SOFTWARE FOR THE APPLICATION OF MULTIFRACTAL ANALYSIS IN THE CLASSIFICATION OF METASTATIC BONE TUMORS

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ABSTRACT

Multifractal analysis emerged as an accurate tool for cancer classification, although the process needs complete automation in order to be applied in medical diagnostics. After the multifractal analysis has been performed, the results must be processed and properly classified. This paper presents the automation of the diagnostic process. The goal is to successfully apply multifractal analysis as an auxiliary diagnostic tool.

KEYWORDS

Diagnostic agent, metastatic tumor, multifractal analysis

1. INTRODUCTION

The World Health Organization warns that in the next 50 years the number of cancer patients will increase by 50% compared to 2000. That is, the number of cancer patients will be 15 million people annually. Due to the constant increase in the number of patients, it is necessary to introduce new diagnostic tools for better and faster diagnosis. In this paper an auxiliary diagnostic agent for the classification of metastatic bone tumors by primary carcinoma was introduced. Namely, it has been established that there are statistically significant differences between microscopic medical images with a view to their classification, in terms of determining primary carcinoma in cases of intraoseal metastatic carcinoma [1]. In order to apply the results in a diagnostic, it is necessary to automate the process of obtaining the results from the microscopic image to the classified sample.

2. MULTIFRACTAL ANALYSIS

Multifractal analysis is a continuation of fractal analysis, introduced by mathematician Benotit Mandelbrot, in the second half of the twentieth century. Fractals related to natural forms, such as mountains, shores and river basins, the structure of plants, blood vessels, lungs, which can not be described by Euclidean geometry.

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Natural objects and phenomena do not exhibit fractal properties strictly, even when they are self-similar, but can have statistical self-similarity. For example, the structure of the seashore, the appearance of a relief or cloud, the structure of some biological systems or signals, exhibit self-similar properties, but in different scales the shape is not exactly the same [1]. While fractal analysis describes forms characterized by strict mathematical properties, the multifractal analysis defines fractal properties in natural objects and phenomena. Their application in medical diagnostics is presented in paper [2].

The cancer cell is one of the natural forms that can be expressed through fractals. It is characterized by chaotic, poorly regulated cell growth [1], which is not a feature of healthy organisms. A healthy cell defines a form that helps in their functioning, while the appearance of cancer cells is usually abnormal. Abnormalities are expressed in a size that is either lower or higher than a healthy cell, because cancer cells do not have a particular function. Irregular growth also occurs in the nucleus and cytoplasm of the cell. Namely, the core of the malignant cells is higher than in healthy cells, while the cytoplasm is scarce and its color is intensively colored or very faint [3]. For the multifractal analysis of the obtained digital medical images in [1], as well as obtaining multifractal analysis parameters, the following programs were used: ImageJ, for image analysis [4], and ImageJ Plugin, FracLac [5], multifractall analysis program.

Digital images of three groups of metastases of the intraoseal cancer were observed:

- metastatic renal cell cancer, shown in Figure 1,
- metastatic breast cancer, shown in Figure 2,
- metastatic lung cancer, shown in Figure 3.

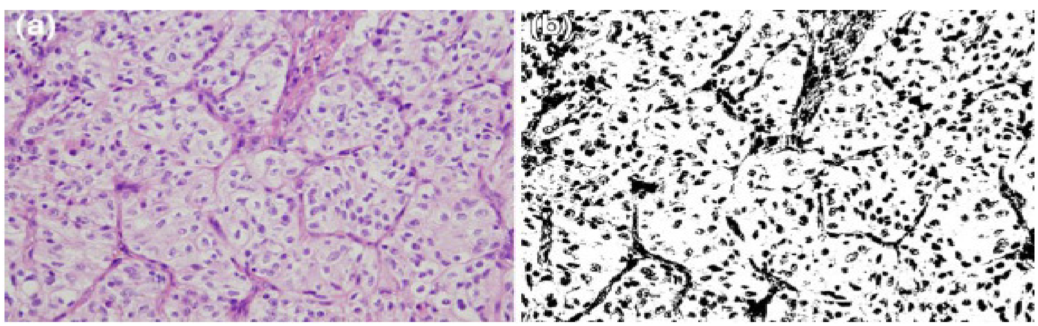

Figure 1. Metastatic renal cell carcinoma: (a) Microscopic imaging; (b) Binary form, obtained using the FracLac program

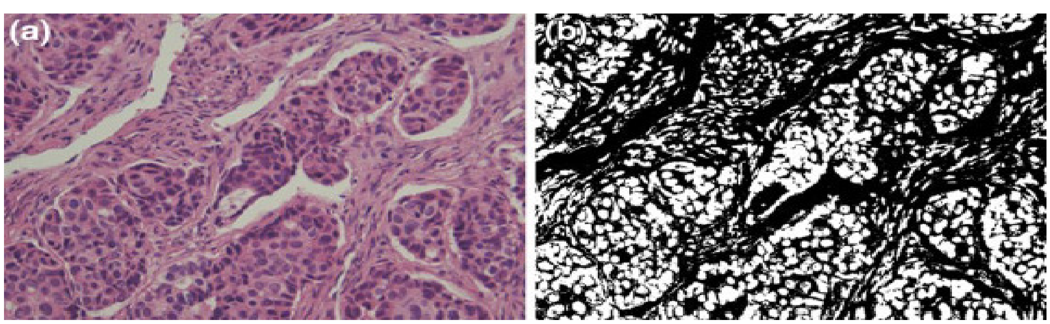

Figure 2. Metastatic breast cancer: (a) Microscopic; (b) Binary form, obtained using the FracLac program

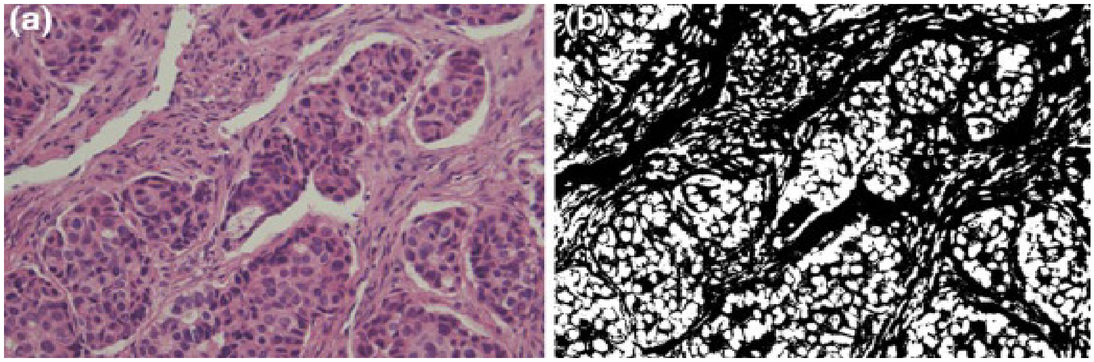

Figure 3. Metastatic lung carcinoma: (a) Microscopic image; (b) Binary form, obtained using the FracLac program

After applying the FracLac software to the metastasis images, the following multifunctional parameters for data classification are obtained:

- D_{max} - fractal dimension
- Q - is the exponent of the fractal dimension
- α_{min} - the minimum value of the Hõlder exponent in the results
- $f(\alpha)_{min}$ - the value of the continual function for α_{min}
- α_{max} - the maximum value of the Hõlder exponent in the results
- $f(\alpha)_{max}$ - the value of the continuous function for α_{min}.

3. AUTOMATIZATION

The idea of this project is to create a platform that will enable an easy and simple work environment for the end user, as well as a basis for further research and improvement of the described techniques. The end user will receive a unique interface through which he can even get the results in just a few clicks even without detailed knowledge of multifractal analysis and neural networks (or even software packages that served as the basis, ImageJ and FracLac).

The project is called "DECIM" according to the techniques underlying its processing. The great obstacle in the practical application of these techniques is the complexity and heterogeneity of the software that needs to be used to get the result. The classification currently requires more complex steps in several software packages, with manual inter-steps, such as copying and converting files. The goal of DECIM is to be a unique solution, robust software that takes on the complexity of the process and allows the user to arrive literally from within the next ten seconds from the microscopic image to the classification result, with minimal interaction.

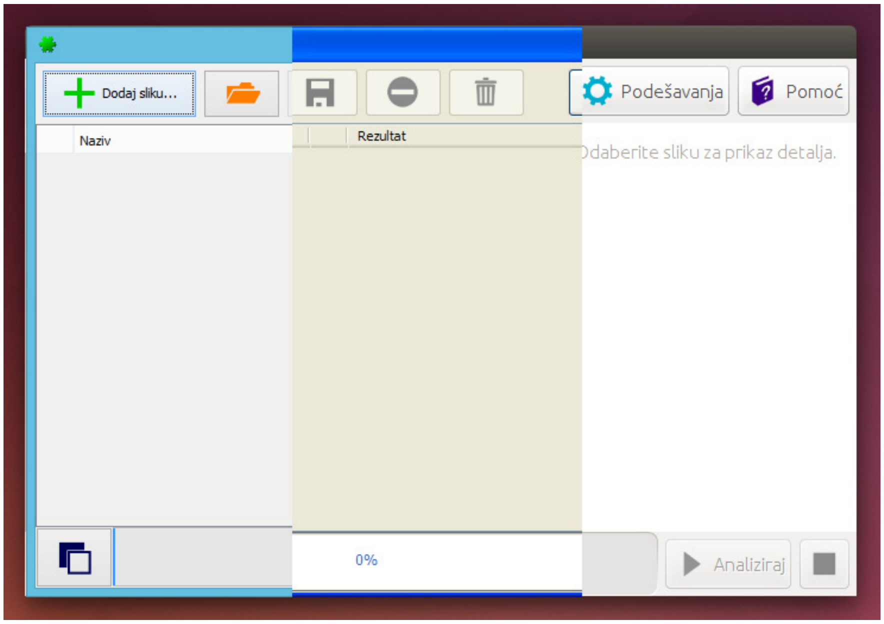

Figure 4. Start window of DECIM program on Windows 8, XP and Ubuntu 14.04

In the initial window (Figure 4), microscopic images can be added in standard digital formats (BMP, JPEG, PNG), either through the normal "Open" dialog, either by dragging images onto the DECIM window. During the typical work, this is all that is needed for preparation, only it is left to start the analysis using the "Analyze" button and the results will be displayed in the window as soon as they are finished (Figure 5). By selecting individual images, more detailed information about each classification can be found.

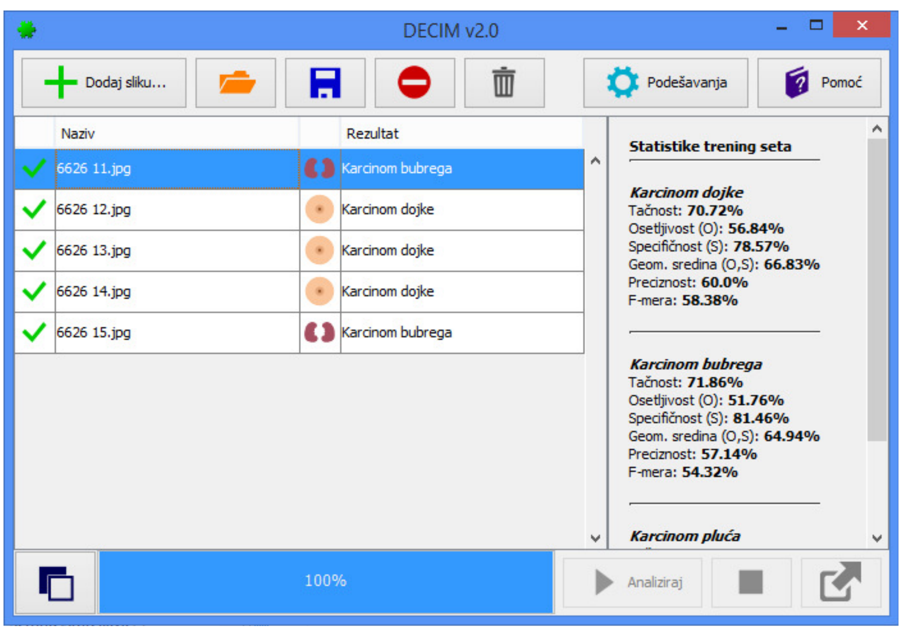

Figure 5. Classification of 5 images completed, with details in the right frame

With the ultimate goal of simplicity in mind, special attention is paid to the installation process of this program, which is compiled to automatically check and adjust the environment needed for the operation of DECIM, such as the presence of Java JRE environment (which can come and packaged with the program), the presence of Octave software [6] (it can also come bundled, if not already present) and the installation of the VC 2010 runtime component required for Octave on Windows platforms. In the program, many checks of errors and auto-detection were installed, so as to minimize the user's technical details. The whole project is designed so that for most average users, without special technical knowledge and without the need for manual interventions, this software "simply works".

4. PLATFORM

The software is made in Java programming language, which allows it to portability and work on multiple platforms (Figure 4). It is based on free and no cost software (Octave, ImageJ, FracLac), and can also run on free Java implementation (OpenJDK), on a free operating system (Ubuntu and other GNU/Linux distributions), which means that analysis through it without any additional costs for the software is possible. Of course, common commercial platforms, such as Oracle Java JRE and all modern versions of Windows and MacOS operating systems are supported. Apart from the simplicity of using the initial version of this program, the ambition of this project is that it is also a platform for further improvements in the process of analysis and classification. Due to the nature of this work, it is expected that the analysis will become better over time, or that specific variants will be developed for some specific cases.

One of the modules in the initial version is an improved method of converting color microscopic photos into a binary (black and white) form in relation to the method that ImageJ uses (Figure 6). Conversion to binary form is necessary, as the multifractal analysis method works with binary images. When converting a color image into a binary image, the key is to select the threshold of the light, that we consider the boundary between black and white. ImageJ calculates the global threshold by constructing histogram and selecting threshold that converts roughly the same image surface into black and white (Figure 7).

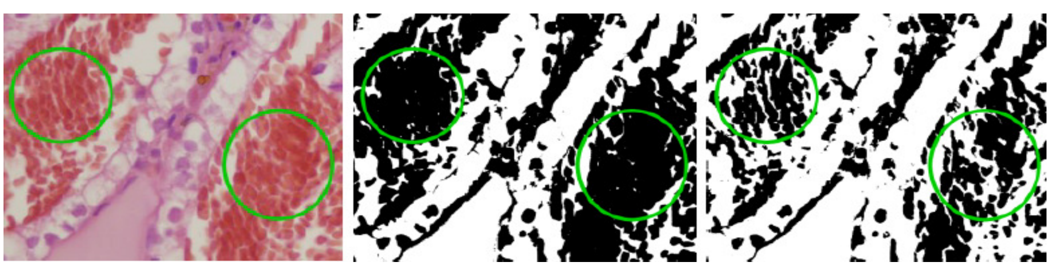

Figure 6. Different image processing techniques for fractal analysis: (a) Original; (b) The technique used by ImageJ; (c) A special technique in DECIM that emphasizes local contrast and thus reveals more detail

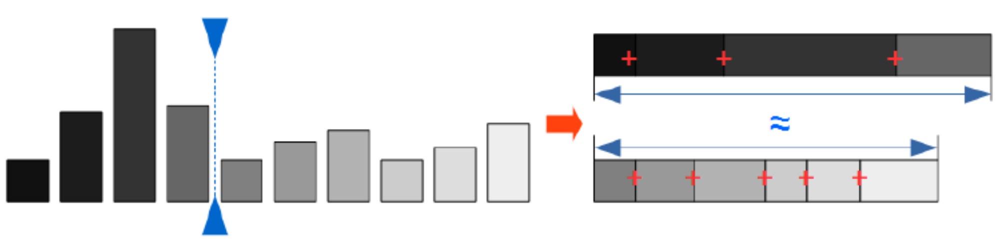

Figure 7. The principle of selecting the threshold for binarization as implements ImageJ

This will not always give the most accurate image repression, especially if some parts are brighter or darker than the global ones. More details in a binary image can be obtained by calculating a local threshold based on the environment, a particular radius, each pixel, instead of using one global value for the whole picture (Figure 8). Such a binarization is achieved by constructing a blurred version of the image (Gaussian blur) in which then each pixel will actually be the weight sum of its environment. Then, calculating the delta image, each pixel resolution will describe the difference between the original image pixels and its immediate surroundings, promoting local contrast.

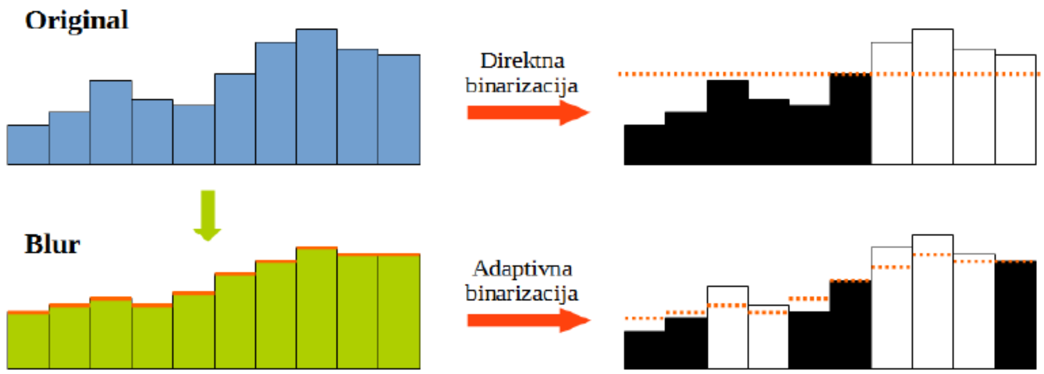

Figure 8. Principle of adaptive binarization work

Although the program is configured to "easily run" immediately after installation and can be used immediately for classification, it also allows modularity and extensibility. Whether it is new training data for the neural network, or new software components for preprocessing and image analysis, DECIM will allow easy use of new components through an already familiar interface. Again, this should be easy for users and, accordingly, whenever possible, the use of new components will be reduced to inserting one, easy to distribute, files into the program, similar to how the same sample images are used in the program. The idea is that DECIM will be a platform and it will present a simple interface that users will be familiar with and that will not change significantly, regardless of any new advances in fractal analysis or neural network classification, or some completely new techniques.

5. MODULARITY

DECIM realizes its modularity through the plug-in system, some of which are already installed in the initial version of the program, while others can easily be added by users after installation. In accordance with the purpose and mode of the program, a system has been developed that supports five module types, namely: image loader, image preprocessor (image processing), image analyzer, classificator and data exporter (export of classification results). The system extends through special "plug-in" files that can be automatically retrieved from a specific folder, if the user places it there, or during work, by dragging a new file into the program window, similar to images and sheets. A user can have multiple modules of the same type, choosing which one to use in the settings box.

The connection between the modules makes a special "Wiring" object (analogue to a wiring, a serial connection of the module) which at each moment has one ordered five modules (one of each type) that make up the image processing chain. Wiring also allows intercommunication between the modules through the provided interfaces, in order to allow the modules to check their environment and requirements (modules can depend on other modules), and then to call the desired parameters to other modules. This is important, because for the correct results the complete chain must be adjusted exactly as it was set up, when the neural network is created, otherwise the correct correlation between the analysis parameters and the classification results is lost.

Modules can be very easily created in the form of new Java projects that include the attached JAR library and implement one of the predefined interfaces (module type). This project can then be executed as a new JAR file, put into the plug-in folder and will be automatically scanned without any additional steps. The role and functionality of the modules are as follows:

A. Image Loader

The first module in the chain is the one that reads the microscopic photo from the file. Along with the program, a simple module of this type is included, which uses built-in image capture capabilities in Java implementations (JPEG, BMP, GIF, PNG and WBMP are guaranteed to be present). However, due to the application in medicine, it should also be possible for further extensions to read somewhat less popular, specialized image formats.

B. Image Preprocessor

The second phase is a pre-image processing, intended for use with multifractal analysis or some other method of analysis requiring conversion of colors or some other kind of pre-processing. There are two modules for binarization, described in the previous chapter, as well as a special "pass-through" module, which only transmits the image, in the event that no special processing is required (without disturbing the processing chain).

C. Image analyzer

The first of the two main modules is the image analysis module, in the form obtained after the pre-processing phase. Currently, this module is implemented the fractal analysis technique described above. The module is implemented as a compatibility shell for the FracLac plug-in to the ImageJ software, allowing it to work within the DECIM module. The output from this module can be in the form of a file, a sequence of whole or real numbers, or a block of binary data, in order to support possible future analysis methods, that have a different concept and format of output data.

D. Classificator

The second of the two most important modules is the one that, on the basis of the data obtained from the analysis, makes the final classification and gives an answer for each individual image. Here, the described neural network is introduced, which takes the parameters of multifractal analysis for inputs, and gives one of the three organs at the output, which considers to have the best correlation. This module is also responsible for determining the number of classes and their names - the rest of the system respects the information obtained from here. So with the new classifier, it is possible to classify with a different set of organs, and considerably more than three organs, or classify some completely different kind of objects and properties.

E. Result exporter

Although the results are visible within the program window, the need for export and further processing of results is envisaged, enabling complete DECIM to be part of a larger processing chain. A module of this type can save files (HTML report, or Excel table, etc.) or to display an arbitrary GUI window, that implements the module itself, having all the results and original images available.

6. CONCLUSIONS

Fractal analysis and classification through a neural network are interesting new techniques with a lot of potential and they are useful diagnostic tools. The purpose of this project is to bridge the typical distance between scientific research papers and new experimental methods/tools that are really applicable in practice. The practice requires robust, stable and reliable tools, and this is precisely what this project seeks to be - a tool that is practical, which will bring with it the convenience of the described classification techniques, as well as the potential for simple future extensions and improvements.

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