Polytehnic University of Bucharest
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Doctoral Thesis
Utilizing fractal analysis in early diagnosis and increasing the confidence level of neuroimaging

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- Fractal analysis;
- Lacunarity analysis;
- Conectome;
- Tract reconstruction;
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Introduction

The intuitive understanding of a process or physical phenomenon starts with observation, then after we have observed the phenomenon, we postulate the causal chain of events that made our observation possible and then after we have a satisfactory causal model we test our theory trying to replicate the observed phenomenon.

The rigor necessary to create a satisfactory model, able to express and integrate all the details and nuances of physical observation led people to the development of a mathematical apparatus capable of describing schematically and as completely as possible the studied physical phenomenon.

Thus, the proposed purpose of this paper is to illustrate the evolution of a physical phenomenon from observation, to the application of exotic phenomenological nuances of the process inside devices, as well as the possibility of a deeper understanding of the world around us by applying the model observed in -a series of new parameters in order to highlight some initially hidden behaviors.

The object of this study evolved from determining topographic features from MRI images using fractal analysis to extracting anatomical features from EEG signals using gap analysis.

During the paper, various experimental applications of lacunar analysis were explored, focusing on the idea that lacunar analysis can be used to reconstruct morphofunctional / structural features of the brain.

First experimental Application

FRACTAL ANALYSIS OF NEUROIMAGISTICS. LACUNARITY DEGREE, A PRECIOUS INDICATOR IN THE DETECTION OF ALZHEIMER'S DISEASE

1. Introduction

The healthy human brain contains tens of billions of neurons, specialized cells that process and transmit information via electrical/physical and chemical signals. Most neurons have three basic components: a cell body, multiple dendrites, and an axon, respectively.

The function and survival of neurons depend on several key biological processes. Neurons are a major player in the central nervous system, but other cell types are also key to healthy brain function. In fact, glial cells are by far the most numerous cells in the brain, outnumbering neurons by about 10 to 1. These cells, which come in various forms-such as microglia, astrocytes, and oligodendrocytes- surround and support the function and health of neurons [1].

The healthy brain is well studied, with reference works available to the general public. We will not deal with this in our article. We will study here a serious problem that arises when the brain gets sick, one way or another, and the nature of the disease must be discovered and healed. And last but not least, whether it is a malign or benign disease, if it is curable with the existing therapeutic means or not, would also be investigated. A question in itself refers to the fact whether we can discriminate if the disease affects only isolated neurons, whole neurons or the brain, in its assemblage. The answer is obtained by the fractal analysis of the images taken on the brain, or the so-called neuroimagistics domain under discussion.

The development of magnetic resonance imaging (MRI) techniques has defined modern neuroimaging. Thereby, since its inception, tens of thousands of studies using techniques such as functional MRI and diffusion weighted imaging have allowed for the non-invasive study of the brain [2].
Fractal analysis is a way of measuring phenomena when the details of design are as important as gross morphology. It has been applied to fields as diverse as music, finance [3], materials technology [4-8], and search and rescue, in addition to topics such as signal processing (EEG/ECG), diagnostic imaging, tumor morphology, vasculature [9, 10] and overall brain structure [11, 12].
In particular, fractal analysis is the method by which we investigate medical images, respectively the MRI images. In this effort to obtain the fractal dimension
[13] of the image and the degree of its lacunarity, we can draw firm conclusions about the disease and its stage of development. The disease that is the subject of our research is Alzheimer's disease and its manifestation through the presence of lacunarity, as a measure of its evolution or stagnation so easily evidenced.

As you can see, Alzheimer's appears in the brain images as a lacunar formation. This lacunarity in the brain takes time, and as it grows, leads to the anomalous functioning of the brain, and obviously of the human body.

2. The voxel and parameters of interest

A voxel analogous to a pixel represents image data values, depicted in a 3D space. In the case of medical imaging, the position is represented on the Ox and Oy axes, while on the Oz it is represented in a gray scale the tissue resistance to the incident radiation. More precisely, the black color is being practically transparent to the radiation while the white color represents the reflectivity level.

The medical imagining is not a continuous process, requiring a space of a few millimeters in between the scanned areas, in order to keep the image contrast. The smaller the space in between the

images, the greater the informational density, but there is also the risk of cross-talk (the tissues previously radiated influence the new scanning area). Therefore, one of the essential parameters is the gap between scans, entitled scan density. To optimize the algorithm we have used the standard voxel size of 512x512x12 (the standard voxel size for MRI).

3. The box counting technique

Several methods to measure fractal dimensions and lacunarity have been used. As is well known, the box counting technique implemented in digital image analysis software is employed with priority [14]. As expected, box counting is a way of assessing the distributions of background and non-background pixels in binary digital images representing extracted patterns from the real context of the original image.

The differential box-counting (DBC) method is one of the frequently used techniques to estimate the fractal dimension (FD) of a 2D gray-level image. Undoubtedly, this is a serious development of the classical box counting method, which takes into account the gray scale of the voxels, through the height of the « boxes » which it computes. The parameters introduced are the length, width and height of the boxes, respectively, which are being counted by the algorithm under discussion. Below, we will propose an improved differential box counting method. In their work from 2014, Y. Liu et al. suggested improved DBC method for computing FD of grey scale image [15]. For this reason authors took into account the difference of boxes where the greatest and least intensity value falls. In this regard they took grey scale image of range $M \times M$ in a three dimensional surface plane, where x and y plane represents the pixel location and third plane called z indicates grey level of an image. Then the entire number of pixels has been scaled down to block of size l × l where $M/2 \geq l \geq 1$ and l is an integer denoting box size. Afterwards we have to compute $r = l/M$. For every scaled down block, there is a pillar of boxes of size $s \times s \times s'$, where s' represents height of each box, $G/s' = M/s$ and G is the entire amount of grey levels. Let the least and greatest grey levels be denoted by I_{min} and

I_{max} respectively in the (i, j)th block. Then the total quantity of boxes essential to cover up in z direction is $n_{r\text{old}}$ and after shifting the δ positions from $n_{r\text{old}}$, $n_{r\text{new}}$ is calculated [16].Maximum of $n_{r\text{old}}$ and $n_{r\text{new}}$ is taken as n_r.

The fractal dimension (D_{IDBC}) is calculated with the regression plot between log(N) versus log(1/r).

In overlapping or "sliding" box counting, the number of pixels per box is assessed using for each caliber, rather than a fixed grid, a single element that is systematically moved over the entire image such that the element may overlap with a previous placement at the next placement. The distribution is determined from the number of pixels per box as a function of box size or scale ($\varepsilon\varepsilon$), which is inversely proportional to the box size. Lacunarity at a particular $\varepsilon\varepsilon$ is denoted as λ_S calculated as the squared coefficient of variation, CV, for pixel distribution:

where σ is the standard deviation and μ the mean of the pixels per box at $\varepsilon\varepsilon$ [17].

To arrive at a single number, the values for λ_S can be summarized as the mean $\lambda$for the total number of calibers (E) used:

A normal limitation of box counting is that the pixel distribution depends on how an image is scanned. For some patterns more than others, placing the non- overlapping box counting grid at different orientations yields different results.

4. The convolutional neural network

The convolutional neural network (CNN) consists of an input layer, an output layer and many hidden layers in between. Convolutional Neural Networks are very similar to ordinary

Neural Networks. They are made up of neurons that have learnable weights and biases. Each neuron receives some inputs, performs a dot product and optionally follows it with a non-linearity. The whole network still expresses a single differentiable score function: from the raw image pixels on one end to class scores at the other. In addition, they still have a loss function (e.g. SVM/Softmax) on the last (fully-connected) layer and all the tips/tricks developed for learning regular Neural Networks still apply [18].

- The **Convolution** passes the images through a set of convolutional filters which are being activated as function of some image particularities.
- The **Rectified linear unit (ReLU)** allows the training of the neural network in a more rapid and efficient way, by assigning all negative values to 0 and keeping the positive values. ReLU stands for rectified linear unit, and is a type of activation function. Mathematically, it is defined as $y=max(0, x)$. ReLU is the most commonly used activation function in neural networks, especially in CNNs. If you are unsure what activation function to use in your network, ReLU is usually a good first choice. This process is also called activation, for only the activated characteristics, which are being sent to the next layer.
- **Pooling** simplifies the output through the reduction of the number of parameters necessary for the learning of the network, by using a nonlinear down sampling process. It is common to periodically insert a Pooling layer in-between successive Conv layers in a ConvNet architecture. Its function is to progressively reduce the spatial size of the representation to reduce the amount of parameters and computation in the network, and hence to also control overfitting. The Pooling Layer operates independently on every depth slice of the input and resizes it spatially, using the MAX operation. The most common form is a pooling layer with filters of size 2x2 applied with a stride of 2 down samples every depth slice in the input by 2 along both width and height, discarding 75% of the activations. Every MAX operation would in this case be taking a max over 4 numbers (little 2x2 region in some depth slice).

5. Algorithm of the fractal dimension and lacunarity degree determination

The input of the program is a set of medical images taken in 3 mm slices with a voxel of standard 512x512x12 size. The first step for diagnostic determination is the image processing through the differentiable box counting method (determination of the image fractal dimension as well as the lacunarity degree).
Once we have obtained a value for the image lacunarity, it is important to also see the diffusion/ clustering degree of the lacunar structure. Due to the fact that mathematically speaking the lacunarity is rotation variant, the box counting algorithms to obtain the image lacunarity as well as the diffusion/clustering degree of the lacunarity are ran 4 times with a 90 degrees offset between iterations. The obtained values are averaged to avoid the spikes.
After obtaining the diffusion/clustering degree of the lacunarity, we will isolate the lacunar structure in order to determine its self-standing fractal characteristics (we treat the lacunar structure as a fractal). This step practically allows us for subsequent refinement of the neural network classification process, the isolation allowing for a more rigorous comparison between the lacunar structure and other similar structures sampled from clearly diagnosed Alzheimer patients.
After the comparison of the lacunar structure to the database and the determination whether a similar structure has been generated in a patient carrying Alzheimer’s disease, the data determined from the isolated lacunar structure is added to the data coming from the initial image.
With all the imaging data obtained, the lacunarity degree, the lacunarity diffusion/clustering as well as the fractal characteristics of the lacunar structure itself, the data is then taken by a convolutional neural network for final classification.
Functionally the algorithm starts with an MRI image and does a contour feature extraction. Then using the scale invariant property of the images fractal dimension, we can easily estimate to a certain degree the inner structures of the brain, after some more image processing. This allows us to detect lacunar structures that would normally be hard to detect by eyesight alone. As you can see even with contour feature extraction alone, the differences between the patients and the control subjects are more easily visible.
In Fig. 3 we present the block diagram of the algorithm used to detect structures associated to Alzheimer's disease, estimating the fractal dimension and the lacunarity, according to the program developed below.

```
Excerpt from the program we have
developed Start
Load image       // input the
image M = image.height ,N
= image.width; s = 2; //the
origin size of box While(s
≤ M/2)
If (s < 13||M/s == 0) r = s/M; //define the r , r is
the scale For(i < M/s;j < N/s) nr(i, j) = (CMA ×
pa − CMI × pi)/s × s
Shift block in (x, y) plane with σ pixels nr(i, j) = max(nr old, nr
shift)
En
d
For
En
d If
 Nr old =
 P(nr); s +
 +;
Fit(log Nr, log(1/r)) //the least
square method Obtain FD ;
Lacunarity =( ( Fit(log Nr, log(1/r)))/ (mean(s,g)))^2; //
g is the possile lacunarity
orientations within the box of size s

Plot( Lacunarity)= Lacunarity + 1;

Load Plot(Lacunarity)          //
input the image M =
image.height ,N = image.width;

 s = 2; //the origin size of box

While(s ≤ M/2)

If (s < 13||M/s == 0) r = s/M; //define the r , r is the scale

For(i < M/s;j < N/s) nr(i, j) = (CMA × pa − CMI × pi)/s × s

Shift block in (x, y) plane with σ pixels nr(i, j) = max(nr old, nr
shift)

En
d
```

```
For
En
d If
 Nr old =
 P(nr); s +
 +;
Fit(log Nr, log(1/r)) //the least
square method Obtain FD ;

End;
```

6. Results and Discussion

Lacunarity is another measurement often used in conjunction with fractal dimension to describe the texture of a shape or fractal [20, 21]. In this study fractal dimension and lacunarity measurements were leveraged to differentiate between benign and malignant tissues and to classify the different brain morphologies exhibited by formatted cell lines**.**

For various benign and malignant subtypes, the fractal dimension (Fig.4) and lacunarity (Fig. 5) of benign, biphasic and lacunarity tumor samples were calculated using the program described above. We have considered the normal physiological brain zone as the benign area, the complete mixed zone as the biphasic area, and the tumor itself as the lacunarity area respectively, with a small margin taken from the rest of the tissue.

In the figures below, unique fractal evaluation and connected implications of brain morphology in malignant tissue are shown.

Due to some missing or damaged samples the resulting number of images analyzed was 36 with lacunarity, 19 biphasic and 15 benign controls. As shown in Fig. 4 and Fig. 5, biphasic and lacunarity tissue samples had significantly higher fractal dimension and higher lacunarity compared to benign tissue ($p < 0.0001$).

A low p-value (such as 0.01) is taken as evidence that the null hypothesis can be ‘rejected’. Statisticians say that a p-value of 0.01

is ‘highly significant’ or say that ‘the data is significant at the 0.01 level’.
Although the difference between biphasic and lacunarity tissue was not found to be statistically significant, lacunarity tissue tended to have a comparable fractal dimension, but it encountered higher lacunarity of lacunarity tissue than biphasic tissue. These results suggest that fractal dimension and lacunarity analysis may be a useful and rapid method to differentiate between benign and malignant tissues.

7. Conclusions and future work

In this paper, the brain radiographies were analyzed to find out the fractal dimension and lacunarity of benign, biphasic and lacunarity tumor samples. For this purpose, the radiographies were processed in the manner presented in a previous chapter of present work, to remove the noise and just keep the formatted cell lines. Then, the neuro-image was transformed into binary format and the differential box- counting (DBC) method was applied to reach the results.
The algorithm used to detect structures associated to Alzheimer's disease, estimating the fractal dimension and the lacunarity, has been developed by the authors.

Between the biphasic and lacunarity tissues a statistically significant difference was not found, as lacunarity tissue tended to have a comparable fractal dimension, but it encountered higher lacunarity of lacunarity tissue than biphasic tissue. These results suggest that fractal dimension and lacunarity analysis may be a useful and rapid method to differentiate between benign and malignant tissues.

Therefore, both fractal dimension and lacunarity demonstrated high accuracy as predictors of benign and malignant tumor and to classify the different brain morphologies.

The software developed in this paper can be fully integrated into a medical equipment, which can be used in detection and monitoring of brain diseases or other organs.

Second Experimental Application

Fractal analysis study of the axonal tracts

MRI IMAGING - HISTOLOGICAL INTERPRETATION

Magnetic resonance imaging (MRI) is an investigation procedure of the internal structure of the body that has many applications, especially in the medical field. Through this method, sections of the human body are obtained in the form of images, where various anatomical structures are rendered in different gray shades, depending on the chemical composition of tissues and the method of obtaining the data.

The MRI imaging protocol involves a series of repetitive radio pulses with a certain frequency, which differs depending on the study methods (T1 or T2), followed by the

measurement of the echo resulting from the relaxation of the nuclei (Figure 1). Differences between tissues in the NMR signal are due to the density and mobility of hydrogen atoms, mainly found in water molecules. Thus, in T1 it is observed that dark areas correspond to water-rich tissues, bone tissue or cerebrospinal fluid, whereas the luminous areas overlap with areas where there are mainly fats. With T2 imaging, hydrated areas and bones will be brighter, while greasy areas will appear brighter [1].

The main types of tissues that can be seen in a cerebral MRI scan are nervous tissue, bone tissue, meninges, blood vessels, and areas filled with cerebrospinal fluid. Nervous tissue is made up of neurons and auxiliary cells, called glial cells. The neurons are formed from neuronal bodies and elongations, dendrites and axons, the latter being very long and often surrounded by auxiliary cells called Schwann cells, which secrete a fatty substance called myelin. In the nervous system, segregation of neuronal bodies and neuronal elongations in different areas is most often encountered. The place where the neural bodies are found is called gray matter, and the place where neuronal elongations are found is called white matter, because the white matter areas appear lighter in the open eye view of a tissue section.

White areas appear lighter because the axonal elongations here are surrounded by the myelin sheath, that maintains electrical isolation and which is lipidic and white in nature. For this reason, in T1 MRI scans the white matter appears lighter than the gray matter due to the presence of lipids, while in T2 the gray matter is lighter in color than the white one. In addition, bone tissue appears light in T1 and dark in T2, and cerebrospinal fluid, due to the water content appears darker in T1 and luminous in T2 [2].

In order to be able to interpret MRI scans in clinical contexts, it is necessary to know how the tissues affected by illnesses are rendered in these images in terms of brightness. These anomalies can easily be detected when they appear in images as brighter or darker than the surrounding nervous tissue. Thus, they may be characterized as hyperintense when brighter than other infected areas, hypointense, when they are darker and isointense when they do not have a significant difference from the rest of the body's nervous tissue. (Figure

2, in affected tissues). For example, in T2, a meningioma surrounded by edema appears whiter than the surrounding areas, while a meduloblastoma appears darker in a T1 image [2]. The conditions that may appear hyperintense in T1 imaging are subarachnoid haemorrhages, tumors and acute stroke. Areas that appear darker in T1 may be edema, ischemia, and subacute stroke. However, T2 imaging is more often used to detect pathological aspects in MRI images where better contrast of these affected areas is obtained. Both tumors and cerebral infarction, ischemia and edema appear brighter in these areas [2]. These aspects are very important for the present study because a hyperintense or hypointense region can be completely or partially eliminated from the processed contour image, and will have other morphological characteristics (it will present lacunarity) [3], another symmetry and, implicitly, another fractal dimension. But even if the affected areas are taken into account, the fractal dimension can be affected because these areas have structural abnormalities.

ANATOMICAL CONSIDERATIONS

The anatomical structures subjected to fractal analysis in this study are the brain cerebral white matter traces extracted from MRI scans. Due to the limited spatial resolution of MRI imaging, best suited for this study are the major connections between cortical or specialized cortical areas, cortex and subcortical structures, as well as connections involving the claustral area, which is an important connectivity node.

The main white matter formations that can be highlighted by MRI scan processing mostly involve connections to the cerebral cortex. These formations are of three types depending on the cortical areas with which they are connected [4]:

- Association fibers - fibers that connect cortical areas in the same brain hemisphere
- Commissural filaments - fibers that connect homologous areas of the two brain hemispheres, such as those connections that make up the Corpus Callosum
- Projection fibers - fibers that connect the cortex with subcortical areas. They have a radial arrangement in the brain, which is why they are called "Corona Radiata" [4].

Finally, the ventricular system of the brain consists of empty spaces filled with cerebrospinal fluid. For a correct interpretation of MRI images by the fractal analysis algorithm, these empty spaces should not be confused with other brain structures, but they should be taken into account because their size may vary in various brain-related disorders [2].

Purpose of the study

Areas of interest for the present study are the white matter areas, which represent the axonal prolongations of the neurons. If at the cellular level these extensions are made between neurons (connections called synapses), macroscopically, the white matter areas form connections between different areas of gray matter through a series of axonal tracts. MRI imaging does not provide a sufficiently good spatial resolution to easily delineate these cordons in the white matter mass, and therefore this paper proposes an approximation of the major connectivity pathways, starting from the morphological characteristics of the white matter using the skeletonisation algorithm. These trajectories thus extracted will be subjected to fractal analysis to identify distortions associated with pathologies. To validate the

structure of these major connectivity pathways, the study aims to make future correlations with diffusion MRI data (DTI or DSI).

Description of the algorithm

To extract the information needed for fractal analysis, it is necessary to understand the structure of Neuroimaging Informatics Technology Initiative (NIFTI) files. The internal structure of this file type (extension ".nii") contains both a metadata header and the image itself. Also, the file can be compressed or not with the DEFLATE algorithm. If the file is compressed, it will have the extension ".gz". Using the header fields we can extract information about the transformations

used, the size of each voxel, the units of measurement used to describe the size, the applied image rotation and the beginning and end index of the slice, to generate a three-dimensional vector (or quadri-dimensional vector for functional MRI images where the storage of several images arranged sequentially, separated by a defined time interval is required) that can further be processed for fractal analysis.

In order to efficiently process MRI images in fractal analysis, a pre-processing stage is required. The goals of this stage are:

- masking the region of interest by filtering the skull
- noise reduction (for functional MRI images)

STRUCTURAL MRI SCANS PROCESSING

The first step in processing this type of MRI images is to filter the skull to highlight the gray matter area. For this purpose, it is necessary to overlay the mask pattern for gray matter, MNI152, over the original image, only voxels intersecting the mask being retained. The MNI152 model is a symmetrical brain image formed by applying 6 iterations of linear and non-linear transformations over 152 T1 anatomical MRI images. After applying the mask, in some cases, a part of the skull will remain unfiltered. To eliminate this unwanted area, due to the discontinuity between the gray matter area of the brain and the skull part left after applying the first filter, we apply a filter that only keeps the largest voxel-connected region.

The processing algorithm is comprised of the following stages:

- Separation of MRI scan in 2D constituent slides, taken on the axial plane
- Binarizing each slice (switching from a monochromatic image to a binary image) by applying a hysteresis threshold filter. This filter keeps the pixels that have a value greater than a threshold defined as a parameter of the filter, called the high threshold. The next criterion is to preserve the areas of the image connected by the regions in the image that passed the first criterion and which, at the same time, have a value greater than another threshold, called the low threshold
- Skeletonization of each slice of the image by successive application of the thinner operator
- Estimation of the fractal dimension using a box-counting algorithm

Bidimensional skeletonization is a binary image processing method that largely preserves the connectivity of the

structures present in the original image, eliminating redundant information by approximating the brain connections with a series of minimal width segments (Figure 3). These features make skeletonization a useful process to apply in the fractal geometry study of an image. The skeleton image is generated by iteratively applying a thinning operator to the binary image until convergence is reached, the stage when the operator application does not change the image [5].

The three-dimensional algorithm retains many of the features of the two-dimensional one. Differences consist in the use of a three-dimensional structuring element defined by a 3x3x3 size array and the application of the algorithm over the entire volume of voxels, unlike the two-dimensional algorithm that is applied individually to each constituent slice (Figure 4) [6]. Thinning is accomplished by iteratively applying the hit-and-miss transformation operation from the original image. This transform uses a 3x3 matrix called the structuring element, translating its origins successively over all the pixels in the original image, and comparing the structuring element with the matrix of the same size formed by the pixels below it. If the two matrices are equivalent, the pixel underlying the structuring element will take the value 1, otherwise it will take value 0.

FUNCTIONAL MRI SCANS PROCESSING

The connectome of a functional MRI image (Figure 6) highlights the dependence (or lack of dependence) in brain activity between brain regions. It is displayed in a graph form where the nodes represent regions of the brain and the lines represent the interactions between them [7]. Due to their inherent nature, the processing of functional MRI scans requires a different approach to the preprocessing of anatomical MRI images. The first step is to generate a mask that will filter the signals outside the gray area. The mask is constructed taking the average of the whole series of images, followed by an approximation of the region of interest by edge detection. The mask application is then applied to each image in the series.

Applying a Gaussian filter to each image in the series results in a noticeable reduction of noise through blurring. Applying this filter, however, has the disadvantage of reducing spatial details. Therefore, the filter is applied in a conservative way, making a compromise between noise reduction and preservation of spatial detail of the image. One

way to estimate a patient's connectome is to extract the covariance matrix (Figure 5) to determine the activity correlation between different regions of the brain. However, this approach has disadvantages that reduce its viability. First of all, a simple correlation between two cortical regions is not enough to determine with certainty their interdependence [8]. Also, there is a high probability that two regions will have at least a reduced correlation, which leads to overcrowding of the graph and further difficult processing. A better method of extracting the functional connectome is by generating the inverse (precision) covariance matrix. This array highlights the dependence of each region on the other nodes, which is an indicator of statistical utility greater than covariance in the connectivity analysis. For estimating the precision matrix, the lasso method is used [9].

CONCLUSION

Despite the limited resolution of the MRI images used, the two-dimensional skeletonization of the axial plane slides as well as the three-dimensional skeletonization of the entire MRI imagery satisfactorily approximates the overall connectivity of the areas of interest. The algorithm used can be applied later with minor modifications in the analysis of other structures that lend themselves to this type of approach, such as the study of blood vessels, lungs, skeleton, etc. The property of this method of highlighting the morphological connectivity of a structure can make it useful even in various engineering applications.

Third experimental application

EXTRACTIONS OF INTRINSIC FEATURES USING THE LACUNARITY HIGHLIGHTED FROM FMRI SOURCES

1. Introduction

The human brain is one of the most complex systems observed in nature, and the phenomenological simultaneity of physical, chemical and electrical interactions presents a series of problems in continuous research, starting, without question, from mapping how our brain interacts with reality. To solve this problem, multiple software / programs have been developed on the computer and thousands of visualizations of brain processes have been implemented, among which we list EEG (Electroencephalography), MRI (Magnetic Resonance Imaging) and FMRI (Functional Magnetic Resonance Imaging) brain scan [1-2].

Among other nicknames used in place of MRI (Magnetic Resonance Imaging), we can mention that the most common other names are some of the following accepted synonyms, such as nuclear magnetic resonance imaging (NMRI) and magnetic resonance tomography (MRT).

Magnetic resonance imaging (MRI) is a medical imaging technique used in radiology to form pictures of the anatomy and the physiological processes of the body. MRI scanners use strong magnetic fields, magnetic field gradients, and radio waves to generate images of the organs in the body. MRI does not involve X-rays or the use of ionizing radiation, which distinguishes it from CT and PET scans [3]. MRI is a medical application of nuclear magnetic resonance (NMR) which can also be used for imaging in other NMR applications, such as NMR spectroscopy.

Historically speaking, the prime researcher who has developed a way to generate the first Magnetic Resonance Images (MRI), in 2D and 3D, using gradients, was American chemist Paul Lauterbur, in 1973. More precisely, Lauterbur described an imaging technique that removed the usual resolution limits due to the wavelength of the imaging field, laying the foundations of MRI technique [4].

The purpose of this paper is thus easy to state and refers to exploring the hypothesis of using the analysis of lacunarity in order to determine the degree of correlation with the topological structures (fractals) existing in the brain.

In order not to compare apples to pears (as funny it is expressed with concern), it is assumed that the lacunarity is a measure of the discernibility of a structure or signal, i.e., more precisely, the larger the lacunarity (more empty space) the easier to distinguish an object from its background, and the opposite case, when the lacunarity is low (dense space), it is even more difficult to distinguish an object or signal from its established background [5-6]. The results of fractal and lacunarity analyzes, in the case of FMRI images, are predictable fixed values, as we expect, by the way.

We will explore the relevance of MRI in the characterization and diagnosis of pathology and diseases of the brain, especially in relation to strokes and dementia. We will also review the imaging sequences and post processing applications available for exhaustive examinations of the brain [7].

2. Some of the FRMI procedures

As stated above, we mention it once again, but with immediate application on the subject of this article. Thus, as it has become commonplace in the medical world, nuclear magnetic resonance imaging it is first and foremost a method of investigating the internal structure of organs that has applications especially in the medical field.

Through this method, sections are obtained through the human body in the form of images, where the various anatomical structures are rendered in various shades of gray, depending on the chemical composition of the tissues and the method of obtaining data. Magnetic resonance images can be obtained by several methods, below are the methods T1 and T2, of interest for the present study.

A MRI device consists of a series of coils, located in a cylindrical chamber, thermally and magnetically insulated, in the center of which the patient will sit. From outside to inside the main components are the following [8]:

- a superconducting electromagnet, cooled with liquid helium, which emits a constant and high intensity magnetic field,

- a series of coils that can emit gradient magnetic fields, in the 3 spatial directions, important for locating the NMR signal,
- a coil for transmitting or receiving radio signals.

The high-intensity magnetic field produced by the superconducting coil orients the hydrogen nuclei in the patient's body in two directions of spin, which correspond to different energy levels [8]. Under these conditions, there is a surplus of nuclei oriented in the direction of the magnetic field, characterized by its own magnetic field, much weaker. Under the influence of radio waves, the nuclei aligned with the magnetic field lines can be excited at the higher energy level, antiparallel, if the radio frequency corresponds to the Larmor precession frequency of these nuclei, thus they resonate [9].

The working protocol in MRI imaging involves a series of repeated radio pulses with a certain frequency, which differ depending on the study methods (T1 or T2), followed by measuring the echo resulting from the relaxation of the nuclei. The differences between the tissues in the NMR (Nuclear Magnetic Resonance) signal are due to the density and mobility of hydrogen atoms, mainly found in water molecules. Thus, in the T1 method it is observed that dark areas correspond to tissues with a higher degree of hydration, bone tissue or cerebrospinal fluid, while light areas overlap with areas where there is mainly fat. By T2 imaging, hydrated areas and bones will be brighter while areas with fat will appear brighter [10].

Fig. 1. Calculation graphical method of T1 and T2

In Figure 1 a calculation graphical method of T1 and T2, (T1 recovery in blue color and T2 decay in black color) is represented.

2.1 Tissue types observed by medical MR imaging

The main types of tissues that can be observed in brain MRI are nerve tissue, bone tissue, meninges, some blood vessels but also areas filled with cerebrospinal fluid. Nerve tissue is made up of neurons and auxiliary cells, called glial cells. Neurons are made up of neural bodies and extensions, dendrites and axons, the latter being very long and often surrounded by helper cells called Schwann cells, which secrete a substance called myelin. In the nervous system there is most often a segregation of neural bodies and extensions in different areas. The place where neuronal bodies are found in particular is called gray matter and the place where extensions are found is called white matter, because areas with white matter appear lighter in color when observing a section through tissue with the naked eye. Areas with white matter appear lighter in color because the axonal extensions present here are surrounded by the myelin sheath, which plays a role in electrical insulation and which is lipidic in nature and whitish in appearance. Also for this reason, in T1 MRI imaging the white substance appears lighter in color than the gray matter, due to the presence of lipids, while in T2 imaging the gray matter is lighter in color than the white one. In addition, bone tissue appears light in color in T1 imaging and dark in T2 and cerebrospinal fluid, due to its water content, appears darker in T1 and brighter in T2 [11].

The areas of interest for the present study are the white matter areas, which as stated above represent the axonal extensions of the neurons. If through these extensions connections are made at the cellular level between neurons (connections called synapses), at the macroscopic level, the areas of white matter form connections between different areas of gray matter through a series of axonal cords. MRI imaging does not provide a good enough spatial resolution to easily delimit these cords in the mass of white matter and therefore this paper aims to approximate the major pathways of connectivity, starting from the morphological characteristics of the white matter, using the method of skeletonization. These trajectories thus extracted will be subjected to fractal analysis in order to identify distortions associated with certain pathologies. In order to validate the structure of these major connectivity pathways, the study aims to correlate in the future with the data obtained by diffusion imaging (DTI or DSI).

Another type of tissue successfully investigated by MRI was lung tissue, after the systematic application of the skeletonization procedure, in what can be called, without modesty, a new way in fractal analysis of pulmonary medical images [12]. The work gathered, in two years from the publication, a record number of citations.

3. Fractal analysis of MR images

Diverse methods have been used successfully to evaluate the lacunarity [13] and fractal dimensions [14-15]. The ones utilized in this paper engage the box counting mechanism implemented in digital image analysis software. We have written about the fractal dimension and how it is calculated in countless works. We will make a brief report only about measuring the lacunarity of an MR image, especially about its mathematical part [16-18].

Lacunarity at a certain value ε indicated as λε, is considered as the squared quotient of variation, CV, for a real pixel distribution obtained where σ is the standard deviation and μ the mean of the pixels per box at $\varepsilon\varepsilon$. To arrive at a single number, the values for λs can be summarized as the mean λ for the total number of calibres (E) used:

Fig. 2 shows the general logical scheme for the Fractal Analysis Algorithm of FMRI images, designed for this occasion.

Fig. 2. Logical scheme for the Fractal Analysis Algorithm of FMRI images

This algorithm begins with box counting to determine lacunarity factor and often stops with highlighting the structure associated with Alzheimer's disease.

The algorithm used for the fractal analysis of MRI images is described below (only the beginning and its end). The main part of the agenda/mathematical content is missing, this program being subject to patent action as original software.

Load image

//input the image

M = image.height ,N = image.width; s = 2;

//the origin size of box

.....

…….

Fit(log Nr, log(1/r))
//the least square method Obtain FD ;
End; .

4. Results and discussion

The BOLD (blood-oxygen-level dependent) contrast mechanism has a complex relationship with functional brain activity, oxygen metabolism, and neurovascular factors. Accurate interpretation of the BOLD signal for neuroscience and clinical applications necessitates a clear understanding of the sources of BOLD contrast and its relationship to underlying physiology.

In general, the physiological components that contribute to the BOLD signal are known, and the steady-state BOLD models that enable quantification are calibrated of functional changes, what is constituted in a separate challenge paradigm. The principles derived from these biophysical models are then used to interpret BOLD measurements in different neurological disorders in the presence of confounding vascular factors related to disease.

In Figure 3, theoretical BOLD signal response is represented. Thus we have T2 * on the ordinate (oy axis) and on the abscissa (ox axis) we have the time, measured in seconds.

Note. This graphic representation describes the principal/basic of the BOLD signal in functional Magnetic Resonance Imaging (FMRI). Today, researchers in the medical field use modern FMRI to determine which regions are most active from a neuronal point of view or for detecting changes in the brain's blood flow, at least.

The BOLD signal is a valuable tool for detecting changes in neuronal activity in the human brain.

The graph, represented in the Figure 4, is the histogram of the Bold signals, so on the ox axis it is Raw signal value, and on the oy axis is found the Signal frequency. It is mainly used for choosing the real value of lacunarity threshold.

Observation. Difference between raw value and physical value. The raw value of a signal is the value as it is transmitted in the network. The physical value of a signal is the value of the physical quantity (such as speed, temperature, etc.).

In Figure 5, a fractal and a lacunarity analysis on the map generated by the EEG signal, against the background of the overlapping RMI representation is presented. It can be noted the appearance varies over time due to the Bold signal and the subject going through a series of exercises, which target specific areas of the brain.

In Figure 6, a fractal lacunarity visual analysis on the cerebral map generated, having the areas of interest of yellow color, respectively with an intensity of level 1.68e + 4, as interpreted from the attached color band, located in the range (-1.68e + 4, + 1.68e + 4).

The software program is done through a medical imagining suite taken in 3 mm slices with a voxel of standard 512x512x12 size. The prime step for diagnostic determination is the image processing by the instrumentality of the differentiable package/box counting procedure (for deduction of lacunarity degree, ultimately)

In Figure 7 a recorded electroencephalogram is presented. It is about a graphical representation having on the abscissa (x-axis) the frequency (Hz) and on the ordinate (y-axis), the logarithm of the energy or power ratio (dB) of signal received, respectively.

The electroencephalogram (EEG) is a non-invasive evaluation that detects, potentiates and records the bioelectrical activity of the brain. The neuronal cells that make up the cerebral cortex emit post-synaptic potentials with electrical value that can be taken, recorded and evaluated using an electroencephalogram. The goal of this

investigation is to provide the doctor with information about the electrical activity of the brain in the context of clinical manifestations of a possible brain damage.

The detailed presentation of the designed software was made within the articles found in the bibliography, in a complex but more general way than the one in the present study [19].

5. Conclusions

In the paper, the brain RMI has been analyzed to find out the fractal dimension and lacunarity of benign tumor samples. By easy to understand reasons, the RMN images were processed in the manner presented in an above section of current study to remove the noise and just keep the formatted cell lines. After that, the neuro-image was transformed into binary format and the differential box-counting (DBC) method was applied to arrive of expected results.

The software algorithm developed here, to identify special formations associated to grave Alzheimer's disease, leads at the estimation of the fractal dimension and the lacunarity, with great accuracy. In principle, however, the article develops an algorithm for identifying abnormal structures in the brain, which has happened. These structures were chosen, through MRI pictures / recordings used, from those of patients susceptible to Alzheimer's syndrome. For these reasons, we said that we estimated the fractal dimension and the lacunarity to identify serious Alzheimer's disease. We made a quantitative determination of this disease and expressed a superior diagnosis, as a level of confidentiality!

About it, we can say that it is original and has been detailed in absolute premiere by the authors.

In the end, it can be said that extractions of intrinsic medical features using fractal lacunarity took place, highlighted from FMRI sources.