

ROBUST ALZHEIMER'S DISEASE DIAGNOSIS USING RADIAL BASIS CLASSIFIER

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Abstract

Alzheimer's disease (AD) is the most common cause of dementia in aged people and affects more than 30 million individuals worldwide. The particular evolution of AD patients and their increasing dependence on the close affective environment provokes an important social repercussion, as the cognitive functions of the patient gradually disappear and his individual essence blurs. This project presents a novel computer-aided diagnosis (CAD) technique for the early diagnosis of the Alzheimer's disease (AD) based on Radial basis Function Neural Network (RBFNN) with bounds of confidence. The CAD tool is designed for the study and classification of functional brain images. For this purpose, two different brain image databases are selected: a single photon emission computed tomography (SPECT) database and positron emission tomography (PET) images, both of them containing data for both Alzheimer's disease (AD) patients and healthy controls as a reference. These databases are analyzed by applying the Fisher discriminant ratio (FDR) and multiresolution wavelet filter for feature selection and extraction of the most relevant features. The resulting multiresolution wavelet -transformed sets of data, which contain a reduced number of features, are classifier by means of a RBFNN-based classifier with bounds of confidence for decision.

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INTRODUCTION

Alzheimer's disease (AD), also known in medical literature as Alzheimer disease, is the most common form of dementia. There is no cure for the disease, which worsens as it progresses, and eventually leads to death. It was first described by German psychiatrist and neuropathologist Alois Alzheimer in 1906 and was named after him. Most often, AD is diagnosed in people over 65 years of age, although the less-prevalent early-onset Alzheimer's can occur much earlier. In 2006, there were 26.6 million sufferers worldwide.

A. Computer Aided Diagnosis (CAD) Techniques

For the past several decades, researchers in the medical imaging field have focused on bringing new imaging modalities to clinicians while improving the performance of existing systems [4], [5]. Nowadays, signal processing engineers are beginning to take the next step by introducing software improvements, enabling computers to help clinicians to make sense of such an amount of noninvasive medical information. Computer aided diagnosis (CAD) is a general term used for a variety of techniques applied to whatever kind of medical data, such as to medical images, to assist physicians in their diagnosis work. CAD systems help physicians by either identifying patterns that might have been overlooked or by providing a road map of suspicious areas, making their efforts more efficient.

II. FEATURE SELECTION AND REDUCTION

Each voxel of a brain functional 3-D image contains information of the corresponding brain point. However, not all the voxels have the same level of relevance in terms of discrimination between groups of subjects. In this case, two groups of subjects are defined: Alzheimer's disease patients, labeled as AD, and subjects not affected by this disease, labeled as NOR. Thus an initial feature selection based on discrimination capability is typically selected, obtaining a vector of discriminant voxels for each participant. In addition, the selected discriminant voxel vectors can be projected onto a different subspace. This subspace is chosen so that only a few variables represent the most discriminant features of each patient images in each database.

A. Intensity Normalization

Previous to any kind of feature selection, the data sets have to be normalized in intensity in order to be able to compare images according to their voxel normalized intensity levels. Regarding the intensity normalization, the normalization to the maximum intensity level may introduce

problems in some images that can have peak intensity values due to noise. Thus, these images are badly normalized as the normalization is based on wrong noisy voxels. In this work, in order to avoid these possible normalization errors, it is applied intensity normalization based on the mean value of a group of voxels with the highest intensity values. According to [18], the mean value of the 0.1% voxels with the highest intensity levels is selected for the intensity normalization.

B. Fisher Discriminant Ratio for Feature Selection

The Fisher discriminant ratio (FDR) criterion is characterized by its separation ability as shown in [19]. For the two-class case, it may be defined as follows:

$$\text{FDR} = \frac{(\mu_1 - \mu_2)^2}{\sigma_1^2 + \sigma_2^2} \quad \text{where } \mu_i \text{ and } \sigma_i^2 \text{ denote the } i^{\text{th}} \text{ class mean value and variance for each}$$

input variable, respectively. C. Nonnegative Matrix Factorization for Feature Reduction .

Nonnegative matrix factorization (NMF) is a technique for finding parts-based, linear representations of nonnegative data, being a useful decomposition tool for multivariate data. This technique is especially suitable for nonnegative data sets such as functional images in general, and for the PET and SPECT brain images of this work in particular, where all the variables consist of positive values. Given a nonnegative data matrix A , NMF finds an approximate factorization $A \approx WH$ into nonnegative matrices W and H .

III. SUPPORT VECTOR MACHINE (SVM) BASED CLASSIFIER WITH BOUNDS OF CONFIDENCE

SVM BACKGROUND

Support vectormachine (SVM) is a widely used technique for pattern recognition and classification in a variety of applications for its ability for detecting patterns in experimental databases. SVM has become an essential machine-learning method for the detection and classification of particular patterns in medical images. In the literature, it can be found several fields in which SVM are applied: cancer, tumor, or nodule detection, vascular analysis, dementia detection etc. Regarding image modalities, SVM has been applied to a variety of image types: magnetic resonance images (MRI), SPECT or PET, ultrasound images, etc. SVM techniques consist of two separate steps: first of all a given set of binary labeled training data is used for training; then new unlabeled data can be classified according to the learned behavior. SVM separates a given set of binary labeled training data by means of a hyperplane that is maximally

distant from the two possible classes (in our particular case, NOR an AD classes). The objective is to build a function with the training data, as expressed in (6), able to properly classify new unclassified data.

CAD TOOL EXPERIMENTAL SETUP

1. FUNCTIONAL BRAIN IMAGE DATA SETS

In order to validate the performance and outcomes of the designed NMF SVMbased CAD tool for Alzheimer's disease detection, two different databases are used. The first one involves SPECT brain images, whereas the second one consists of PET brain images. These two databases, described below, contain spatially normalized functional brain images of different subjects. This normalization step ensures that a given voxel in one patient refers to the same brain position than the same voxel in another patient. Then, the intensities of the functional images are normalized to the maximum intensity. This normalization is computed for each image individually by referring each voxel to the average value of the %0.1 highest intensity voxels, in order to allow statistical comparison among different subjects.

2.SPECT DATABASE:

This baseline SPECT data set is taken from the internet. Each patient was injected with a gamma emitting technetium-99m labeled ethyl cysteinat dimer (99mTc-ECD) radiopharmaceutical and the SPECT scan was acquired by means of a three-head gamma camera Picker Prism 3000. Brain perfusion images were reconstructed from projection data by filtered backprojection (FBP) in combination with a Butterworth noise filter. The SPECT images were labeled by experts of the "Virgen de las Nieves" hospital using two different labels: NOR for subjects without any symptom, and AD for Alzheimer's patients. The complete SPECT database consists of 97 patients: 41 NOR and 56 AD.

3.PET DATABASE.

This PET data set selected for the validation of the CAD tool was obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database.¹ Launched in 2003 by NIA (National Institute on Aging), NIBIB (National Institute of Biomedical Imaging and Bioengineering), and FDA (Food and Drug Administration), the ADNI main purpose was focused on the measurement

of the progression of Alzheimer's disease (AD) in its initial stages. The ADNI, coordinated by M. W. Weiner (VA Medical Center and University of California, San Francisco), is the product of the effort of a variety of researchers from a wide number of academic institutions and private corporations. 800 participants from USA and Canada were recruited: approximately 200 participants without symptoms as a reference, about 400 MCI subjects, along with their temporal evolution over three years and 200 patients with early AD symptoms, with their progression in two years.

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