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Applications of fractals in medicine

Kaoutar Lamrini Uahabi and Mohamed Atounti

Abstract. The mathematical concept of fractals characterized irregular and broken objects, with details on all scales of observation and whose dimension can be non-integer. A fractal organization controls the structures at all levels of the human body. Euclidean geometry is powerless to study irregularities in these structures. For cons, the fractal analysis tools allow us to model it with an impressive realism. We discuss in this work the contribution of fractals in the diagnostic of the diabetic retinopathy, by a non-invasive method. We will take two samples of each ten retinal images, one is normal and the other is pathological. We will calculate the fractal dimensions for each sample. The comparison of the values obtained for the two samples have led to a significant result, allowing distinguish between normal retinas of pathological retinas.

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1. Introduction

The human body is full of a multitude of very complex structures, this is the case of the respiratory tract and the prodigious bronchial ramification, some parts of the heart, the renal system, the large blood and capillary networks, etc ... These structures, real physical systems are of geometric and functional complexities. A precise approach of these phenomena necessarily passes through a stage of mathematical modeling. Euclidean Geometry is unfortunately powerless to resolve such problems. It actually applies only in the cases of smooth and regular shapes. Thus, a point has a dimension equal to zero, a line has a dimension one, a plane has a dimension two and a volume has a dimension equal to three. Fractal geometry, meanwhile, deals with such dimensions ranging for example between one and two or between two and three, etc. The fractal dimension is in fact the size of the irregular curves [7]. And it's this specificity that offers huge benefits in the field of medicine. Indeed, the structures of the human body are real fractal objects, which allows a modeling and hence a quantification of these phenomena, through the fractal analysis [3]. The science of fractal objects uses specific mathematical objects of non-Euclidean geometry. The term "fractal" is used to refer to self-similar objects and having the same details in different scales. The fractal dimension is a measure of the density of the fractal in the space it occupies [21]. A fractal is a localized object in space that can be decomposed into a growing number of similar or identical elements ever smaller. This is a self-similar object, meaning that its smallest elements are copies of his greatest elements. In the case of some fractals, the smallest elements of the structure are exact copies of larger elements. For most of fractals found in nature, smaller elements are similar, not identical, to the larger elements. The tree is an example of fractal; it has

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a growing number of branches but still smaller. A fractal can also be an established process at a particular position in time, and has a growing number of increasingly low amplitude fluctuations. A fractal can also be a set of numbers from experimental data, with a growing number of ever smaller numbers. This system has a surprising property; it predicts the system values accurately for short periods of time, but do not allow for the same forecasts over long periods of time [15].

In this work, we will stick to one of the important applications of fractals in the medical field, namely diabetic retinopathy; very common complication of diabetes disease. It causes changes in the morphological structure of blood vessels in the diseased retina. Although they represent only 5% of body volume, blood vessel diameter nourish every cell of the human body. As they occupy an infinite surface contained in a finite volume, the capillary and blood vessel diameter have very complex properties [6]. For this, various vascular exploration techniques do not allow an objective quantification of the architecture of vessel diameter, although this factor is of major importance to distinguish between what is physiological and what is pathological [16]. The retina is the only location where blood vessels can be directly visualized in vivo, by a non-invasive method [17]. The blood vessels in the retina branch a number of times each time forming a vessel tree that is similar in characteristics to the branch it came from. There are some reports of measuring fractal properties of blood vessel patterns of the retina; most have involved manual segmentation of the blood vessel patterns [4], [22] and [23]. Now with reliable automated vessel segmentation, attention is turning to analyzing the retinal vasculature as a fractal [1], [6].

In the present paper, we will discuss in the two first sections, the contribution of fractals in the diabetic retinopathy, using the fractal dimension, which is the main tool of fractal analysis. In section 3, we will define the pathology of the diabetic retinopathy and compare the classical method of diagnosis of the disease and the new method based on fractal geometry, which is a non-invasive method. In section 4, we will take two samples of twenty retinal images, one of them is composed by ten normal retinas and the other by ten pathological retinas. We will estimate the box counting dimension, as fractal dimension for each sample. For this, we use the Image J fractal analysis software. Thereafter, we will try to compare the values obtained for the two samples and we will discuss the results.

2. Fractal dimension

Box-counting or box dimension is one of the most widely used fractal dimensions. Its popularity is largely due to its relative ease of mathematical calculation and empirical estimation. Let F be any non empty bounded subset of R^n. The lower and upper box-counting dimensions of a subset $F \subset R^n$ are respectively defined by [7], [11], [12], [19]:

$$\underline{dim}_B(F) = \underline{\lim}_{\delta \to 0} \frac{log N_\delta(F)}{-log\delta}; \quad \overline{dim}_B(F) = \overline{\lim}_{\delta \to 0} \frac{log N_\delta(F)}{-log\delta} \tag{1}$$

If these are equal then the common value is referred to as the box-counting dimension of F and is denoted by [7], [11], [12], [19]:

$$dim_B(F) = \lim_{\delta \to 0} \frac{log N_\delta(F)}{-log\delta} \tag{2}$$

If this limit exists, where $N_\delta(F)$ is any of the following:

(i) the smallest number of closed balls of radius $\delta > 0$ that cover F;

(ii) the smallest number of cubes of side δ that cover F;
(iii) the number of $\delta - mesh$ cubes that intersect F;
(iv) the smallest number of sets of diameter at most δ that cover F;
(v) the largest number of disjoint balls of radius δ with centers in F.

3. Fractals and diabetic retinopathy

In the field of ophthalmic pathologies, diabetic retinopathy has one of the most common complications of diabetes disease. Figure 1 shows a diseased retina.

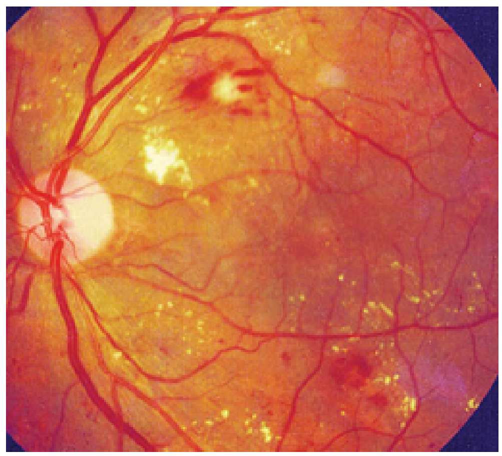

FIGURE 1. Diabetic retinopathy.

Diabetic retinopathy is damage to the blood vessels of the retina in people with diabetes. This condition develops silently and in a sneaky way for many years. Only a regular screening test would diagnose such interference in its infancy. Note that diabetic retinopathy is a leading cause of blindness in people with diabetes. This disease affects up to 80 percent of all patients with diabetes for 10 years or more [24]. Despite these intimidating statistics, research indicates that at least ninety percent of these cases could have been reduced if they had received adequate treatment on time [9]. This shows the great importance that has the early diagnosis of such condition. The usual and classical technique for screening for diabetic retinopathy is based on the examination of the fundus of the eye, performed by an ophthalmologist after pupil dilation. This type of examination is easily understood that varies according to the judgment of the treating doctor, and that a large part of subjectivity persists, especially in cases of early attacks.

In recent decades, new methods of screening for diabetic retinopathy have been tried. The method of making photographs of the fundus without pupil dilation, using a digital camera is the most relevant. It is a non-invasive method and can be performed by a technician within a short time [2]. It allows us to take digital photographs, which are transmitted to a central database for testing. To process these data (retinal images), several methods have been tried and reported in the literature. But it seems that the methods using fractal analysis are the most consistent and the most likely to give very accurate results (Figure 2). The fractal dimension is the main tool of fractal analysis [5]. This is one of the parameters used to characterize the complexity of blood networks. Based on the estimation of the fractal dimension [20],

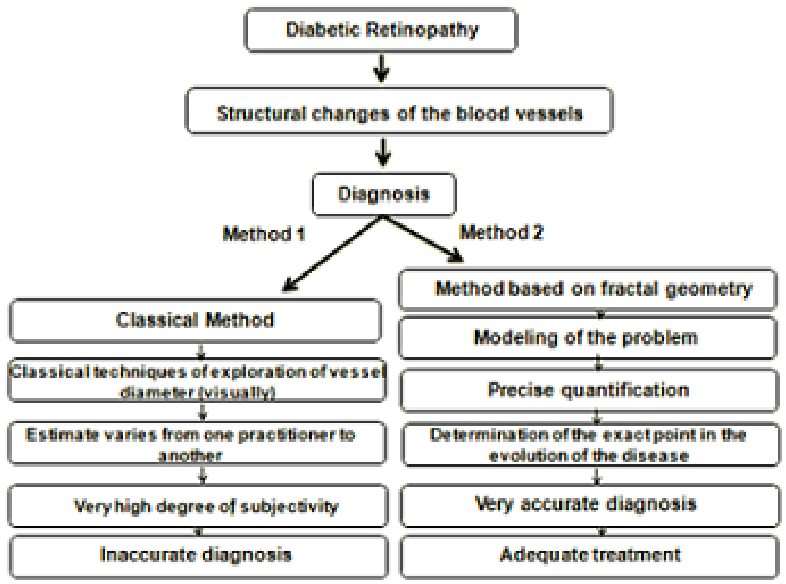

FIGURE 2. Diagnosis of diabetic retinopathy: the enormous interest of the method using fractals.

using different algorithms or different methods, several studies on the mechanism of formation of the vascular network of the retina have provided impressive results and therefore have given rise to new and very important interpretations.

4. Results and discussions

In the present work, we specifically used the box-counting dimension as fractal dimension. We took a number of images of the retina from the base STARE database (http://www.ces.clemson.edu/ ahoover/stare/). The first sample, denoted sample A, consists of ten images of normal retinas; the second, denoted sample B contains ten images of pathological retinas [18]. The evaluation of the calculated results is made by comparing the values obtained for the two samples. For each group, a fractal dimension calculation was performed. We note by D the value of this fractal dimension. It is calculated by the method ImageJ. This method can display, edit, analyze, process, save and print 8-bit, 16-bit and 32-bit images. It can read many image formats including TIFF, GIF, JPEG, BMP, DICOM, FITS and "raw". It supports "stacks", a series of images that share a single window. It is multithreaded, so time-consuming operations such as image file reading can be performed in parallel with other operations. (http://imagej.nih.gov/ij/).
It can calculate area and pixel value statistics of user-defined selections. It can measure distances and angles. It can create density histograms and line profile plots. It supports standard image processing functions such as contrast manipulation, sharpening, smoothing, edge detection and median filtering. (http://imagej.nih.gov/ij/).

In Table 1, the results of calculations of fractal dimensions are grouped for the sample A of normal cases (images of healthy retinas).

number of image	Retinal image	D
1	im0077.ah	1.578
2	im0081.ah	1.554
3	im0082.ah	1.578
4	im0162.ah	1.651
5	im0163.ah	1.641
6	im0235.ah	1.598
7	im0236.ah	1.585
8	im0239.ah	1.588
9	im0240.ah	1.594
10	im0255.ah	1.634

Table 1. The values of fractal dimensions D for the sample A.

The shapes of the distributions of the blood vessels of human retinas are very complex and very different from one person to another, even in the case of normal retinas. This greatly complicates the comparison of the distributions of these networks. The complexity is even greater when treating pathological retinas. For this, the fractal geometry may characterize more precisely these irregular shapes. Figure 3, extracted from STARE database(http://www.ces.clemson.edu/ ahoover/stare/), shows the fractal shape of the distribution of blood vessels of a normal retina.

im0163


FIGURE 3. Image of a normal retinal vessel network (file im0163.ah).

For a sample A, the graph in blue of Figure 4 represents the fractal dimension associated with each normal case of human retina. This curve shows a more or less linear appearance. The values of fractal dimensions are roughly the same for the ten cases studied.

number of image	Retinal image	D
1	im0001.ah	1.539
2	im0002.ah	1.549
3	im0003.ah	1.508
4	im0004.ah	1.522
5	im0005.ah	1.590
6	im0044.ah	1.540
7	im0139.ah	1.565
8	im0291.ah	1.519
9	im0319.ah	1.444
10	im0324.ah	1.567

Table 2. The values of fractal dimensions D for the sample B.

In Table 2, there are the results of calculations of the fractal dimensions for the sample B containing pathological cases (images of diseased retinas). Figure 5, obtained from STARE database (http://www.ces.clemson.edu/ ahoover/stare/), highlights the

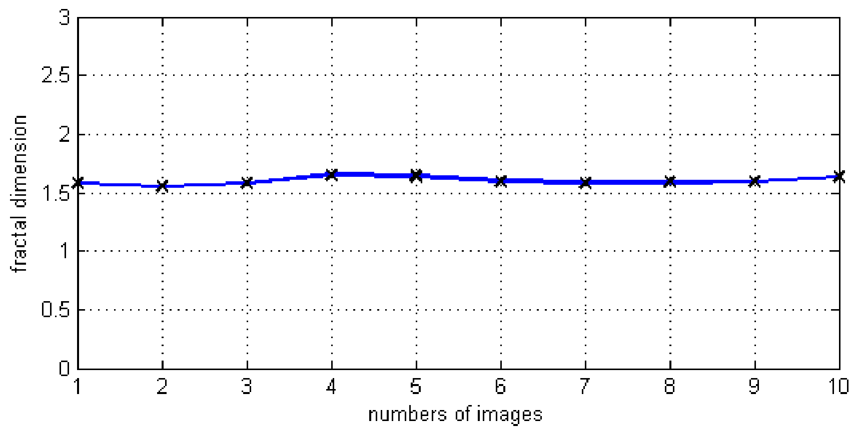

FIGURE 4. Graph linking the values of fractal dimension associated with the images of sample A (normal retinas).

broken and fractured appearance of the structure of blood vessels of a pathological retina.

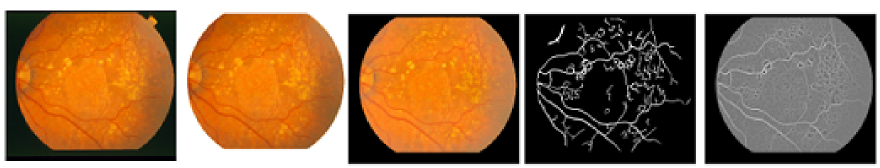

FIGURE 5. Image of a pathological retinal vessel network (file im0003.ah).

In the case of the sample B, Figure 6 shows the graph (shown in red) representing the fractal dimension for each pathological case. One can easily notice the broken shape of this curve. This shows the variation of the fractal dimension of a pathological subject compared to another. This variation is due to different degrees of impairment of the blood vessels of the retina in question. The clinical indication of changes in fractal dimensions (Figure 6) is very important because it allows a very precise classification of stages of deterioration of the retinas.

Figure 7 (comparative figure) shows the comparison of the results for both samples A and B. It is clearly seen that the fractal dimension for sample B (pathological retinas) is significantly lower than that of sample A (normal retinas).

From a statistical point of view, the increasing of the numbers of cases in each sample could give conclusive results. This can be very useful in the quest of automatic procedures of diagnostic.

Conclusions. The human retina has a complex vascular network, having a fractal structure. For this, the fractal geometry, in contrast to Euclidean geometry, provides a more accurate method of modeling of this vascular network. Two samples of each ten retinal images, one is normal and the other is pathological, were studied. The comparison of the values obtained for the two samples have led to a significant result, allowing differentiate normal retinas of pathological retinas. An increase in numbers of cases studied could enrich these results. Such results are of major importance for

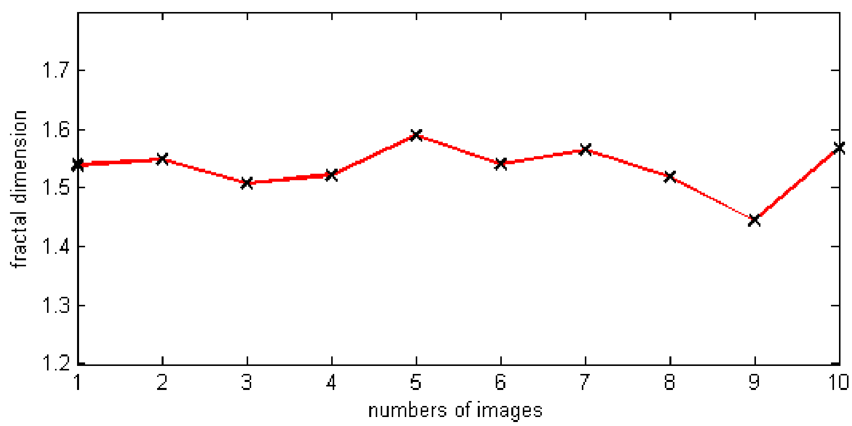

FIGURE 6. Graph linking the values of fractal dimension associated with the images of sample B (pathological retinas).

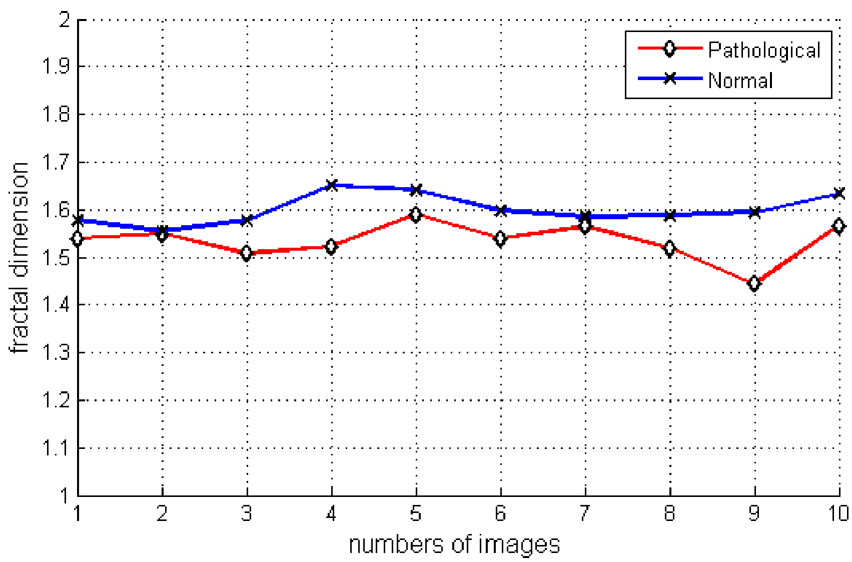

FIGURE 7. Comparison of curves of fractal dimensions of sample A and sample B.

the diagnosis of diabetic retinopathy in general and for early diagnosis in particular, where the method took its rise. Fractal analysis of vasculature formed in human retinal image can be used as a non-invasive technique for detection of early retinal vascular diseases. Indeed, it would be very useful to arrive eventually to determine a reference value which would be a true indicator between normal cases and pathological cases. On the other hand, such a value would give a very precise indication of the degree of achievement and the stage of the disease. These measures will also be useful for the control of the severity of the disease and the evaluation of the progress of treatment over time.

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(Kaoutar Lamrini Uahabi, Mohamed Atounti) Laboratory of Applied Mathematics and Information Systems, Department of Mathematics and Computer Science, Multidisciplinary Faculty of Nador, University Mohammed First of Morocco, 62702 Selouane - Nador, Morocco
E-mail address: lamrinika@yahoo.fr, atounti@hotmail.fr