Semi-Automatic Segmentation of Multiple Sclerosis Lesion in 4D Modality

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***Abstract*—The automatic and computerized recognition of Regions of Interest (ROI) is a crucial step in the process and analysis of medical images. The reasons are many and include the increase of available medical image data, the wide variety of devices and methods for image acquisition and the need to provide mechanisms making the analysis more accurate and the clinicians' job faster. Within the study on multiple sclerosis, the goal is the recognition of the damaged brain areas by processing images captured through magnetic resonance imaging. In this context, the proposed work is a study on the relationship between brain images obtained by magnetic resonance imaging, using different types of acquisitions. The goal is to understand whether it is somehow possible to identify the different regions of the brain, through a process of segmentation, using a method which allows the user's independence. The employed volumes are acquired in three different modalities T1-weighted, T2-weighted, and PD for synthetic database; T1-weighted, T2-weighted and FLAIR for real database. The purpose of this paper is to provide the doctor with a tool helping with diagnosis and detecting the possible areas of doubt. Two databases were taken into account, a synthetic one and a real one, and for the synthetic database the parameters of the confusion matrix have been calculated.**

***Index Terms*—segmentation, fuzzy processing, connectedness, T1-weighted, T2-weighted, PD, FLAIR, MS lesion**

I. Introduction

The encephalon and spinal cord Magnetic Resonance Imaging (MRI) has assumed great importance both diagnosing and in monitoring the course of neurological pathologies.

Multiple sclerosis [1] is a disease which affects the central nervous system, (i.e., brain and spinal cord) and is also called demyelination syndrome since it is characterized by a progressive degeneration, of myelin up to its destruction. Myelin holds a key role in the functioning of the central nervous system. It functions like a sheath and allows the nerve fibers to perform a rapid pulses transmission. It also integrates the messages which, from the brain and the spinal cord, branch off to other parts of the body and vice versa go to the center from the periphery. The areas in which the myelin are damaged or destroyed are also called "plaques" or areas of demyelination. MRI allows to highlight the typical plaques of MS and to follow their evolution over time.

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These areas in time undergo a hardening process or rather a healing process. Hence the multiple sclerosis names: "sclerosis" for the presence of healed lesions (plaques), "multiple" for the fact that the lesions can affect various areas of the central nervous system. There are different types of MS lesions, which can be classified as follows: focal damage (harm); Global damage (nerve degeneration); heterogeneous lesions characterized by histopathological variability (demyelination, reduced density of axons, gliosis, axonal loss).

In the context of digital image processing techniques, this paper shows how to exploit the potential of the segmentation process for the detection of regions of interest like the MS plaques from 4D datasets such as multiparametric MRI volumes.

A new method is proposed where no specific use of pathology information is required. In fact, the user is only asked to point with the mouse the main non-pathological brain tissues for a subsequent automatic segmentation.

The areas, which are not recognized as healthy tissues, will be classified as doubtful regions, being possible candidates for the pathology signs.

After a segmentation step it is possible to apply a cluster analysis allowing an optimal separation of the pathological area from non-pathological areas.

Within the vast problem of segmenting medical volumes, the present method fits the need to look more volumes at a time since different acquisition modalities are used.

Generally, to assess separate volumes, is very demanding, as the doctor has to visually inspect the volumes simultaneously and look at the same object in different ways. The goal of this work is to provide the physician with a useful tool helping him in the detection and quantification of multiple sclerosis plaques.

The different acquisitions of brain images are related to magnetic resonance conventional modalities: T1-weigthed, T2-weigthed, PD and FLAIR [2].

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II. STATE OF THE ART

In [2] an analysis of the state of the art is made concerning the following problem: over 80 different methods for the recognition of damaged areas are identified but only 47 have a qualitative verification with at least a real image. This analysis leads to the conclusion that although different methods offer promising results, the problem of finding a method which works well in all possible cases and therefore, can be used on a large scale, is still unresolved.

Among the different approaches, paper [3] proposes a model which allows an identification of the damaged regions starting from the concept of visual saliency.

In [4] many features are extracted through an image segmentation process, and are subsequently used in a classification process implemented by random forest approach.

In [5] results of lesion segmentation are based on supervised approaches because, in order to obtain the initial segmentation of brain tissues, they make a registration with the statistical atlas. This method is almost totally dependent on the user's intervention.

The statistical parametric methodology proposed by [6] uses a four-dimensional feature space (intensity, position (x, y), and time). Gaussian mixture modelling (GMM) and Expectation-Maximization (EM) algorithm are used to determine the parameters of the model.

In article [7], there is a collection and very good summary of the most popular methods for the semi-automatic segmentation of the various body's regions as regards different diseases. In particular, for the brain's district, both automatic methods based on fuzzy connectivity, the neural network model, and fuzzy c-means clustering are analyzed.

With regard to the detection of multiple sclerosis plaques, in the literature, many works have already been proposed, for example, those described in the article [8], where through a nearly automatic system, multiple sclerosis plaques in the brain are detected from two different methods of acquisition, T1-weighted and T2-weighted.

This paper proposes an extension allowing the use of multiple modalities. For the moment, three of them are analyzed, but it is possible to increase the number of volumes processed simultaneously, namely integrating different modalities. This prepares the groundwork for a possible classification of regions recognized, so as to obtain a useful tool for the early detection of the disease.

III. METHOD

The method shown in Fig. 1 starts from three volumes acquired at the same time but with different characteristics. In this case, for reasons of clarity, synthetic images have been used, which simulate three different modalities, such as T1-weighted, T2-weighted and Proton Density (PD). Inside the volumes depicted in Fig. 1, three distinct objects and background are present. The user selects regions or tissues that are recognized as healthy parts within the volume by pointing one voxel inside each region.

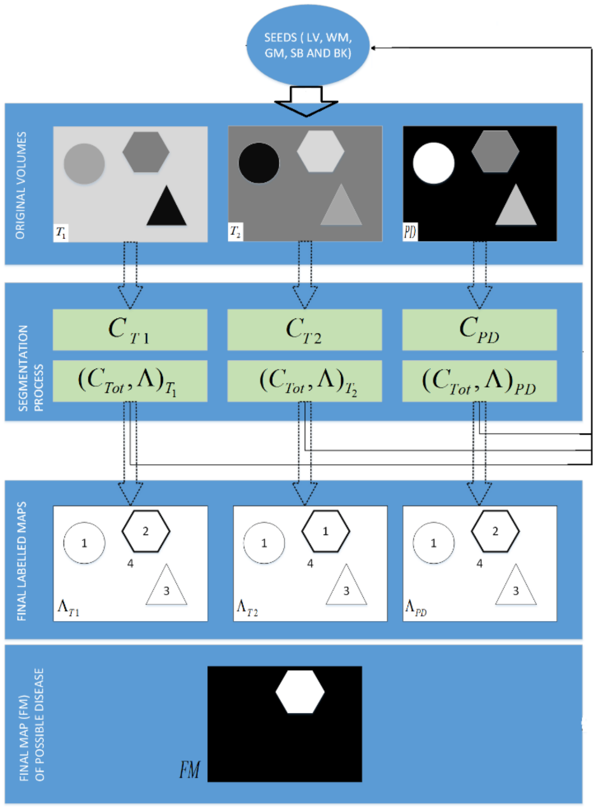


Figure 1. Graphical representation of the method used.

As next step the automatic processing of the method begins. Here the software autonomously realizes the region growing process, which associates to each voxel a value related to the intensity and topological similarity, with respect to one of the seed voxels selected by the user in one volume. This step is iterated for all seeds selected by the user and for all the given original volumes. Thus, a 3D map is generated where each voxel is associated with a fuzzy membership value for each of the seeds selected by the user and for each volume.

Using fuzzy union for each modality a map is achieved containing the label values for each selected seed. Finally, a process of identification of discordant points is applied, and a single final image is provided.

In particular, as reported in previous articles [8] and [9], for each volume and for each seed the segmentation process creates a Fuzzy χ-map:

$$\forall\ v_i \subset V\ \chi_{v_i}^{v_a} = 1 - \left|\eta_{(v_i)} - \eta_{(v_a)}\right| \qquad (1)$$

where V is a generic 3D square lattice, $v_i \in V$ with $i=1...,|V|$, is the i-th voxel, $\eta_{(v_i)}$ is a fuzzy field intensity value within the unit real interval [0,1], v_a is the seed point.

Consequently, fuzzy-intensity connectedness (or χ-connectedness) map, $C_{\chi^{v_a}}$, is defined as

$$\forall v_i \subset V \; C_{\chi^{v_a}} = \max_{P(v_a,v_i)} \left[\min_{z \in P(v_a,v_i)} \chi^{v_a}(z) \right] \quad (2)$$

where $P(v_a, v_i)$ is a path, i.e., a connected sequence of voxels from v_a to v_i.

For each volume analyzed, connectivity information independently derived from each seed *t* (from a set of cardinality *T*) are merged into a single "Total-Connectedness Map" through a process of fuzzy union:

$$C_T = \bigcup_{t=1}^{T} C_\chi t \quad (3)$$

A labeling map Λ is created where each region is associated with a different label value depending on the seed corresponding to the maximum in C_T. At this point, there are three volumes, one for each acquisition modality, where each region is identified by a label.

To obtain the Final Map (FM), the software compares all voxels of the labelling map volume. If the voxel labels agree, a zero value is associated to that voxel in the final map (black), vice-versa if at least one of the three labels is discordant, the value 255 (white) is assigned, as shown in the example of Fig. 2.

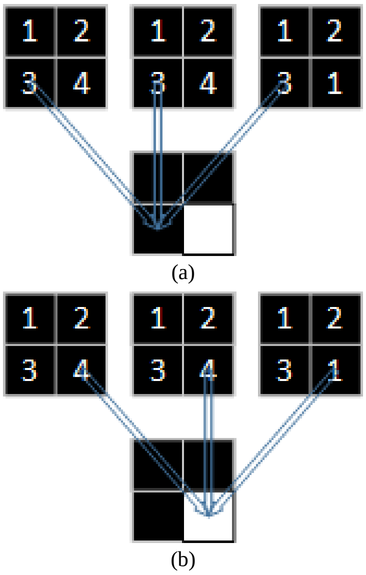


Figure 2. Graphic explanation of the final map creation concept

The rationale of this process is that if a region is well identified by all three volumes it is supposed to be correctly recognized, otherwise, the result indicates a doubtful region, and so the possible pathology regions.

Finally, it may be that within the group of doubtful points, noise points are present in addition to possible disease, thus generating false positives. For this reason, to better show the results, a morphological operation was applied in order to regularize the boundaries.

IV. Results and Discussion

The database used, suggested by [2], is a standard way to validate the proposed method. The BrainWeb [10] dataset is composed by volumes whose size is $181 \times 217 \times 181$ voxels, spatial resolution being 1 mm^3. The database section including volumes affected by Multiple Sclerosis (MS) disease was chosen.

The second database taken into account is also suggested by [2] and is a real database related to MS lesion segmentation MICCAI challenge 2008 ([11]), MRI scanner with slice thickness of 1mm and in-plane resolution of 0.5mm.

The healthy tissues addressed by the proposed method include: lateral ventricle, white matter, grey matter, spinal bulb, caudate nucleus, and background. After the segmentation process, for each labelled tissue, the mean value was measured from each modality of acquisition. For the synthetic DB (SDB), the results are shown in Table I and plotted in Fig. 3, Fig. 4 and Fig. 5.

TABLE I. Identification Value of the Regions for SDB

Label N.	Regions	Acronym	T1 Mean Value	T2 Mean Value	PD Mean Value
1	Lateral Ventricle	LV	43	248	241
2	White Matter	WM	148	116	195
3	Grey Matter	GM	108	151	226
4	Spinal Bulb	SB	118	141	218
5	Caudate Nucleus	CN	100	158	220
6	Background	BK	0	0	0
	Discordant Points	DP	119	237	250

TABLE II. Identification Value of the Regions for RDB

Label N.	Regions	Acronym	T1 Mean Value	T2 Mean Value	FLAIR Mean Value
1	Lateral Ventricle	LV	27	210	31
2	White Matter	WM	84	52	81
3	Grey Matter	GM	58	75	104
4	Spinal Bulb	SB	35	55	75
5	Caudate Nucleus	CN	73	74	97
6	Background	BK	2	2	2
	Discordant Points	DP	67	106	152

For Real DB (RDB) the results are shown in Table II and plotted in Fig. 6, Fig. 7 and Fig. 8. In both cases it is clear that discordant points are characterized by values different with respect to the healthy classes, thus they should belong to a new class correlated with the pathology.

In Fig. 9, for a case from SDB, on the left, one slice of the original T1-weighted volume, T2-weighted volume and PD volume are shown; on the right, the original left slices are overlapped with the segmented plaques coloured in cyan. As it can be seen, the segmentation proposed is almost completely comparable with a manual segmentation operated by the user.

The proposed method is semi-automatic since only the insertion of the initial seeds is required. In addition, the segmentation results do not change when changing the order of picking seeds and their position inside the healthy tissue they represent. For these reasons, the method turns to be totally user-independent.

We proceed now verifying whether the results obtained with the synthetic databases are extensible in some way to the case of real images. To this purpose, T1, T2, and FLAIR volumes from the available real database are taken into account. To limit the work to the central area of the brain a mask was manually built allowing its isolation. Fig. 10 refers again to an axial section of the volume: on the left, the original volumes are shown; on the right the plaques segmentation result is overlapped in colour.

As it is can be seen, results are very reliable also regards the real case. In Fig. 11, there is a zoom of FLAIR image for a better visualization of MS lesion.

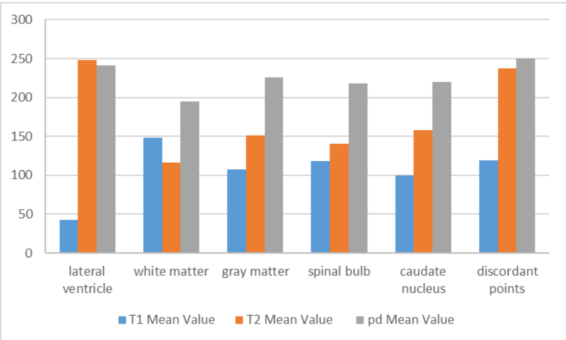


Figure 3. SDB - Graphical representation of the mean values calculated for the labeled regions, and the remaining discordant points (DP)

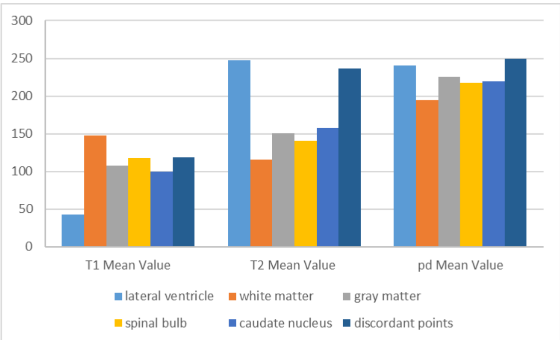


Figure 4. SDB - Graphical representation of the mean values calculated for the labeled regions, and the remaining discordant points (DP)

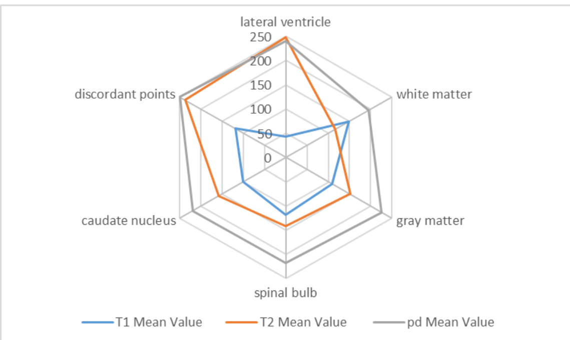


Figure 5. SDB - Graphical representation of the mean values calculated for the labeled regions, and the remaining discordant points (DP)

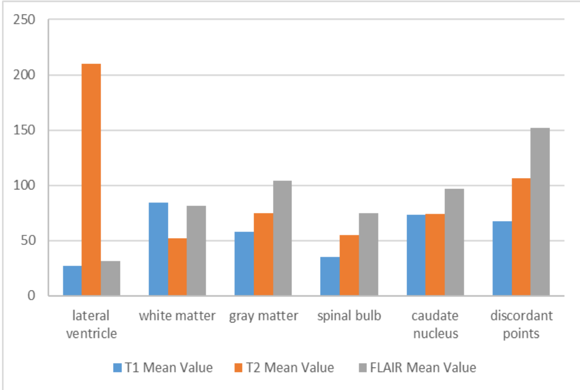


Figure 6. RDB - Graphical representation of the mean values calculated for the labeled regions, and the remaining discordant points (DP)

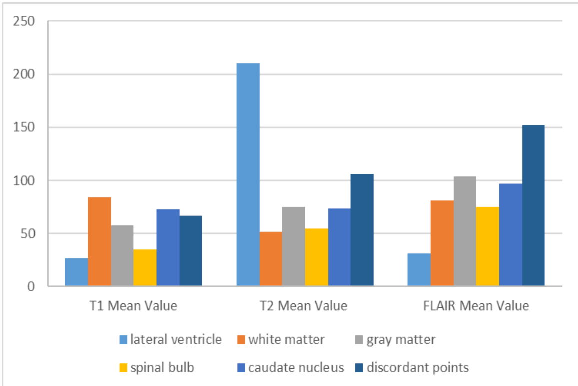


Figure 7. RDB - Graphical representation of the mean values calculated for the labeled regions, and the remaining discordant points (DP)

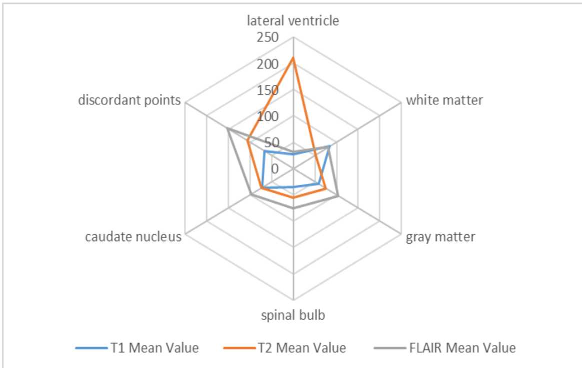
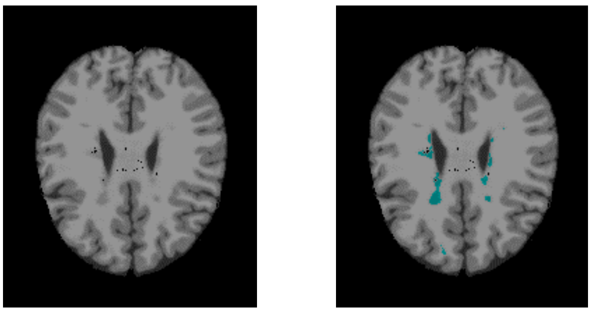


Figure 8. RDB - Graphical representation of the mean values calculated for the labeled regions, and the remaining discordant points (DP)



(a) (d)

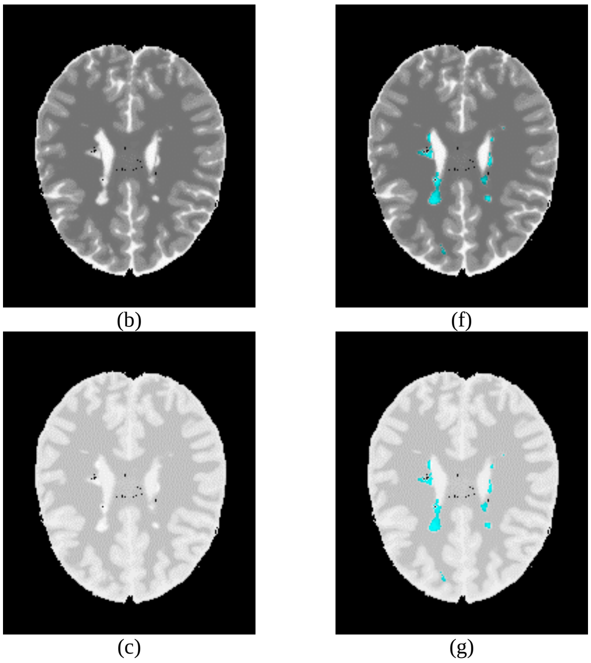


Figure 9. SDB One sample slice from (a) Original T1-weighted volume; (b) Original T2-weighted volume; (c) Original PD volume; (d) slice (a) overlapped with MS segmentation in cyan; (f) slice (b) overlapped with MS segmentation in cyan; (g) slice (c) overlapped with MS segmentation in cyan.

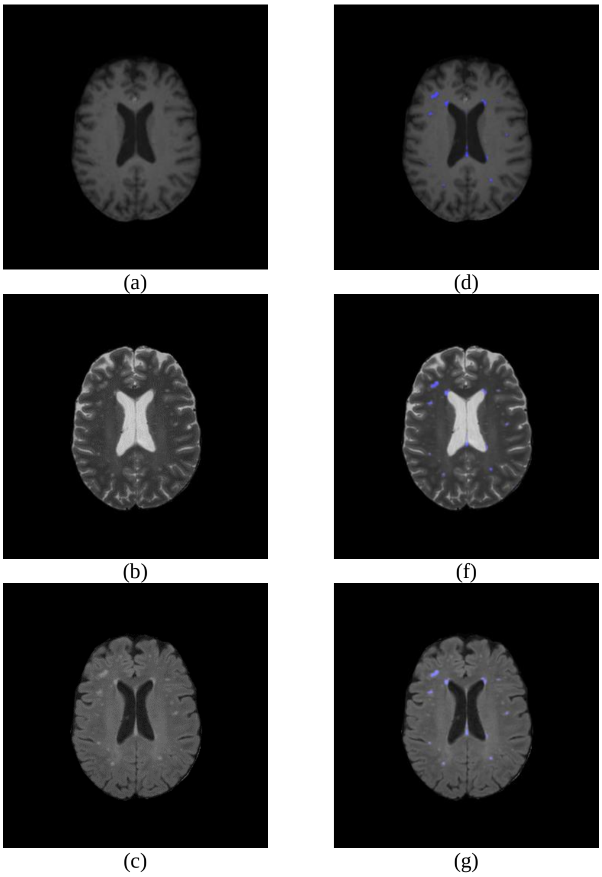


Figure 10. RDB – One sample slice from (a) Original T1-weighted volume; (b) Original T2-weighted volume; (c) Original FLAIR volume; (d) slice (a) overlapped with MS segmentation in cyan; (f) slice (b) overlapped with MS segmentation in cyan; (g) slice (c) overlapped with MS segmentation in cyan.

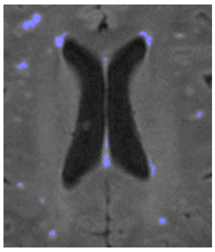


Figure 11. RDB - Zoom of FLAIR volume for better visualization.

V. Conclusion

The aim of this work is to obtain a segmentation which allows extracting, with multiple magnetic resonance imaging acquisitions made simultaneously, and recognition of the regions of interest, as in this case the multiple sclerosis plaques.

This has been demonstrated using pre-segmentation as a tool provided to the doctor for the detection of multiple sclerosis plaques. The use of multiple volumes at the same time reduces the workload for the doctor and allows to report the possible areas of doubt and therefore of pathology. The method was tested both on synthetic and real databases. The obtained results are very reliable and conform to the expected outcome.

Possible future works with quantification of the plaques found, especially their size and number, can be performed further, to propose a follow-up scheme for monitoring the disease. All processing time was only one minute and 40 seconds with three volumes with size $181 \times 217 \times 181$ voxels, five seeds, and with a personal computer Intel® Core™ i7 3610QM Processor.

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Luca Patrone was born in Albenga, Italy on October 26, 1985. He graduated in March 2015 in Genoa at the Medicine and Surgery University. He developed a thesis named: "Exercise-induced asthma: the role of the cholinergic system". After his graduation he started a 4 years' master named "The healthy aging" who includes knowledge in aesthetic medicine, diabetology, psychiatry and palliative medicine. He also started a six-month master in emergency medicine. From November 2015 he works as doctor on duty. Enrolled in "Ordine dei Medici Chirurghi e degli Odontoiatri" of Imperia (equivalent to General Medical Council in UK). Recently he became interested in scientific research directed to the diagnosis of multiple sclerosis pathology in the brain.

Silvana G. Dellepiane graduated in 1986 with honours. In 1990 she received the PhD degree in Electronic Engineering and Computer Science. In 1992 she became a Researcher (Assistant Professor) in the Department of Biophysical and Electronic Engineering (DIBE), Università degli Studi di Genova, where she is an Associated Professor in the Telecommunication area, belonging to DITEN department. She has taught in Signal Theory and Pattern Recognition. At present she is professor of Electrical Communications, Statistical Methods, Signal and Image Processing and Recognition, in the courses of Telecommunications Engineering and Bioengineering. She is responsible for the NUMIP research area of the Signal Processing and Telecommunications (SP&T) laboratory at DITEN. Prof. Dellepiane has gained wide scientific and technical experience in multi-dimensional data processing. Her main research interests include the use of context and fuzzy systems for multi-dimensional data processing, segmentation, supervised methods for the processing of remote sensing SAR images, and non-linear adaptive processing of digital signals. Her application domains are, mainly, telemedicine and remote sensing. Silvana Dellepiane is a reviewer for various journals. She was invited at some international conferences and schools for tutorials and lessons. She has participated, at the organization and scientific levels, in the research activities concerning various CNR, ASI, MIUR and UE projects. She has been a member of the Technical Committee "Bio Imaging and Signal Processing" of IEEE Signal Processing Society.