A SOFTWARE PLATFORM TO ANALYZE MR IMAGES BASED ON 3D FRACTAL DIMENSION

Application in Neurodegenerative Diseases

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Abstract: Previous studies carried out by our group have demonstrated that 3D fractal dimension algorithms detect changes in apparently normal magnetic resonance (MR) images of the brain in patients suffering early stages of Multiple Sclerosis. In addition, 3D fractal dimension has also been demonstrated to be useful for detecting brain abnormalities in other cerebral diseases, as in Alzheimer's disease and in children born after intrauterine growth restriction. Thus, 3D fractal dimension detection has been proposed as a valuable and powerful diagnostic tool. To our knowledge, no user-friendly software is available to obtain the 3D fractal dimension of volumetric MR images. In this paper, we present an optimized Web platform that allows computing the 3D fractal dimension value for uploaded MR images in an interactive user-friendly way. Moreover, and because the computational cost of the involved algorithms is very high for interactive use, we have focused our efforts on the optimization of the appropriate algorithms using the parallel computing power of current GPUs and multi-core CPUs.

1 FRACTAL DIMENSION

A geometry object self-similar at different scales is a fractal. Fractals are described by fractal geometry, which was first proposed by Benoit Mandelbrot (Mandelbrot, 1983). In contrast to Euclidean geometry, where the dimension value is 1 for a line, 2 for a plane and 3 for a volume, fractal dimension (FD) is a non-integer number that characterizes an irregular shape. Thus, FD is 1 for a straight line, but it has a value between 1 and 2 for an irregular line; however, the Euclidean dimension is 1 for both a straight line and an irregular one. With this simple example, we may figure out how the FD describes a natural object in a better way than Euclidean dimension does. Fractal theory has also been proposed as an unifying theory for different results in biomedical research that previously were apparently not related among them (West et al., 1987).

One accepted procedure to obtain the FD of an object, in a metric space, is the box-counting method. It is based on cover the object with grids of boxes with different sizes, and, for each size, to estimate how many boxes are filled by the object. (Hou et al., 1990).

2 FRACTAL DIMENSION IN NEUROLOGICAL DISEASES

The characterization and quantification of the brain morphology using FD analyses, in health and disease, is getting increased attention and interest from the biomedical community. Most recent studies focus on 2D analyses from individual MR or SPECT images (Zhang et al., 2008), where the two-dimensional FD (2DFD) no longer fulfils the complexity of the structure. To obtain the 2DFD, general and wide-use image analysis programs are available, such as *ImageJ* (http://rsb.info.nih.gov/ij/), and even others more specific for FD calculation such as *HarFA – Harmonic and Fractal Image Analysis* (http://www.fch.vutbr.cz/lectures/imagesci/).

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The cortex of the human brain is highly convoluted, and structural changes in this complex region has been related to developmental disorders (for example, epilepsy or cerebral palsy), and also associated with neurodegenerative diseases such as Multiple Sclerosis or Alzheimer's disease. Even thought some of these alterations are easily detected in MR and computerized tomography (CT) images, many of them consists of subtle structural changes difficult to detect and quantify. As previously suggested (Fernández and Jelinek, 2001), FD is a good quantitative descriptor of not only the convolutions of the cerebral cortex but also the white matter. Thus, the structural brain abnormalities taking place in several diseases can be revealed by changes in its FD (Thompson et al., 1996; Kiselev et al., 2003; Liu et al., 2003). Moreover, and as stated before, FD approaches are particularly useful to detect those subtle changes that cannot be conventionally identified in MR images (Free et al., 1996), and to characterize disorders without an apparent structural abnormality of the brain matter, such as schizophrenia and obsessive-compulsive disorders (Ha et al., 2005). Until now, most studies has been focused to obtain the 2DFD of MR images of specific coronal sections, and some authors even did a step ahead developing pseudo-3D extrapolations. Thus, no so much efforts have been made in the three-dimensional FD (3DFD) structural characterization, an approach that may include relevant information otherwise lost in the study. In this sense, FD changes of the aged white matter have been detected both in MR images both at the pseudo-3D level and in 3D (Zhang et al., 2006; 2007).

Multiple Sclerosis is a neurodegenerative disease mainly characterized by the appearance of white matter lesions. The different manifestations of the disease can be associated with its progression and, because the onset of symptoms and the development of visible damages in the MR images are related, an early detection of the structural alterations of the brain are crucial for clinical making decision including an appropriate treatment. The most critical to detect are the early stages of Multiple Sclerosis, in which the white matter appears as apparently normal in the MR images, even thought some of the underlying cellular and molecular processes are taking place (inflammatory cellular infiltration, axonal degeneration and even gliosis). Magnetization transfer imaging has been proposed as a promising method for detecting changes in apparently normal white matter in Multiple Sclerosis. However, this method not only shows some contradictory results in terms of their sensitivity, but it is also expensive and difficult to be included in the daily clinical diagnostic procedures in most hospitals (Filippi et al., 1999). Our research group has recently demonstrated that changes in both the white matter (Esteban et al., 2007) and grey matter (Esteban et al., 2009) are well-characterized by the FD (2D and 3D respectively) using MR images which are apparently normal in early stages of Multiple Sclerosis. This approach has been proposed as an useful tool for an early diagnostic of the disease and, therefore, clinical decision making. In addition, we have also detected changes in the 3DFD of the brain in one year-old children who had intrauterine growth restriction (IUGR), when compared with premature infants without IUGR and full-term controls (Esteban et al., 2010).

3 COMPUTER GRAPHICS, VOLUME MODELLING AND ALGORITHM OPTIMIZATION WITH GPU

Volume modelling is an important area of Computer Graphics. Volume modelling gives solutions based on the description of the volume occupied by the represented objects, instead of the traditional representation based on the surface. An important effort to provide biomedical applications is being developed in this area, mainly in 3D modelling and visualization of scientific data obtained from techniques such as CT, MR imaging or microscopy (Muraki and Kita, 2006).

Just as the pixel is the basic element in a 2D image, the voxel is the basic unit for representing 3D volumes. Thus, volume modelling focuses on providing techniques related to the construction, processing and display of real structures by using voxels. As commented above, the most generally accepted approach for calculating the 2DFD is the so-called box-counting method. Following the same principles, calculating the 3DFD implies the construction of the volumetric representation (using voxels) of the objects that are being studied.

The typical way to obtain volumetric representations from a set of medical MR or CT images is to construct a 3D matrix by stacking Z images of X x Y pixels each. From this 3D matrix, there are a wide variety of algorithms to display, processing or reconstruction of the region of interest in each case study (Muraki and Kita, 2006; Lorensen and Cline, 1987).

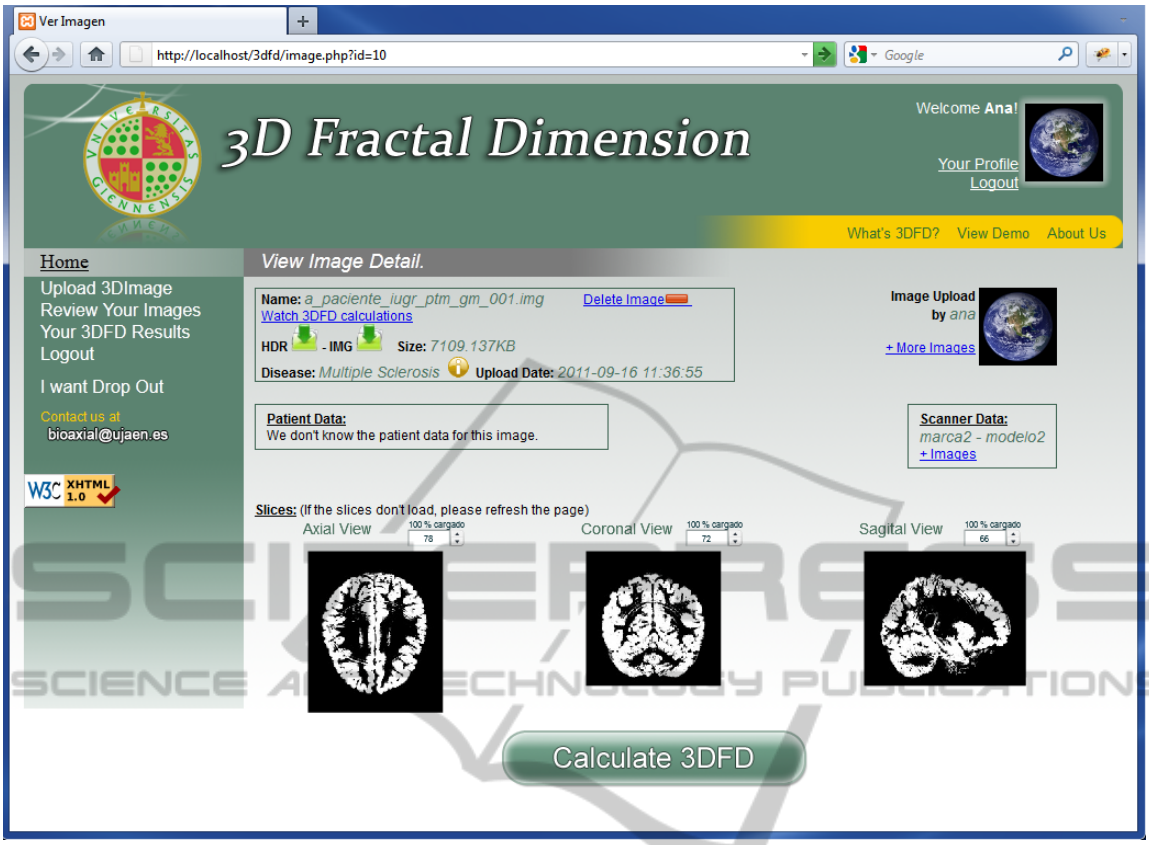

Figure 1: 3DFD web application. Brain data uploaded to the server.

There are alternative representations for a 3D volume that maintain their topologic essence and are more compact, such as the so-called skeletons. This representation may allows an accurate classification of the represented volume (Cornea et al., 2007).

The computational cost of the algorithms that process 3D volumes is usually very high, especially when acceptable levels of precision are required. Thus, the searching for efficient solutions is crucial to provide interactivity to user-friendly applications. The ability to program the Graphics Processing Units (GPUs) of any current mid-range PC has revolutionized many fields where high computational cost algorithms are required (Owens et al., 2007). The evolution of these GPUs and their low cost, especially compared with traditional parallel computers, place them as one of the most interesting solutions when the programmer wants to optimize data-parallel algorithms.

Many volume modelling algorithms are based on performing independent operations on each voxel. For these cases, applying GPU-based optimizations is very suitable. Iso-surface extraction algorithms, segmentation of medical images, or interactive visualization of volumes are examples of such algorithms (Stone et al., 2008; Fan et al., 2008).

GPU programming is based on the classic graphic display pipeline. However, using the GPU to code algorithms that are not related with graphics may be quite complicated, since it requires knowledge of the architecture and the operation of the graphic processor. For this reason, several GPU programming paradigms, that do not require any knowledge of graphics, have recently emerged. NVIDIA CUDA (Luebke, 2008) and OpenCL (Khronos group, 2010) stand out among these new paradigms. These programming models exploit the inherent GPU parallelism by writing simple programs (threads) running into hundreds of thousands of parallel invocations on the GPU. There are many examples of successful use of GPU optimization in the biomedical area (with improvements in time between x10 and x100), such as CT reconstruction or interactive MR imaging visualization (Xu and Mueller, 2007; Zhao et al., 2009).

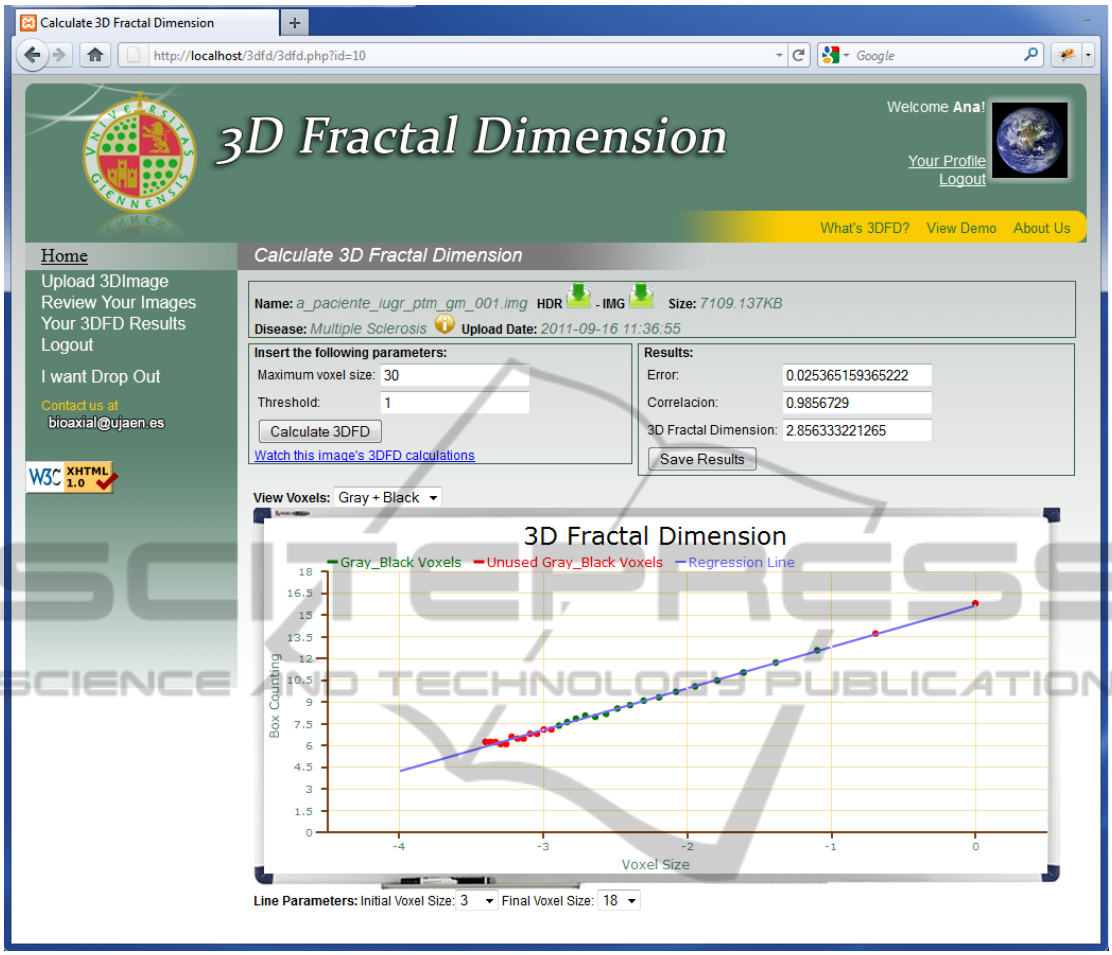

Figure 2: 3DFD web application. Box-counting and 3DFD calculation.

4 A SOFTWARE PLATFORM TO CALCULATE THE 3DFD OF MR IMAGES

A general software to compute the 3DFD of MR images has been developed by our research group in previous studies, which has become a very useful and high social-interest tool (Ruiz de Miras et al., 2011). The different exiting hardware and software platforms to obtain the MR images, the wide profile of potential users of the software, and the need for constant maintaining and updating in this kind of programs, imply that the software has to be made available to the scientific community in the most flexible and user-friendly way. Thus, we have decided to integrate our software into a Web platform, a project with the aim of providing a universal access through a simple Web browser. A Web platform instantly gives the user the latest version of the software and, when correctly related to a database, a large number of medical images, uploaded by different users, can be collected, classified and analyzed, which otherwise cannot be accessed to and managed.

Figure 1 and Figure 2 shows sample snapshots of our developed web platform. In the first one, the main data of an uploaded 3D image, including the set of slices, is showed. The interactive computation of the 3DFD for the uploaded 3D image is showed in Figure 2. The obtained results are represented in the scattered graphic for slope analysis, allowing us to discard the initial and final points out of linearity. The final value of 3DFD is the slope of the resulting regression line, which can be directly stored by pushing the "*Save Results*" button. The value of the box-counting and image segmentation input parameters (*maximum voxel size* and *threshold*, respectively) can also be tuned, thus obtaining different 3DFD values which can also be also stored

in the database.

The computational cost of the different algorithms needed to calculate the 3DFD is very high, which is a handicap when interactivity and fast feedback to the user are essential, as in data analysis Web platforms. The algorithms required in the engine are those related to volume visualization, box-counting calculation for different voxel resolutions and the computation of the curve-skeleton of the represented 3D image. Because all these algorithms can be reduced to individual operations on each voxel of the volume, and taking into account that these operations can be run in parallel using the recent hardware and software platforms based on GPU programming, we have adapted and improved them to be run on these massively parallel platforms. Thus, the degree of interactivity needed to integrate the 3DFD calculation, in a really useful and user friendly Web platform, has been achieved.

The most time-consuming algorithm is the curve-skeleton calculation; in our case we selected and implemented the thinning approach as the most appropriate (Palágyi and Kuba, 1999). A 3D curve-skeleton is a very compact representation of a three dimensional object, and its 3DFD provides very good and reliable results.

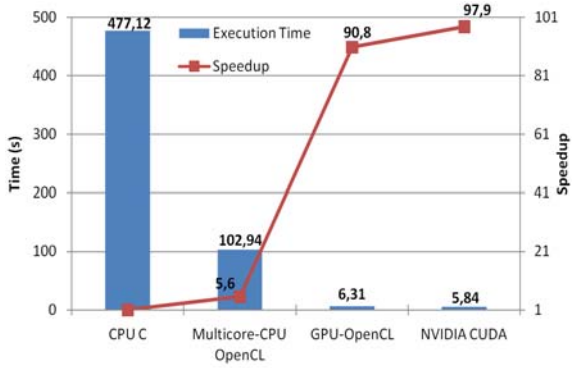

Figure 3: Curve-skeleton generation time and speedup for executions over 512 x 512 x 512 voxelized models. GPU executions on the NVIDIA GTX 580. CPU execution on Intel i7-920, an eight-threaded CPU.

A standard calculation of a 3D skeleton takes around 8 minutes to be obtained, which is a very time-consuming process. After the 3D thinning algorithm multi-threaded implementation, for GPU and multi-core CPUs, we obtained a substantial execution-time improvement, when compared to the traditional mono-threaded version. We used two parallel programming models: CUDA and OpenCL. Figure 3 shows the running time of each parallel version, where the speedup achievement using the optimized parallel algorithms for the GPU is showed to be improved 97,9x against the CPU single-process version, and more than 19x over the CPU multithreaded version, being this two interesting results.

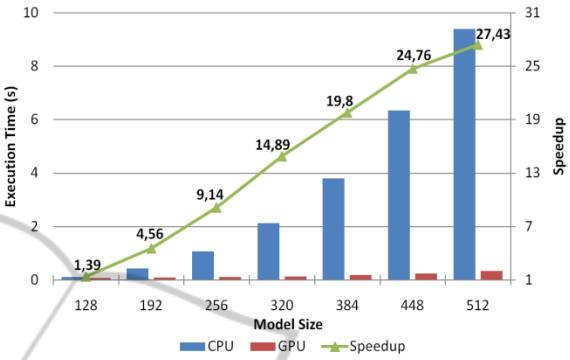

Figure 4: Box-Counting optimization. C-CPU algorithm (mono-threaded) vs. CUDA-GPU algorithm (multi-threaded). Execution time and speedup.

We have also designed and implemented a parallel optimized version of the box-counting algorithm. This algorithm run faster in CPU than the curve-skeleton calculation, taking just a few seconds, which may be considered a good execution time. However, the execution time may be tediously longer when performing the box-counting calculation on a set of *n* case studies. In addition, the segmentation threshold (which is an input parameter, as seen in Figure 2) may need to be tuned and, thus, several runs have to be executed using different *m* threshold values. Thus, the execution time has to be multiplied by *n* and *m* in the simplest case. Figure 4 shows the CUDA implementation runtime of the box-counting algorithm. The obtained results detected an average 27-fold improvement for the best case, thus decreasing the execution time from around 28 seconds to only one second when using the highest model of resolution (512 x 512 x 512 pixels).

5 CONCLUSIONS

We have developed effective and efficient algorithms to obtain the FD from 3D images, obtaining a complete brain characterization. These algorithms have been drastically optimized and implemented in a user-friendly Web platform that currently is in the last stage of testing by our research group and selected medical staff. This advanced platform will be available soon to the scientific community and we hope it may be a useful

tool for early diagnosis of several neurodegenerative diseases.

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