional space in which the data is linearly separable. When this hyperplane of separation is projected back to the input space (Σ), it has the form of a non-linear curve. The new feature space can be of unlimited dimension and thus the hyperplane separating the data can be very complex. The function $K(x, x_i) = \Sigma(x)^T \Sigma(x_i)$ is known as kernel function and in this work, each SVM model is trained using a gaussian kernel (i.e. a Radial Basis Function kernel) defined by the following expression:

$$K(x, x') = \left(\frac{\|x - x'\|^2}{2\sigma^2} \right) \quad (13)$$

where $\sigma \in \mathfrak{R}$ is a kernel parameter and $\|x - x'\|$ is the dissimilarity measure.

Combining the SVM method with the Bagging technique it is possible to improve the stability and accuracy of the machine learning algorithm, reducing the variance and avoiding the overfitting. In this work, the Bagging technique is also used to solve the problem of the unbalanced classes caused by the different number of healthy and pathological patches extracted from a retinal fundus image. Given T pathological patches and K healthy patches where $K \gg T$, the bagging technique can be applied in order to balance the classes. In first place, a random permutation of the healthy patches is carried out. After that, M different SVM models can be trained using groups of L healthy patches and the L pathological patches. The final number of classifiers can be calculated as $M = \text{round}(K/L)$.

An overview of the proposed method is presented in Figure 6. The flow chart shows the different steps of the pre-processing and feature extraction stages.

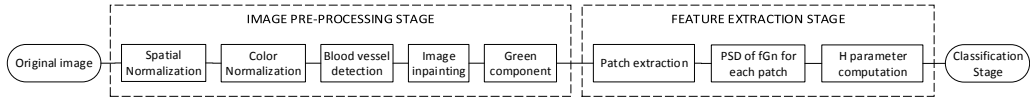


Figure 6: Flow chart of the pre-processing and fractal analysis stages.

3. Results

3.1. Statistical significance analysis of the fractal dimension

The main purpose of this work is to analyse the ability of fractals to discriminate between pathological and healthy retina. For this reason, in the first experiment a statistical analysis of the fractal dimension, described by the Hurst exponent variable, is carried out.

From the 47 color fundus images with exudates of the E-OPHTHA_EX database, 10991 healthy and 2151 patches with lesion are extracted. Figure 7(a) shows the average PSD of the fGn computed from each labelled patch. As it can be observed, the lines that describes these curves (red and green) will be characterized by different slopes and these slopes will define the H parameter or fractal dimension.

The statistical significance of the fractal dimension variable according to the two populations under study is analysed by means of the students t-test [34]. A random selection of 2151 healthy patches is carried out in order to balance the groups. Figure 7(b) shows the box comparison of H parameter. The p-value obtained from the t-test $p < 0.001$ is statistically highly significant, so this fact is promising in order to use the fractal analysis to detect automatically the bright lesions typical in DR and AMD retina background.

3.2. Automatic exudate detection using fractal analysis

An automatic system combining the different stages detailed in Figure 6 was developed by the authors. This computer-aided diagnosis system is used with the aim to demonstrate the ability of fractal dimension to discriminate between healthy and pathological texture.

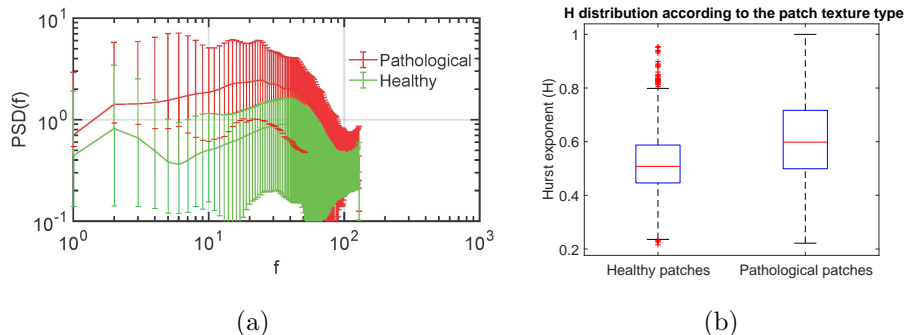


Figure 7: (a) Average PSD comparison between the two populations, pathological (in red) and healthy (in green) and (b) Hurst exponents \pm SD estimated using GSE for the healthy and pathological groups.

To avoid biased results produced by training and testing sets selection, in this work we use an external k -fold cross-validation procedure. For each database under study, the whole dataset composed by N images is divided into k partitions. Then patches extracted from the images belonging to $k - 1$ partitions are used for training a classifier as described in Section 2.4.3, and the patches extracted from the remaining partition of images are used for testing. The procedure is carried out k times, leaving out a different partition in each repetition.

The optimal patch size (N_w) and the overlap ($\Delta x, \Delta y$) used to extract the local features were obtained through an internal v -fold cross-validation process with $v = 8$ folds. Note that this technique is applied to the “patch” instances extracted from the fundus images. From this process, a patch size $N_w = 64$ pix. and an overlap $(\Delta x, \Delta y) = 32$ pix. were obtained as optimal parameters for the local analysis in the exudate detection task. Regarding to the classification stage, a Radial Basis Function (RBF) kernel was used. RBF kernel is characterised by two parameters (C, γ) . The parameter C trades off miss-classification of training examples against simplicity of the decision surface, while the parameter γ defines how far the influence of a single training example reaches. Internal v -fold cross-validation was used in the experiments in order to “grid search” the optimal parameters. Several pairs of (C, γ) values were tried and the one with the highest cross-validation accuracy was selected for each k partition [31].

In addition, the problem of unbalanced data is solved using the Bagging technique with $M = 7$ classifiers. It is important to note that in the test stage, each SVM classifier predicts one label for each patch and the final decision is obtained using a voting algorithm. The individual decision of each classifier is pondered by the probability assigned in the classification. The final assignment of the class is made according to the sum of all weighted decisions. If this sum is greater than 0.5, the patch is classified as pathological texture, while if the sum is less than 0.5 the tissue is classified as healthy. The whole classification strategy is summarized in Figure 8.

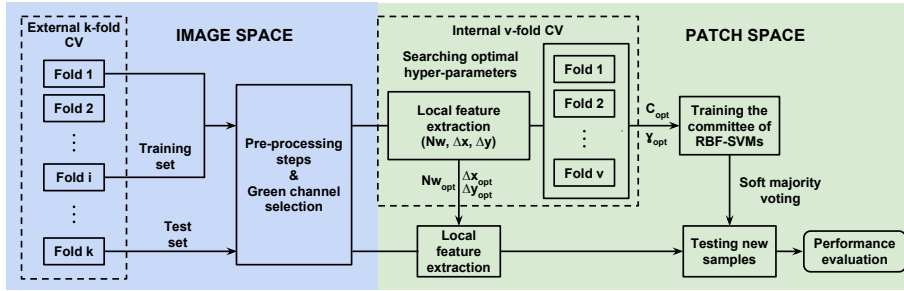


Figure 8: Overview of the classification strategy.

Table 2 shows the evaluation of the classification performance for the two public databases detailed in Section 2.1. The classification of the retina background patches extracted from the 14 images that compose the test set are evaluated by using six metrics. Accuracy (ACC) measures the fraction of correct predictions by the total number of cases. Sensitivity (SENS) and specificity (SPEC) measure the proportion of positive and negative cases which are correctly identified as such, respectively. The positive and negative predictive values (PPV and NPV respectively) measure the proportion of positive (negative) cases classified correctly according to the gold standard and the total number of positive (negative) predictions determined by the classification system. Finally, the area under the ROC curve (AUC) relates the hit rate to the false alarm rate and it is an extended way to measure the predictive modelling accuracy [35]. This measure allows to establish fair comparisons where there is a strong

350 imbalance between classes [36].

Database	ACC	SENS	SPEC	PPV	NPV	AUC
E-OPHTHA_EX	0.6980	0.6149	0.7488	0.2981	0.9213	0.7168
DIARETDB1	0.8361	0.6047	0.8657	0.3448	0.9459	0.8176

Table 2: Results of the classification patch process using the fractal descriptor.

As we can observe, fractal dimension presents a promising ability to describe patches with lesions allowing the discrimination from the healthy texture. It is important to note that using only two features (the Hurst exponent in two directions), the classifier is able to correctly classify 69.8% of all the instances
355 extracted from the test images of the E-OPHTHA_EX database and 83.61% of all the patches extracted from the test images of the DIARETDB1 database. From the SPEC and NPV measures of Table 2 it is possible to determine the great capacity of fractal analysis for modelling the healthy tissue. Regarding to the sensitivity and positive predicted values, results suggest the difficulty
360 of discriminating a large test set using two features. With the objective of improving this aspect, texture information is incorporated to the feature vector combining the Hurst parameters with another descriptor.

Figure 9 shows the visual representation of the exudate detection in one representative image of each database. In this figure, red squares indicate the
365 true positives, green squares the false positives and the blue squares reveal the false negative detections.

3.3. Fractal dimension combined with Local binary patterns

As we demonstrated above, fractal analysis is able to describe pathological retinal tissues with around 70% and 83% of success in each database under
370 evaluation. However, the SVM classifiers involved in the bagging process are using only two features, the Hurst exponent or fractal dimension in $L = 2$ directions, to perform the discrimination. In order to improve the accuracy of the bright lesion detection, the fractal descriptor is combined with Local Binary

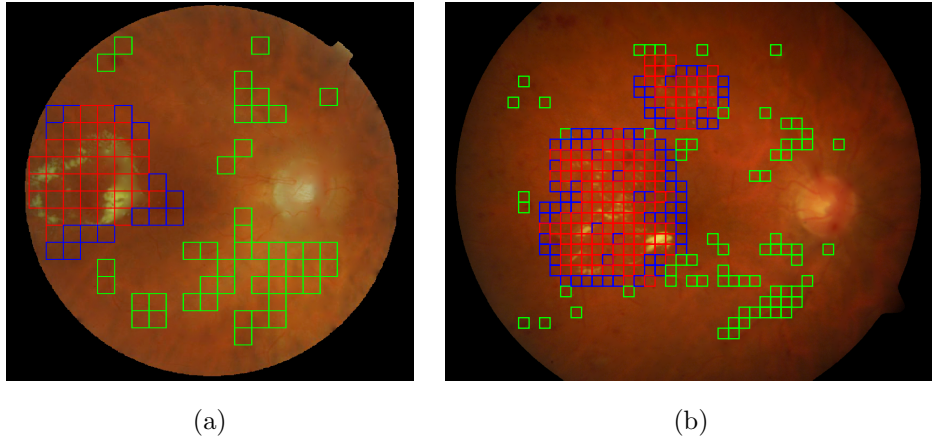


Figure 9: Automatic exudate detection in two retinal images using the fractal dimension as unique feature. (a) Representative image (DS000U30.jpg) from the E-OPHTHA_EX database and (b) representative image (image014.png) from DIARETDB1 database. Red squares indicate the true positives, green squares the false positives and the blue squares reveal the false negative detections.

Patterns (LBP). LBP is a powerful grey-scale texture operator used in many
 375 computer vision applications. This descriptor establishes a label for each pixel
 taking into account its neighbourhood which is defined by a radius R and number
 of points P . Many variants of LBP exist in the literature but the rotation-
 invariant uniform LBP presented in [37] is used in this work. Using this LBP
 variant, ten different texture labels could be generated depending on the binary
 380 string computed in the comparison between a pixel and its neighbourhood.
 When LBP is used for texture description it is common to include a contrast
 measure by defining the Rotational Invariant Local Variance [37]. As a novelty
 in the retina texture description stage, in this work LBP (rotation-invariant
 uniform variant) and VAR are combined following the process proposed by Guo
 385 et al. [38] resulting the LBP variance (LBPV). Both descriptors (LBP and
 VAR) are computed for the whole image and the normalized histogram of the
 LBPV is extracted from each patch.

LBPV is computed in a circular neighbourhood of radius $R = 1$ by defining
 $P = 8$ neighbours. A discrete histogram composed by ten labels or patterns

390 describes each patch extracted from the images. A new model taking only into account this texture information is trained. Table 3 reports the classification performance obtained for the two databases under study.

Database	ACC	SENS	SPEC	PPV	NPV	AUC
E-OPHTHA_EX	0.7212	0.7947	0.6121	0.4178	0.8603	0.7393
DIARETDB1	0.8229	0.8366	0.7990	0.4212	0.8987	0.8125

Table 3: Classification patch performance using as feature vector the ten patterns of the LBPV histogram.

As can be observed in the previous table, the LBPV descriptor presents a good performance in exudate detection. Using the ten features provided by the LBPV histogram, 72.12% and 82.29% of classification accuracy is achieved for each database. Paying attention to the sensitivity and PPV values, the texture information is able to reduce the number of false positives at expense of a drastic reduction of the true negatives detections. Analysing the results showed in Tables 2 and 3, in particular SENS, SPEC, PPV and NPV measures, it is possible to extract a complementary behaviour between the roughness and texture descriptors. In spite of this complementary behaviour, a similar overall performance in the classification is glimpsed attending to the ACC and AUC measures. This fact is exploited in a second test, in which the ten features obtained from the LBPV histogram computation are combined with the fractal dimension computed in two directions (0 and 90 degrees) composing a feature vector that combines texture and roughness information. The same test as we presented in the previous section is performed achieving the results showed in Table 4.

The fact of feeding the classifier with a combination of texture and contrast information (LBPV) and roughness information (FD) provides a powerful system to discriminate between healthy and pathological retinal tissue. A promising trade-off between sensitivity-specificity and PPV-NPV (Table 4) propitiates higher values of AUC. Based on [39], AUC values greater than 0.85 invites to

Database	ACC	SENS	SPEC	PPV	NPV	AUC
E-OPHTHA_EX	0.8477	0.7478	0.8705	0.4061	0.9528	0.8686
DIARETDB1	0.8987	0.8083	0.9023	0.4175	0.9656	0.8812

Table 4: Classification patch performance using as feature vector the fractal dimension combined with the LBPV histogram.

consider the proposed methodology as a “good diagnostic test” for the hard ex-
415 udate detection. The robustness of the proposed system against the variability
introduced by the use of different image databases is another relevant aspect to
emphasize.

The new feature vector provides an accurate bright lesion detection in fun-
dus images. Now, only particular patches composed by less of five percent of
420 pixels with lesion are not identified as pathological tissue. Figure 10 shows the
automatic identification of exudates in the same images that in the previous
section allowing to observe the improvement by visual inspection.

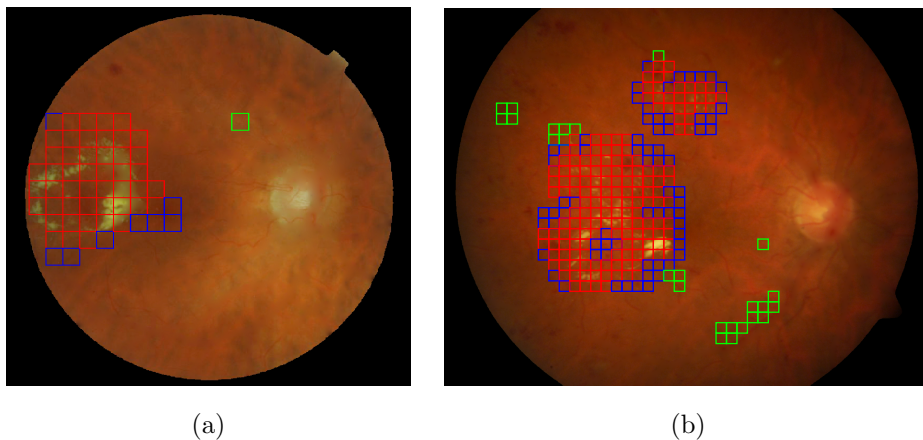


Figure 10: Automatic lesion detection in two retinal images using the LBPV histogram and the fractal dimension as feature vector. (a) Representative image (DS000U30.jpg) from the E-OPHTHA_EX database and (b) representative image (image014.png) from DIARETDB1 database.

Thanks to DIARETDB1 public database, the proposed method for exudate detection can be compared with some state-of-the-art works, in which, the de-

425 tection/segmentation of these lesions is performed by using classical techniques
such as filtering and mathematical morphology. Table 5 summarizes the exu-
date detection results achieved by the proposed method and by other works of
the literature.

Methods	Sensitivity	Specificity	PPV
Sopharak et al.[40]	0.4348	0.9931	0.2548
Walter et al.[1]	0.6600	0.9864	0.1945
Welfer et al.[2]	0.7048	0.9884	0.2132
M.Ghafourian et al.[3]	0.7828	-	-
Proposed method	0.8083	0.9023	0.4175

Table 5: Comparison of exudate detection methods for the 47 retinal images with exudates of DIARETDB1 database.

The proposed method presents the best trade-off between sensitivity-specificity
430 improving the representative methods involved in the comparison. In Sopharak
et al.[40] and Walter et al. [1], poor sensitivity values are achieved. This fact is
quite relevant taking into account that this parameter is directly related with the
quality of predicting positive instances. Sensitivity value is the unique measure
provided by [3] about the performance of its method. Taking into account only
435 one parameter is not possible to establish the goodness of that method. The
algorithm introduced by [2] provides interesting results. However, analysing to-
gether the three parameters of Table 5 it is possible to observe that our method
outperforms the Welfers' one. It is important to note that if AUC parame-
ter would have been included in the works involved in the comparison a more
440 exhaustive comparison would have enabled.

4. Conclusions

In this work, fractional Brownian motion model was used in order to de-
scribe grayscale retinal images allowing the estimation of the fractal dimension.
With the aim of reliably applying fractal analysis in fundus images, a prepro-

445 cessing stage combining resizing, inpainting and colour-normalization methods
was essential due to the high image variability in the databases. After that,
different test were carried out using the E-OPHTHA and DIARETDB1 pub-
lic databases. The local estimation of the Hurst exponent by linear regression
made possible to discriminate between healthy and pathological retinal tissue
450 in a statistical highly significant way ($p < 0.001$). This fact led the authors to
develop an automatic system able to detect the bright lesions using as feature
the fractal dimension and a committee of SVM classifiers. The obtained results
glimpsed the need of creating a more robust feature vector able to avoid the
possibility of underfitting. The normalized LBPV histograms were extracted
455 from the image patches and new experiments using this descriptor showed a
complementary behaviour with respect to the fractal dimension. This fact pro-
pitiated a last experiment, in which, the SVM models were recalculated using as
feature vector a combination of roughness information, provided by the fractal
analysis, and texture information, extracted by the LBPV histograms. This
460 novel approach reached an accurate bright lesion detection. In particular, 85%
and 90% of accuracy was achieved in E-OPHTHA_EX and DIARETDB1 re-
spectively. In addition, the proposed system was able to outperform the most
representative state-of-the-art methods in exudate detection showing the best
trade-off between sensitivity-specificity.

465 In future research, piecewise fractional Brownian motion model will be ex-
plored. In this model, the PSD of the graylevel increments is supposed multi-
fractal, in other words, the spectrum can be divided in fragments and several
Hurst parameters will be extracted by linear regressions. Each patch will be
represented by a fractal signature. Moreover, the authors would like to explore
470 Minkowski functionals and Minkowski tensors [41] with the aim of extracting
new fractal features from fundus images [42]. In addition, fractal analysis will
be used to detect red dark lesions as microaneurysms and haemorrhages. This
fact would allow to automatically discriminate between two of the most frequent
causes of blindness or vision impairment in the world: diabetic retinopathy and
475 age-related macular degeneration.

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