21st International Symposium on
Mathematical Theory of Networks and Systems
July 7-11, 2014. Groningen, The Netherlands

# Classification of Alzheimer′s Disease Using Nonlinear Independent Component Analysis

D. Duncan
Department of Mathematics
University of California at Davis
Davis, CA 95616, USA
dduncan@math.ucdavis.edu

T. Strohmer
Department of Mathematics
University of California at Davis
Davis, CA 95616, USA
strohmer@math.ucdavis.edu

## Abstract

*The goal of this study is to classify magnetic resonance imaging (MRI) of brains of patients with Alzheimer′s Disease (AD) and those without AD and then to identify changes in brain MRI in early stages of AD. A novel approach based on the diffusion map framework, which is considered to be one of the leading manifold learning methods, is used for this classification. Diffusion mapping provides dimensionality reduction of the data as well as pattern recognition that can be used to distinguish brains of patients with AD from brains of patients without AD. A new algorithm, which is an extension of diffusion maps, constructs coordinates that generate efficient geometric representations of the complex structures in the MRI. In addition, this method is adapted to the MRI and accounts for the variability in calibration of the MRI of different patients. The algorithm is tested on MRI data from patients who developed AD and those who did not.*

## 1. Background

Alzheimer′s Disease (AD), the most common type of dementia, currently affects approximately 5.2 million people in the US, with a significant increase predicted in the near future. There are more than 35 million people worldwide with AD; this number is expected to double by 2030 and more than triple by 2050 to 115 million [1]. In AD patients, neurons along with their connections are progressively destroyed, resulting in the loss of cognitive function and eventually death [2]. Therapeutic intervention is most beneficial in the early stages of AD, thus, it is important to identify the disease as early as possible in order to administer medication that will effectively stop the disease.

Mild Cognitive Impairment (MCI) is a stage between normal aging and the development of AD. It has been defined to account for the cognitive state where patients are impaired on one or more standardized cognitive tests but do not meet the criteria for clinical diagnosis of AD [3]. MCI offers an opportunity to target the disease process early, before it is too late to stop the disease from progressing.

Neuroimaging has been shown to be a powerful tool for studying changes in the progression of AD as well as therapeutic efficacy in AD patients. Magnetic Resonance Imaging (MRI) scans are useful for identifying features that can help predict which patients will develop AD.

## 2. Methods

In MRI data, we assume that there are certain features in the brain images of patients with AD. We would like to discover these features to distinguish brains of patients in early stages of AD from brains of healthy patients. Diffusion maps [4] have been a useful tool in reducing the dimensionality of the data as well as providing a measure for pattern recognition and feature detection. Since diffusion mapping may detect abnormal behavior in the data, it can be used to determine differences of brains of patients with AD. However, diffusion mapping assumes access to the underlying process that it aims to reveal. In MRI data, the relationship between the pixels of the images and the underlying brain activity may be stochastic, and the data are assumed to be noisy due to the calibration. Hence, diffusion mapping is not the most suitable approach to use with the MRI data. A recently developed algorithm, which is an extension of diffusion maps, is more applicable in the case of

ISBN: 978-90-367-6321-9

classifying AD [5, 6]. This algorithm assumes a stochastic mapping between the underlying processes and the measurements; the mapping is inverted, and a kernel is used to recover the underlying activity [5]. Thus, the proposed algorithm is more appropriate than diffusion maps for our data.

We propose an algorithm that relies on [5] for extracting the underlying brain activity from the MRI data. The algorithm is an extension of diffusion maps and uses local principal components analysis (PCA). PCA is another dimensionality reduction method. In PCA, the goal is to compute the most meaningful basis to re-express a large and noisy data set. This new basis can reveal hidden patterns and structure in the data as well as remove the noise. An orthogonal linear transformation converts the data to a new coordinate system. The greatest variance in the data is represented by the first coordinate or the first principal component. An important difference between the proposed algorithm and PCA is the use of nonlinear locality in the extension as opposed to PCA, which retains the linear global information of the data. For the MRI data, we perform PCA on local regions of the images and then integrate the local information using a kernel and obtain a single model. We use a data-driven adapted distance between blocks of MRI data to approximate the Euclidean distance between the features from the MRI data that are considered noisy due to calibration differences.

The 3D matrices that are formed from the MRI data are subdivided into vectors that are made up of overlapping neighborhoods around pixels (8x8x8). These vectors from the MRI of patients with AD are compared to the vectors from the MRI of healthy patients to determine if certain features are different that can be used to identify AD.

Given one of these feature vectors, $\mathbf{S}_y(m)$, we compute the local covariance matrix within a set interval, $J$, where $\mu_m$ is the empirical local mean of the feature vectors in the interval.

$$_m = \frac{1}{J}\sum_{m'=m-J+1}^{m}(\mathbf{S}_y(m')-\mu_m)(\mathbf{S}_y(m')-\mu_m)^T, \quad (2.1)$$

We define a nonsymmetric distance using the covariance matrices and a symmetric distance, known as the Mahalanobis distance, and it is shown in [4] that this distance approximates the Euclidean distance between the underlying factors in the data.

$$a_\Sigma^2(m,m') = (\mathbf{S}_y(m)-\mathbf{S}_y(m'))^T\Sigma_{m'}^{-1}(\mathbf{S}_y(m)-\mathbf{S}_y(m')) \quad (2.2)$$

$$d_\Sigma^2(m,m') = \frac{1}{2}(a_\Sigma^2(\mathbf{S}_y(m),\mathbf{S}_y(m'))+a_\Sigma^2(\mathbf{S}_y(m'),\mathbf{S}_y(m))). \quad (2.3)$$

We are able to recover these underlying factors using an eigendecomposition of an appropriate Laplace operator (kernel). A kernel is used to compare the underlying factors, and $\varepsilon$ is the kernel scale set according to the Mahalanobis distance. This kernel defines the local geometries of the graph.

$$W^{m,m'} = \sum_{r\in\mathscr{R}}(A^{m,r}A^{m',r}), \quad (2.4)$$

The kernel is normalized by a diagonal density matrix, which enables us to view the sampling as uniform. Then an eigendecomposition is performed to handle the nonuniform sampling of the data. The eigenvectors found from the eigendecomposition corresponding to the largest eigenvalues provide a parametrization of the features, allowing for significant data dimensionality reduction and capturing the features that may identify patients with AD.

$$\mathbf{S}_y(m) \mapsto [\psi_1(m),\psi_2(m),...,\psi_\ell(m)]^T, \quad (2.5)$$

The proposed method has already proved to be effective in identifying preseizure states in intracranial EEG data by providing a distinction between interictal and preseizure states of a patient with epilepsy [7].

## 3. Data

Alzheimer′s Disease Neuroimaging Initiative (ADNI) is a worldwide project that provides reliable clinical data for the research of pathology principle, prevention, and treatment of AD. Subjects who have mild cognitive decline and memory loss problems are recruited to clinical trials for MRI scans. Over 800 adults aged between 55 to 90 years old have been recruited to participate in the research, including approximately 200 cognitively normal subjects who are followed for 3 years, 400 subjects with MCI who are followed for 3 years, and 200 subjects with early AD who are followed for 2 years.

## 4. Discussion

Independent component analysis (ICA) based methods have been used for analyzing neuroimaging data, such as MRI. Yang et al. used ICA and a support vector machine (SVM) to classify AD MRI data. They first aligned and normalized all MRI scans studied using statistical parametric mapping. Then ICA was applied to

the images to extract features used for classification. Finally, the SVM was used to classify the images based on the independent component coefficients [8].

The key difference in our method and other methods that have been used to classify and detect early onset of AD in patients is the nonlinear and local network approach, which is necessary to eliminate the calibration differences of MRI of patients with different shapes and sizes of brains as well as the use of different scanners and centers collecting data.

## References

[1] Alzheimer′s Association: Alzheimer′s Disease Facts and Figures. Alzheimer′s & Dementia, **6(2)** (2010), 158–194.

[2] J. Ye, M. Farnum, E. Yang, R. Verbeeck, V. Lobanov, N. Raghavan, G. Novak, A. DiBernardo and V.A. Narayan, *Sparse learning and stability selection for predicting MCI to AD conversion using baseline ADNI data*, BMC Neurology (2012), 12–46.

[3] R.C. Petersen, *Mild cognitive impairment clinical trials*, Nat. Rev., **2** (2003), 646–653.

[4] R.R. Coifman and S. Lafon, *Diffusion maps*, Appl. Comp. Harm. Anal., **21** (2006), 5–30.

[5] R. Talmon and R.R. Coifman, *Differential stochastic sensing: intrinsic modeling of random time series with applications to nonlinear tracking*, Proc. Nat. Acad. Sci., (2012).

[6] R. Talmon, D. Kushnir, R.R. Coifman, I. Cohen and S. Gannot, *Parametrization of linear systems using diffusion kernels*, IEEE Trans. Signal Process., **60** (2012).

[7] D. Duncan, R. Talmon, H.P. Zaveri and R.R. Coifman, *Identifying preseizure state in intracranial EEG data using diffusion kernels*, Math. Biosci. Eng., **10(3)** (2013), 579–90.

[8] W. Yang, R.L.M. Lui and X. Huang, Independent component analysis-based classification of Alzheimer′s MRI data J. Alzheimers Dis., **24(4)** (2011), 775–783.