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Dynamical systems in biology and medicine

## On Application of Fractal Analysis Methods to Biomedical Preparation Images

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**Abstract:** We investigate a possibility to apply fractal and multifractal methods to analyze some classes of biomedical preparation images. The Modified Fractal Signature method based on the calculation of the Minkovsky dimension is used. The method is alternative to well-known box dimension calculation. Generalized dimensions (Regny spectrum) and multifractal spectrum are calculated to obtain valuable features for multifractal sets. Different methods for multifractal spectrum calculation are considered. The results of numerical experiments show that for the images under study the direct calculation of multifractal spectrum (pointwise dimensions calculation and the computing thermodynamic averages) is more preferable than the obtaining the spectrum from generalized dimensions with the following using the Legendre transform.

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*Keywords:* dynamic system, attractor, self-organizing systems, chaotic behavior, image analysis, fractal.

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## 1. INTRODUCTION

It is now widely accepted that physical systems that exhibit chaotic behavior are generic in Nature. Since it is possible to follow their trajectories only for short time scales, one must use suitable statistical descriptions to obtain an approximation to system dynamics.

We may consider phase portraits of complex dynamical systems (self-organizing system, for example) and analyze them as images. Stable invariant sets (attractors) of the systems often have complex geometrical structure — they are fractals or

multifractals (unions of several fractal sets, being everyone has own fractal dimension). One can realize a multifractal set image as a result of a measure  $\mu$  distribution.

The multifractal formalism as a method of description of such sets relies on the fact that highly non-uniform probability distributions arising from the nonuniformity of the system often possess rich scaling properties such as self-similarity. Hence we can associate a characterization of the fractal properties of a measure with the nonuniform distribution. The multifractal formalism describes the statistical properties of these measures in terms of their multifractal spectrum or their generalized dimensions.

### **1.1 Fractal dimension calculation**

One of the most widely used dimensions is box-counting or box dimension. (It has been also termed capacity dimension, entropy dimension). This is due to its ease of mathematical description and empirical estimation. It is well-known that the calculation of box dimension may be rather time-consuming. In 1997 Tang et al.[10] proposed the Modified Fractal Signature method based on the calculation of the Minkovsky dimension that coincides with box dimension for non-empty bounded sets in  $R^n$ . The basic idea of this approach is that an image is mapped onto a gray-level function. Furthermore, this function can be mapped onto a gray-level surface, and from the area of such a surface the fractal dimension (fractal signature) of the document image can be obtained. The authors used this dimension to differ the areas of text, background and pictures in digital images. The method seems to be appropriate for different subject areas. So, in [1] this method was successfully applied to the classification of some classes biomedical preparation images. In [7] the authors calculated the Minkovsky dimension to classify (on the focusing degree) the images obtained by radars.

### **1.2 Multifractal spectrum and Regny dimensions**

Cover the support of the measure with disjoint boxes  $\{N_i\}$  of size  $l$  and define for  $i$ th box a measure as  $l^{\alpha_i}$ , where  $\alpha_i$  is a real number. Then the subsets of points ( $E_\alpha$ ) for which values  $\alpha_i$  are equal or close (level sets), are defined. For each subset its fractal dimension  $f(\alpha_i)$  is calculated. So, the image is considered as a union of interwoven subsets, being each of them has own fractal dimension. The set of these dimensions forms multifractal spectrum (MFS). It should be noted that the finding of  $E_\alpha$  sets means a categorization of an image points. In fact, it is the box measure that describes a categorization. Different measures lead to different multifractal spectra. For digital images the measure is defined through pixel intensities. The method of MFS direct determination using the calculation dimensions of the level sets is described in [12].

Multifractal spectrum is widely used in image analysis because it is globally invariant under bi-Lipschitz transform (general transform including brightness changing, rotation, scaling and general texture surface deformations). Hence it may be used as some stable feature for a class of images. So, in [12] the authors apply multifractal spectrum to texture analysis and classification.

Another approach to analyze multifractal sets is to calculate generalized dimensions (Regny spectrum). Let  $\{\mu_i\}$  be a probability measure defined on the set under investigation. Generalized (Regny) dimensions  $D_q$  provide an alternative description of the singular measure. They correspond to scaling exponents for the  $q$ th moment of the measure. The main idea of this approach is to use the statistical sum  $S(q) = \sum_i \mu_i^q$  and consider a set of dimensions  $D_q$  defined by  $D_q = \lim_{l \rightarrow 0} \frac{\ln S(q)}{(q-1) \ln l}$ . It was the first and probably the simplest way to calculate Regny spectrum. Nonetheless, the error analysis in [11] showed that such a way is not sufficiently reliable.

Since MFS and Regny spectrum describe the same measure, one can connect  $\alpha$  and the function  $f(\alpha)$  with the sum  $S(q)$ . As  $q$  is varied, different subsets, which are associated with different scaling indexes, become dominant. In other words, maximum principle allows us to obtain a set of numbers (for different  $q$ ) that are fractal dimensions of subsets in which the sum is maximal. This reasoning technique leads to the following: when  $f(\alpha)$  and  $D_q$  are smooth functions of  $\alpha$  and  $q$ , they are connected by the Legendre transform. It was believed that for measures arising from real experiments it is easier to calculate generalized dimensions and then obtain multifractal spectrum using the Legendre transform. And vice versa — given a multifractal spectrum one can calculate Regny dimensions.

### **1.3 MFS direct determination –moment based method**

But, as was shown in [4], the  $D_q$  corresponding to large negative  $q$  may have large error bars and Legendre transforming the  $D_q$  curve may decrease precision considerably. The authors elaborated a new direct method of determining multifractal spectrum, which is based on a canonical method of computing thermodynamic averages. Both  $f(\alpha)$  and  $\alpha$  are obtained as functions of  $q$ . It should be marked that well-known method for the calculation of Regny spectrum considered in [11] is based on the Chhabra method [4] for obtaining  $f(\alpha)$  with the following calculation  $D_q$  by Legendre transform. This method was successfully applied to the recognition of Carelian petroglyphs [9].

This work continues our investigations relating to the analysis and classification of biomedical preparation images [1, 2]. We use all the described methods to analyze the images of some classes of biomedical preparation and give the results of numerical experiments. The Modified Fractal Signature method was successfully applied to all the classes. Regny spectrum method did not demonstrate reliable results for histological preparation images. At the same time, the MFS direct determination allowed us to classify them.

## **2. MAIN NOTIONS AND METHODS**

### **2.1 Definitions**

**Definition 1.** Let  $F$  be a nonempty bounded set in  $R^n$ ,  $\Omega = \{\varpi_i: i = 1, 2, 3, \dots\}$  — a covering  $F$ ,  $N_\delta(F)$  — the number of sets from  $\Omega$  whose diameters are not greater than  $\delta$ . Let  $\dim_H F$  and  $\dim_T F$  denote Hausdorff and topological dimensions  $F$  respectively.  $F$  is said to be fractal if  $\dim_H F > \dim_T F$ . Box-counting (capacity) dimension is defined by  $\dim_B F = \lim_{\delta \rightarrow 0} \frac{\log_2 N_\delta(F)}{-\log_2 \delta}$ .

**Definition 2 [5].**  $\delta$ -parallel body  $F_\delta$  can be defined by  $F_\delta = \{x \in R^n: |x - y| \leq \delta, y \in F\}$ .

**Definition 3.** Let  $F$  be a nonempty and bounded set in  $R^n$ ,  $F_\delta$  —  $\delta$ -parallel body  $F$ ,  $Vol^n(F_\delta)$  —  $n$ -dimensional volume of  $F_\delta$ . For a constant  $s$ , if  $\delta \rightarrow 0$ , the limit of  $Vol^n(F_\delta)/\delta^{n-s}$  is positive and bounded, we say that  $F$  has Minkovsky dimension  $s$ , which is symbolized by  $\dim_M F$ .

**Theorem 1 [5]** Let  $F$  be a nonempty bounded set in  $R^n$ . Then  $\dim_B F = \dim_M F$ .

## 2.2 Modified Fractal Signature method

In [10] the authors call the used method “Modified Fractal Signature” to emphasize that they did not use traditional fractal dimension (capacity). Alternately the volume of a  $\delta$ -parallel body was estimated to approximate the Minkovsky fractal dimension. Let  $F = \{X_{ij}, i = 0, 1, \dots, K, j = 0, 1, \dots, L\}$  be an image with multigray level and  $X_{ij}$  be the gray level of the  $(i, j)$ th pixel. In a certain measure range, the gray-level surface of  $F$  can be viewed as a fractal. In image processing the gray level function  $F$  is a nonempty bounded set in  $R^3$ . The surface area  $A_\delta$  may be calculated using the volume of a special  $\delta$ -parallel body — blanket with the thickness  $2\delta$ . Denoting this volume  $Vol(F_\delta)$  we have  $A_\delta = Vol(F_\delta)/2\delta$ .

But according to Definition 3 and Theorem 1 we can conclude that if  $\lim_{\delta \rightarrow 0} Vol(F_\delta)/\delta^{3-D} = \beta > 0$ , then  $D = \dim_M F = \dim_B F$ . Therefore, when  $\delta$  is sufficiently small, we have  $Vol(F_\delta) = \beta \delta^{3-D}$ . So, we have  $A_\delta = \frac{Vol(F_\delta)}{2\delta} = \beta \frac{\delta^{2-D}}{2}$ , from which the fractal dimension  $D$  (fractal signature) can be obtained. It should be noted that in practice it is often sufficient to calculate only  $A_\delta$  values.

The covering blanket is defined by its upper surface  $u_\delta(i, j)$  and its lower surface  $b_\delta(i, j)$ . Initially,  $\delta=0$  and  $u_0(i, j) = b_0(i, j) = X_{ij}$ .

For  $\delta=1, 2, \dots$  the blanket surfaces are defined iteratively as follows:

$$\begin{aligned} u_\delta(i, j) &= \max \left\{ \begin{array}{l} u_{\delta-1}(i, j) + 1, \\ \max_{|(m,n)-(i,j)| \leq 1} u_{\delta-1}(m, n) \end{array} \right\}, \\ b_\delta(i, j) &= \min \left\{ \begin{array}{l} b_{\delta-1}(i, j) - 1, \\ \min_{|(m,n)-(i,j)| \leq 1} b_{\delta-1}(m, n) \end{array} \right\}. \end{aligned} \quad (1)$$

The volume of the blanket  $Vol_\delta$  is computed as

$$Vol_\delta = \sum(u_\delta(i, j) - b_\delta(i, j)). \quad (2)$$

It should be noted in [8] that in practice the following formula for the surface area calculation is more preferable:

$$A_\delta = \frac{(Vol_\delta - Vol_{\delta-1})}{2}. \quad (3)$$

This is necessary, since  $Vol_\delta$  depends on all smaller scales features. Subtracting  $Vol_{\delta-1}$ , we isolate those features that change from scale  $\delta - 1$  to scale  $\delta$ . For a pure fractal object property changes do not depend on scale, and measurement between any two different scales lead to the same fractal dimension. In this case both methods for surface area calculation are identical. However, for nonfractal objects we should isolate the effects of smaller scale features. The last formula is applicable for both fractal and nonfractal surfaces.

In practice, the image  $F$  is divided into several non-overlapping subimages and  $A_\delta$  is computed for every subimage using formulas (1)-(3). Then all  $A_\delta$  are summarized. Given  $A_\delta$  the fractal dimension can be obtained. Sometimes it is convenient to study a “map” of the image, where in every cell the corresponding  $A_\delta$  (or fractal dimension) value is written.

### 2.3 MFS Direct Determination – calculation of level sets

Let  $\mu$  be a measure defined through pixel intensities. For  $x \in R^2$  we denote  $B(x, r)$  a square of length  $r$  with center  $x$ . We describe  $\mu(B(x, r)) = kr^{d(x)}(x)$  with  $d(x)$  the density function and  $k$  some constant. The local density function of  $x$  is defined as

$$d(x) = \lim_{r \rightarrow 0} \frac{\log \mu(B(x, r))}{\log r} \quad (4)$$

The set of all image points  $x$  with local density  $\alpha$  is

$$E_\alpha = \{x \in R^2 : d(x) = \alpha\}. \quad (5)$$

Thus we obtain a point categorization  $\{E_\alpha : \alpha \in R\}$  of the image with a multifractal spectrum defined as

$$\{f(\alpha) : \alpha \in R\} = \{\dim(E_\alpha) : \alpha \in R\}. \quad (6)$$

The density function describes how locally the measurement  $\mu$  satisfies the power law behavior. It measures the non-uniformity of the intensity distribution in the square  $B(x, r)$ . It should be noted that in this method the measurement  $\mu(B(x, r))$  is the sum of intensity pixels in the square. The density  $d(x)$  is obtained as the slope of the line fitted to the data  $\{\log r, \log \mu(B(x, r))\}$  by the least square method. Then we take a discrete

set  $\{\alpha_i\}$  from an interval and find for each  $\alpha_i$  the point set  $E_{\alpha_i}$  according to (5). This set contains all the pixels whose densities are close to  $\alpha_i$ . The example of such a set near the source image is shown below with  $\alpha_i \in (1.5, 1.6)$ . The fractal dimension  $f(\alpha_i)$  is computed as the slope of the line fitted to the data  $\{\log \frac{1}{\delta}, \log N(\delta, E_{\alpha_i})\}$ , where  $N(\delta, E_{\alpha_i})$  is the smallest number of sets of diameter less than  $\delta$  that cover  $E_{\alpha_i}$  (i.e. as box dimension).

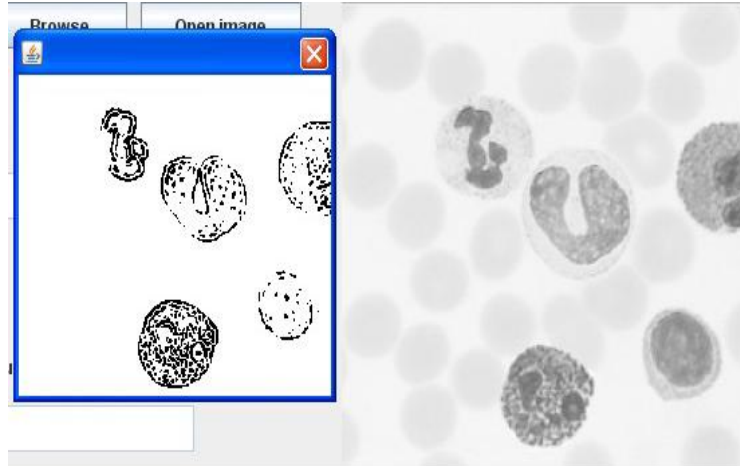


Fig.1 The example of  $E_{\alpha}$  set with  $\alpha_i \in (1.5, 1.6)$

## 2.4 MFS direct determination — moment based method

Let  $p_i(r)$  be a normalized measure of the  $i$ th box (the sum of box pixel intensities divided by the sum of all pixel intensities),  $i \in [1, N]$ ,  $r$  is the box side. Construct a one-parameter family of normalized measures  $\mu(q)$ , where for  $i$ th box  $\mu_i(q, r) = \frac{(p_i(r))^q}{\sum (p_j(r))^q}$ .

According to [3] the Hausdorff dimension of the support of  $\mu(q)$  is given by

$$f(q) = \lim_{r \rightarrow 0} \frac{\sum_{i=1}^N \mu_i(q, r) \ln \mu_i(q, r)}{\ln r} \quad (7)$$

In addition we can compute the average value of the exponent  $\alpha_i = \frac{\ln p_i(r)}{\ln r}$  as

$$\alpha(q) = \lim_{r \rightarrow 0} \frac{\sum_{i=1}^N \mu_i(q, r) \ln p_i(r)}{\ln r} \quad (8)$$

Thus, both  $\alpha$  and  $f(\alpha)$  may be obtained as explicit functions of the parameter  $q$ .

## 2.5 Regny spectrum calculation

Consider an irregular object embedded into Euclidean space and divide it into  $N$  boxes of sizes  $l_i \leq l, i = 1, \dots, N$ , where  $l < 1$  and the size of the object equals 1. Let  $\{\mu_i\}$



be a probability measure defined on the partition. Suppose that  $\mu_i \sim l_i^\alpha$ , where  $\alpha$  is a scaling value that can take the values from some range with a probability density  $\rho(\alpha)l^{-f(\alpha)}$ , and so the probability to get  $\alpha$  from an interval  $(\alpha', \alpha' + d\alpha')$  is  $d\alpha' \rho(\alpha')l^{-f(\alpha')}$ , and a continuous function  $f(\alpha')$  shows the fractal dimensions of the sets on which the exponents  $\alpha'$  may lie [6].

Now we consider the function  $S(q) = \sum_{i=1}^N \mu_i^q$ . It follows that  $S(q) = \int d\alpha' \rho(\alpha') l^{-f(\alpha')} l^{q\alpha'}$ . When  $l$  is small enough  $S(q)$  is maximal for  $\alpha = \alpha(q)$  such that  $q\alpha' - f(\alpha')$  is minimal. On the other hand it is known [5] that there is a unique finite nonzero function  $\tau(q)$ , such that

$$S(q) \sim l^{\tau(q)}, \quad \tau(q) = \lim_{l \rightarrow 0} \ln S(q) / \ln l$$

and  $\tau(q) = q\alpha - f(\alpha)$ ,  $d\tau(q)/dq = \alpha$ , i.e.  $\tau(q)$  and  $f(\alpha)$  are connected by the Legendre transform.

Regny spectrum  $\{D_q\}$  is defined by the equation  $\tau(q) = (q - 1)D_q$ , where  $D_0, D_1, D_2$  are Hausdorf, information and correlation dimensions respectively.

There are several methods to approximate  $D_q$ . We use the method of coarsening partitions developed in [11]. This method follows the idea supposed in [4] and allows us to obtain multifractal spectrum in the terms  $f(q)$  and  $\alpha(q)$ , and then uses Legendre transform to calculate Regny dimensions. Consider  $K$  partitions of an image into boxes with sizes  $r_k, k = 1, \dots, K$ . Let  $\mu_{ik}$  be a measure of the box  $i$  for  $k$ th partition. Let  $N_k$  be the number of the boxes in  $k$ th partition for which  $\mu_{ik} > 0$ . Then  $\alpha(q)$  and  $f(\alpha(q))$  may be calculated by the formulas:

$$\alpha(q) \approx \frac{A_k(q)}{\ln r_k}, \quad f(\alpha(q)) \approx \frac{F_k(q)}{\ln r_k}, \quad (9)$$

where

$$A_k(q) = \frac{\sum_i^{N_k} ((\mu_{ik})^q \cdot \ln(\mu_{ik}))}{\sum_i^{N_k} (\mu_{ik})^q}, \quad (10)$$

$$F_k(q) = \frac{\sum_i^{N_k} \left( (\mu_{ik})^q \cdot \ln \left( \frac{(\mu_{ik})^q}{\sum_i^{N_k} (\mu_{ik})^q} \right) \right)}{\sum_i^{N_k} (\mu_{ik})^q} \quad (11)$$

For a fixed  $q$  values  $A_k(q)$  and  $F_k(q)$  are calculated for all  $K$  partitions. Hence in coordinate systems  $(A_k(q), \ln r_k)$  and  $(F_k(q), \ln r_k)$  there are  $K$  points that have to be approximated by a straight line. Using above formulas and the least-squares method we obtain  $\alpha(q), f(\alpha(q))$ , then  $\tau(q)$  and  $D_q$ .

(It is easily to see that accurate within designation formulas (9)-(11) give approximate values for  $\alpha$  and  $f(\alpha)$  defined by (7) and (8).)



### 3. NUMERICAL EXPERIMENTS

#### 3.1 Modified fractal signature method

Surface areas were calculated for some kinds of connective tissues of animals. The picture shows the images and the graphic illustrates the dependence of normalized surface area on the size of the partition box. Partitions into boxes are chosen depending on the size of the image. Method demonstrates good separability of values for different classes of tissues.

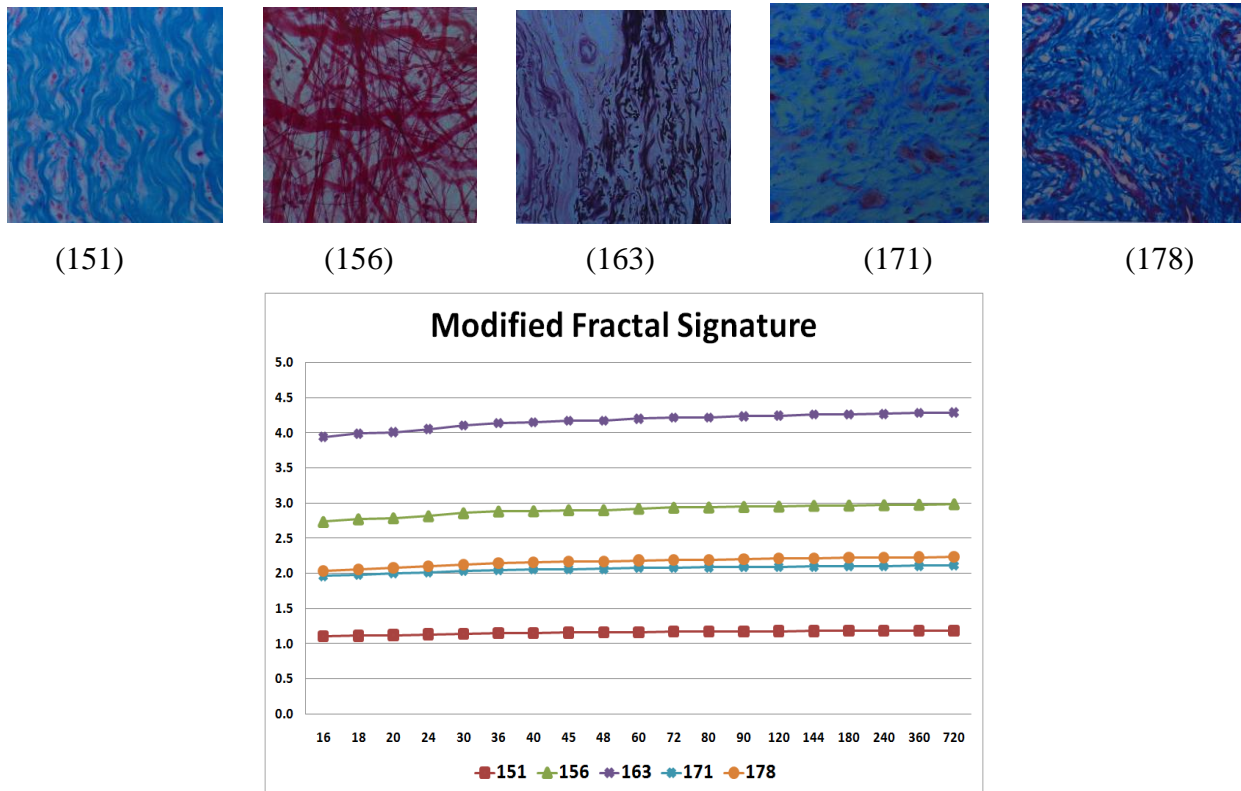
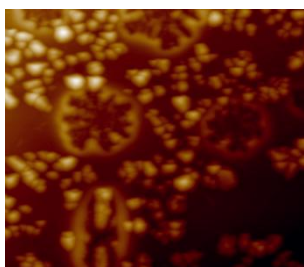


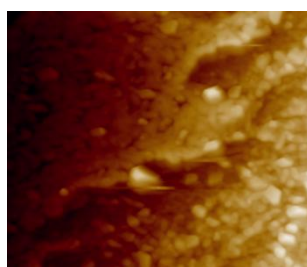
Fig. 2. Normalized surface area values for 5 types of connective tissue.

#### 3.2. Regny spectrum calculation

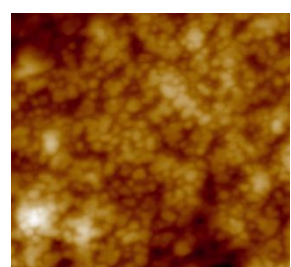
We used images of pharmacological solutions of Ag with different concentrations — zero, small and large. The images were obtained by atomic-force microscope. For every image Regny spectrum was calculated for  $q = 0, 1, 2, 3, 4, 5, 10, 20, 30, 40, 50$ . The box measure is defined as light level of the box concerning to the number of light pixels of the whole image.



Large



Small



Zero

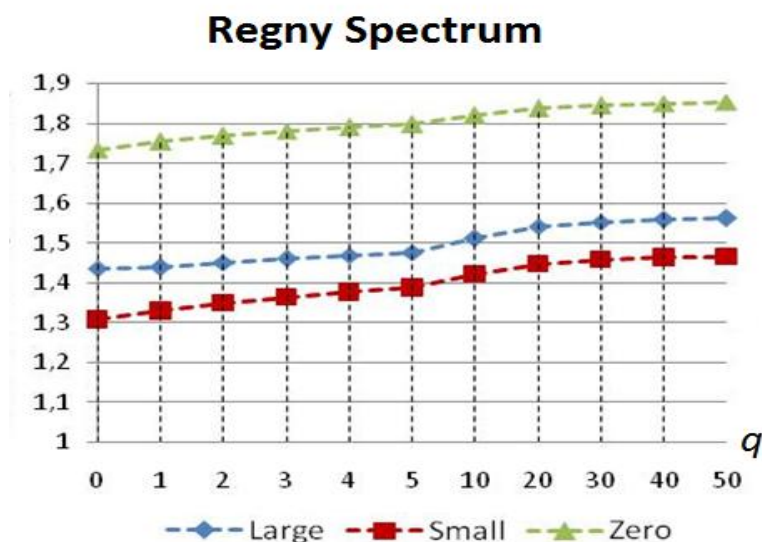
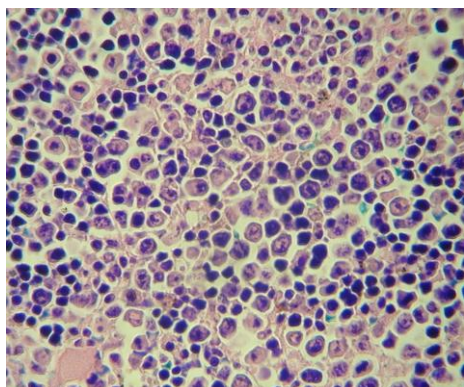


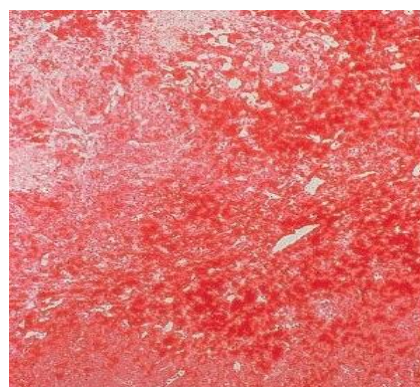
Fig. 3. Regny spectra for Ag solutions with different concentrations

### 3.3 MFS direct determination using level sets

Multifractal spectra were obtained for histological preparations — health and affected liver, and the graphic illustrates their spectra.



Health liver



Affected liver

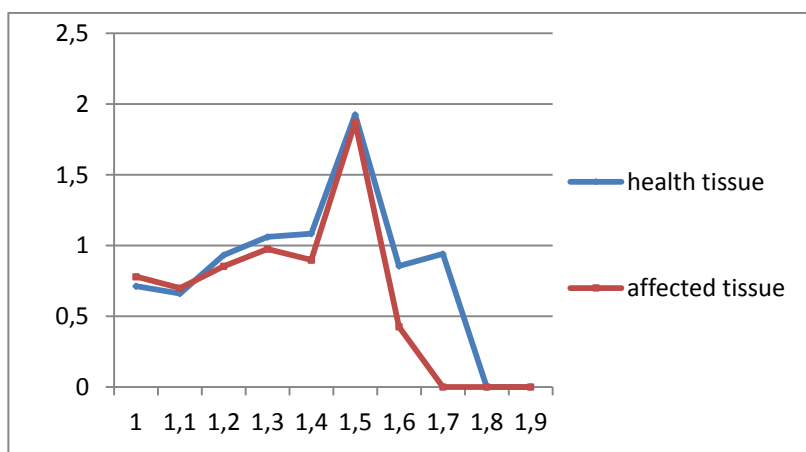
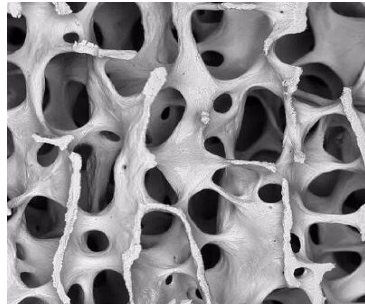


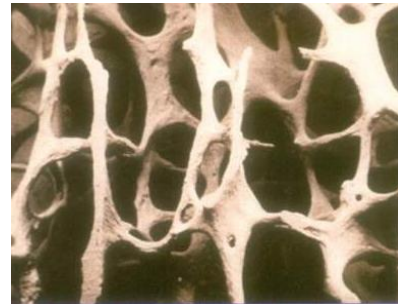
Fig.4. Liver preparation images. Graphics  $f(\alpha)$  obtained by the calculation level sets

### 3.2. Moment based method

Multifractal spectra based on the Moment Method were calculated by using formulas (7),(8) for images of 4 classes of biomedical preparations. The most reliable results were obtained for bone tissue and histological preparation images.



Health bone tissue



Affected bone tissue

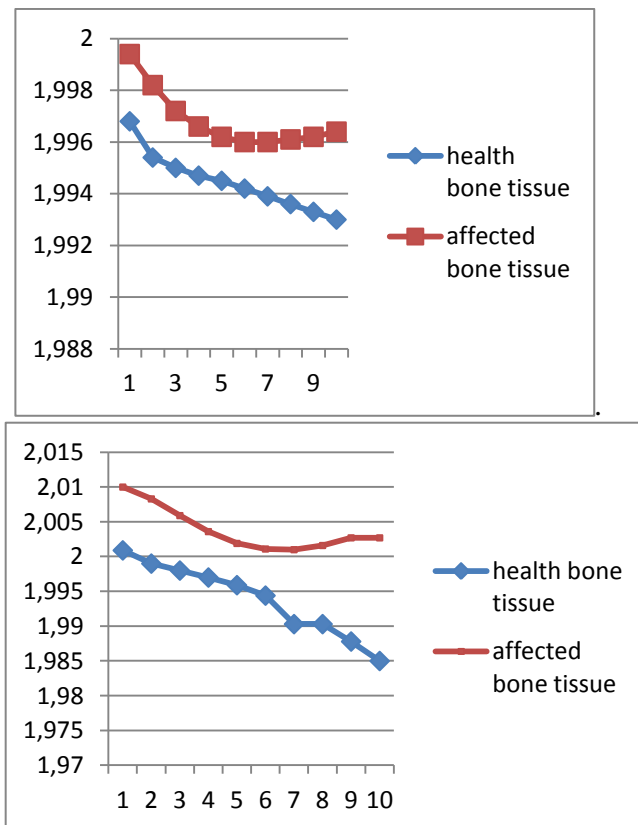


Fig.5. Bone tissue preparation images. Graphics  $\alpha(q)$  and  $f(q)$  obtained by the moment based method.

### CONCLUSION

The results of experiments show the high efficiency of Modified Fractal Signature method for all the classes of images. The MFS direct determination allows us to classify the images of histological preparations, connective tissue and bone tissue. At the same time Regny spectrum method did not demonstrate reliable results for histological preparation images.

## Acknowledgements

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