Segmentation of PET and SPECT Data Using Hidden Markov Random Fields in Order to Improve the Assisted Diagnosis of Neurodegenerative Diseases

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INTRODUCTION

- Structural and molecular brain neuroimages are frequently used to assist the diagnosis of Alzheimer's (AD) and Parkinson's disease (PD).
- During last decades a number of computer-aided diagnosis (CAD) systems that analyze and classify these data with high accuracy have been proposed.
- The classical (straightforward) approach to classify neuroimaging data uses the intensity of all brain voxels as feature, what leads to the small sample size problem [1].
- Two approaches have been proposed to address this problem:
  - To perform a selection of voxels based on the regions that are known to be affected by the disorder under study (previous knowledge).
  - To carry out a dimensionality reduction based on the classic algorithms [2] (does not require previous knowledge).

We propose a method to reduce the dimensionality of neuroimaging data in order to address the small sample size problem and, that way, to improve the performance of CAD systems. Our proposal consists on performing a segmentation of the data based on Hidden Markov Random Field (HMRF) followed by a selection of regions based on the Bhattacharyya distance. Thus, no previous knowledge about the disease is required.

- HMRF is a classical technique successfully used to segment structural data but, as far as we know, it has not been used to segment molecular neuroimages such as those obtained with Positron Emission Tomography (PET) or Single-Photon Emission Computed Tomography (SPECT).
- This method divides each neuroimage into several maps according to both intensity and neighborhood of the voxels (a given voxel is more likely to belong to the same map as the voxels in its neighborhood).

SEGMENTATION BASED ON HMRF

- It assigns a label $l_i \in L = \{1, \dots, M\}, i = \{1, \dots, N\}$ to each voxel in a molecular neuroimage according to both, intensity and neighborhood. Therefore, this procedure results in the division of the voxels of a neuroimage into M maps.
- Let $y = \{y_1, y_2, \dots, y_N\}$ be the locations of the N voxels that form a neuroimage. Each of them is associated to an intensity value d_i. In this procedure we looked for a labeling, $\mathbf{x} = (x_1, x_2, \dots, x_N)$, where $x_i \in L$ is the label assigned to the voxel in y_i. Formally we estimated (MAP criterion):

$$\hat{\mathbf{x}} = \arg\max_{\mathbf{x}\in\chi}\{P(\mathbf{y}|\mathbf{x})P(\mathbf{x})\}$$

  where $\hat{\mathbf{x}}$ is an estimation of $\mathbf{x}$ and considered a particular realization of the Markov random field X [4].
- Using the equivalence between Markov random fields and Gibb distributions [3], previous equation can be written as:

$$\hat{\mathbf{x}} = \arg\min_{\mathbf{x}\in\chi}\{U(\mathbf{y}|\mathbf{x}) + U(\mathbf{x})\}$$

  where $U(\mathbf{y}|\mathbf{x})$ is the likelihood energy.
- Estimating $\hat{\mathbf{x}}$ involves estimating the parameter set $\theta = \{\theta_l, l \in L\}$, where $\theta_l = (\mu_l, \sigma_l)$, since we assumed a Gaussian function for $\mathbf{y}$.
- A k-means algorithm was used to initialize the labeling $\hat{\mathbf{x}}$. Then, an Expectation-Maximization algorithm alternatively estimated the parameter set, θ, and the label set, $\hat{\mathbf{x}}$.
- The HMRF-based segmentation was applied to *ad-hoc* images (one per data modality) composed as the average of all neuroimages in our dataset.
- The resulting maps for a given modality were used as masks to segment all available images of that modality.

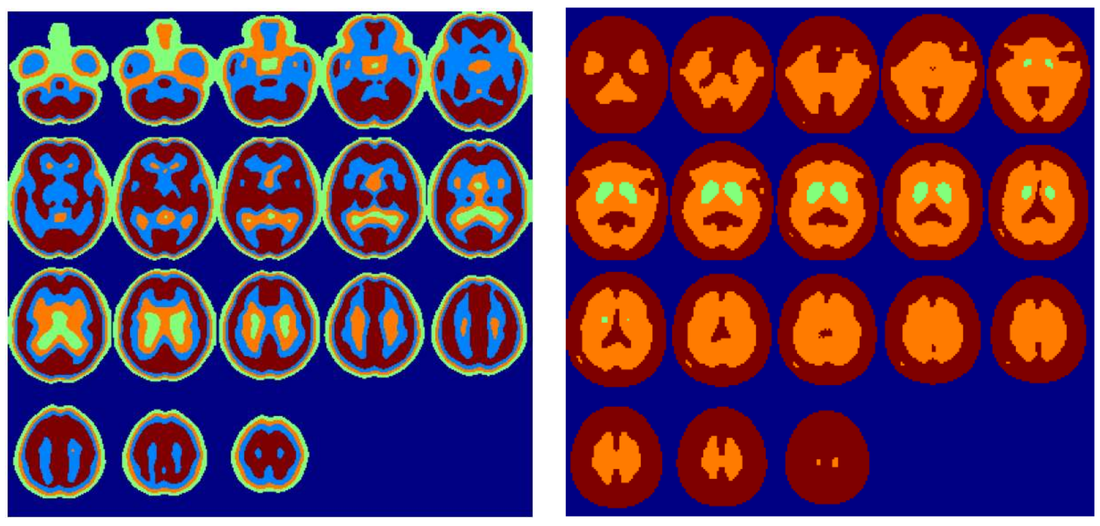
VOXEL SELECTION

- The Bhattacharyya distance was used to select the most discriminative maps among those resulting from the HMRF-based segmentation.

$$B = \frac{1}{8}(\mu_1 - \mu_2)^T \left(\frac{\sigma_1 + \sigma_2}{2}\right)^{-1} (\mu_1 - \mu_2) + \frac{1}{2}\ln\frac{\left|\frac{\sigma_1+\sigma_2}{2}\right|}{\sqrt{|\sigma_1||\sigma_2|}}$$

EXPERIMENTS AND RESULTS

- The proposed method was evaluated using two datasets:
  - **Dataset for AD.** Composed by 97 ^{99m}Tc-ECD-SPECT images from AD patients (56) and healthy subjects (41).
  - **Dataset for PD.** Composed by 189 ^{123m}I-FP-CIT SPECT images from healthy subjects (95) and patients with parkinsonian syndromes (94).
- Both datasets were labeled by experienced clinicians after visual examination of the neuroimages.
- Initially, neuroimages in both datasets were preprocessed following standard procedure:
  - **Spatial registration**. The template matching approach implemented in SPM8 was used.
  - **Intensity normalization**. It was performed by dividing each voxel intensity by the mean intensity of the 0.1% of the voxels with highest intensity.



Maps resulting from the segmentation of the mean image of the "Dataset for AD" (left) and the "Dataset for PD" (right).

- A SVM classifier was trained using the voxels in selected maps to separate patients and controls.

Classifiers using the regions selected by the proposed approach yielded higher accuracy rates than those based on previous approaches.

- The performance was estimated by means of a k-fold approach:

Dataset	Method	Accuracy	Sensitivity	Specificity
AD	Proposed approach	76,29 %	80,36 %	70,73 %
	All voxels as feature	71,13 %	71,43 %	70,73 %
PD	Proposed approach	89,42 %	88,54 %	90,32 %
	Striatal voxels	69,84 %	70,78 %	69,00 %

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3. Y. Zhang et al., "Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm", IEEE Transactions on Medical Imaging, vol. 20, no. 1, pp. 45–57, Jan. 2001.
4. S. Z. Li, Markov Random Field Modeling in Image Analysis, 2nd ed. Tokyo, Japan: Springer, 2001.