Multiway Analysis of Alzheimer's Disease: Classification based on Space-frequency Characteristics of EEG Time Series

C.-F. V. Latchoumane, F. Vialatte, A. Cichocki, and J. Jeong

Abstract*—In this paper, we present a method to detect the early stages of Alzheimer's disease (AD) based on electroencephalogram (EEG) feature extraction. We used a multiway analysis to extract the spatial-frequency characteristics for classification of subjects. The filters obtained from a parallel factor analysis (PARAFAC) model were used to describe the groups and reduce their description to meaningful features in frequency and space, helping the identification of subjects developing Alzheimer's disease. We analyzed 20-second steady state, artifact free EEG time series recorded over 21 leads from age-matched subjects. The subject database included 38 controls, 22 mild cognitive impairment subjects (MCI) and 23 Alzheimer's disease patients (AD). We applied a multiway analysis based on the PARAFAC model to extract the multilinear interactions between groups, frequency, and space. In a divide and conquer scheme, we obtained a classification accuracy of 74.7% comparing the control subjects to the demented subjects, and we obtained a classification accuracy of 75.6% comparing MCI subjects to AD patients. This approach combined the multilinear interaction within the tensor formed by *subjects X frequency power X regions* and provided an interesting interpretation and characterization of Alzheimer's disease in the early stages from a simple set of features. The multiway modeling of EEG recordings applied to the characterization and classification of Alzheimer's disease patients in the early stages has not been employed as yet. Even though the classification results are modest compared with the available literature, this method could help extract more interesting features as well as summarize information for classification or diagnosis at a higher level than subject-by-subject EEG analysis. This method, if combined with other features, could reveal itself to be very promising for diagnosing Alzheimer's patients in the early stages. Moreover, it can be easily generalized as well as improved by numerous linear and nonlinear features of EEGs.

***Index Terms*—Multiway analysis, PARAFAC, classification of Alzheimer's patients, EEG.**

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I. Introduction

Alzheimer's disease is the most prevalent form of neuropathology leading to dementia; it affects approximately 25 million people worldwide and is expected to have a fast recrudescence in the near future [1]. The numerous clinical methods that are now available to detect this disease including imaging [2]-[3], genetic studies [4], and other physiological markers [5], however, do not allow a mass screening of the population. Whereas psychological tests such as MMSE in combination with an electrophysiological analysis (e.g. electroencephalograms or EEG) would be a much more efficient and inexpensive screening approach to detect subjects affected by the disease.

EEG recordings are now used more and more as a method to assess the susceptibility a patient to Alzheimer's disease, but are often obtained during steady states where temporal information does not easily reveal the relevant features for subject differentiation, however it could obtain the excellent reported classification results [6]. In those cases, the spatial-frequency information includes simple indexes that might summarize information valuable in detecting demented subjects, however, the inter-subject variability, especially considering the differences in the progression of the disease, might render the study difficult when undertaken subject-by-subject. In that manner, a multiway analysis would allow the extraction of information that is contained across subjects simultaneously considering the spatial-frequency information. This methodology has been applied to epilepsy detection and has successfully characterized the epilepsy foci in a temporal-frequency-regional manner [7]-[8]. Classification based on multiway modeling has even been performed on a continuous EEGs [9] showing the power and versatility of multiway analyses.

Previous two-way analyses combining PCA-like techniques [6] have shown very interesting results in the classification of subjects and have then assisted in early detection. Thus far, no application of a multiway analysis has been made in this type of database, dealing with subject classification based on EEG characteristics.

II. Method

In this study, we aimed to extract valuable and simple features from the frequency-region map of each subject from each group (i.e. control, MCI, or Alzheimer's patients). We then constructed a multivariate tensor, *subjects X frequency X brain region*, extracted the frequency-space map associated with each model component. The latter mapping was used as a filter to class subjects using linear and nonlinear classifiers. The detail of the method is described as follows.

A. Multivariate Analysis: PARAFAC

The important concept underlying multiway analyses is the extraction of a multilinear structure of the data, which could highlight important interactions, invisible at lower dimensions. In this study, we used a common modeling method for N-way analyses: PARAFAC [10].

The parallel factor analysis (PARAFAC) is often referred to as a multilinear version of the bilinear factor models. From a given tensor, $\underline{X} \in \mathbb{R}^{I\times J\times K}$, this model is able to extract linear decompositions of Rank-1 tensors.

$$\underline{X} = \sum_{r=1}^{R} a_r \circ b_r \circ c_r + \underline{E} , \qquad (1)$$

where $\boldsymbol{a}_r$, $\boldsymbol{b}_r$, and $\boldsymbol{c}_r$ are the r^{th} column of the component matrices $A \in \mathbb{R}^{I\times R}$, $B \in \mathbb{R}^{J\times R}$, and $C \in \mathbb{R}^{K\times R}$, respectively, and $\underline{E} \in \mathbb{R}^{I\times J\times K}$ is the residual error matrix. The operator $\circ$ designates the outer product of the two vectors. The PARAFAC model under optimal fitting conditions (e.g. core consistency analysis) is able to provide a model with the assumption of trilinearity relations between the dimensions (also called modes), thus, will provide a unique fit for the given data.

The fitting of the model depends on the number of components, R, chosen by the users, and for this approach, we opted for validation of the model (i.e. number of components) based on the core consistency [11]. However, the choice of the correct number of components only guarantees that the model does not suffer from overfitting. We could observe that for an optimal number of components, the classification results returned discrete values, which were inversely correlated to the average of the maximum residual values. This correlation indicates that overfitting does lead to a less meaningful model. In addition to the core consistency analysis, we opted for a model with a high average maximum of residual.

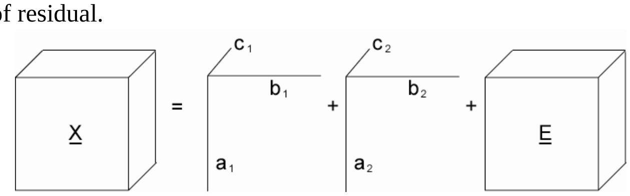

Fig. 1: PARAFAC modeling of a 3-way tensor; each component (R=2) is the outer product of Rank-1 tensor a, b, and c, and E is a residual tensor.

B. From Model to Filter

The multivariate model, with a sufficient number of components and an appropriate fitting (i.e. core consistency [11] and component variability), is able to represent a trilinear interaction between the modes. The sample mode is analogue to the components in the principal component decomposition, thus representing the weight of the common interactions with the two other modes. In addition, the component-wise frequency-region map formed by the frequency mode and region mode could be thought of as a characteristic filter, which combined with the sample weight, would recreate the original data. This same filter could also be used in a discriminant comparison to decide the membership of each sample. We calculated the filters, F_R, as described in Eq. (2):

$$F_R = (b_R \circ c_R) , \qquad (2)$$

where b_R and c_R are the Rank-1 vector of the frequency and region mode in the PARAFAC model, respectively.

C. Subjects & EEG Recordings

The subjects analyzed in this study were taken from a previously studied database [6, 12, 13] and consisted of eyes opened, steady state EEG recordings of duration of 20 s, over 21 leads disposed according to the 10-20 international system and digitalized at 200 Hz. The database contains 38 control (71.7±8.3) subjects, 22 mild cognitive impairment (MCI) subjects (71.9 ± 10.2) who later contracted Alzheimer's disease, and 23 Alzheimer's disease patients (72.9±7.5). The control subjects had no complaints or history of memory problems, and scored over 28 (28.5±1.6) on the mini mental state exam (MMSE). The MCI subjects had complaints about memory problems and scored over 24 at the MMSE (26±1.8). The inclusion criterion was set at 24 as suggested in [13], therefore, encompassing MCI subjects with various cognitive deficits, but in the early stages of Alzheimer's disease. The Alzheimer's disease patients scored below 20 on the MMSE and had had a full clinical assessment. Thirty-three moderately severely demented probable AD patients (mean MMSE score = 15.3±6.4, range = 0-23) were recruited from the same clinic. After obtaining written informed consent from the patients and controls, all subjects underwent EEG and SPECT examination within one month of entering the study. All subjects were free of acute exacerbations of AD related co-morbidities and were not taking medication. The medical ethical committee of the Japanese National Center of Neurology and Psychiatry approved this study.

D. Classification: Contol vs. Demented and MCI vs. AD

We classified the three classes (Ctr, MCI, and AD) using both a quadratic discriminant analysis (QDA) and an artificial neural network (ANN, feedforward two layer perceptron with one input bias). We first separated the control subjects from demented patients, using the F_R filters (see Eq. (3)) extracted from the PARAFAC model (three components were the largest accepted dimension according to the core consistency). For a comparison, we also generated three "reference filters", F_A (Eq. (3)), using the averaged matrix along the samples of each class (Ctr, MCI, and AD):

$$F_A = \overline{X}_c , \qquad (3)$$

where X_c is the matrix of all the samples of one class (e.g. all Ctr subjects or all AD patients). The filters obtained were then applied to the original data, constituting for each subject a database of three descriptive features. We validated the classification models using a leave-one-out approach. The same procedure was applied to a classifier separating the AD patients from the MCI patients. In this context, we used a two-component PARAFAC against the two reference filters of the AD and MCI classes. Combining the two classifiers in cascade (Ctr vs. MCI and AD, then MCI vs. AD, see Fig. 2), it is therefore feasible to separate the data into the three groups.

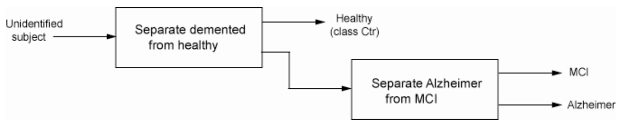

Fig. 2: Classification method – cascade of classifiers.

The filter used for the classification provides additional information, which is especially useful for the interpretation of the spatial-frequency boundary.

III. Results

The best classification results using the ANN and QDA are displayed in Table 1.

Table 1: Leave-one-out classification results. ROC curves for the PARAFAC and references classification results using ANN as displayed in Figs. 3 and 4.

	Ctr / demented (PARAFAC)	Ctr / demented (reference)	AD / MCI (PARAFAC)	AD / MCI (reference)
ANN	25.3%	38.6%	24.4%	35.6%
QDA	25.3%	38.5%	31.1%	35.6%

Generally, the PARAFAC filters strongly outperformed the reference filters (over 10 points for the ANN) for both classification methods.

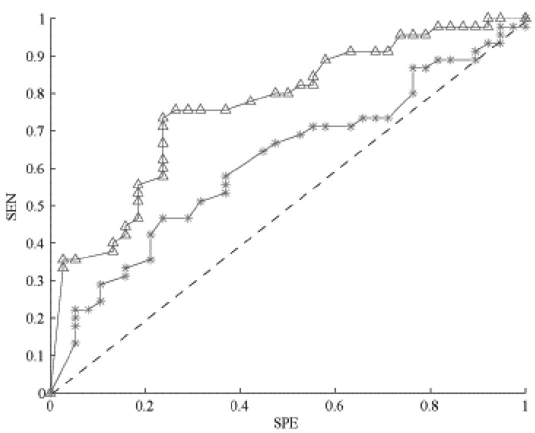

Fig. 3: ROC curve of classification accuracy of control vs. demented subjects; classification results obtained using the original data (stars) and using the filtered data extracted with a three-component PARAFAC (triangle).

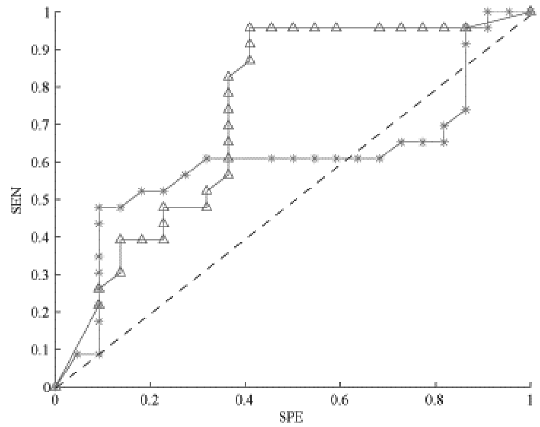

Fig. 4: ROC curve of classification accuracy of AD vs. MCI subjects; classification results obtained using the original data (stars) and using the filtered data extracted with a three-component PARAFAC (triangle).

As shown in Figs. 3 and 4, the performance in the classification based on the ANN shows better results using the information from the extracted filters than using the original data. Especially, the best performance was found to be 74.7% (75.6% sensitivity, 73.7% specificity) for the Ctr vs. demented classification and 75.6% (95.6% sensitivity, 59.1% specificity) for MCI vs. AD classification.

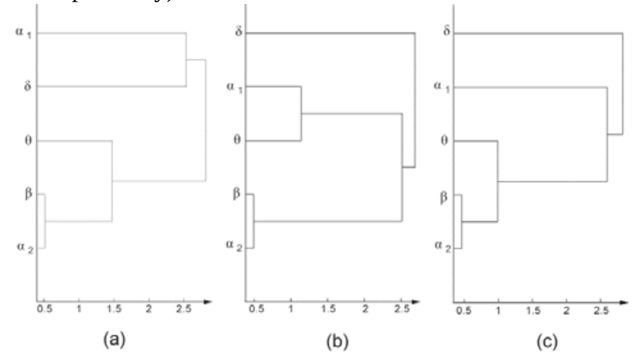

Fig. 5: Classification of frequency bands characteristics. Dendrograms extracted from the clustering of two-components PARAFAC models for (a) control subject, (b) MCI patients, and (c) Alzheimer patients.

Using PARAFAC on each separate group, a clustering of frequency bands (i.e. frequency band mode) can also be obtained [14] in order to study the non linear interactions between the frequency ranges (Fig. 5). The most striking effect we can observe is the evolutions in the inter-relations between the theta range and high frequency (alpha2 and beta) ranges: seemingly, for Ctr subjects and AD patients, the theta range activity is clustered with high frequencies (distance 1.5 and 1, respectively); whereas for the MCI patients, the theta range activity is much less (distance 2.5).

IV. Conclusion

In this paper, we presented a novel method applied to the classification of subjects based on a multiway analysis of their EEG features. This type of application of multiway analysis to EEG features has not yet been implemented for Alzheimer's disease diagnosis. We also showed the possible interpretability of the fitted model not only based on the spatial-frequency filters, but also based on the unimodal clustering for each group's model.

The classification results presented here are modestly good compared with the classification results using the same database in another study [6]. However, this study is the only one to provide a three-class classification result with an overall accuracy of approximately 74%. It is also of important to note that the classification based on the EEG features without feature extraction returns (i.e. classification results of the reference) did not originally result in high accuracy, indicating the originally poor separability of the groups.

Moreover, apart from its crucial uniqueness and its resulting easy interpretability [15], the PARAFEC model used might not be the best model to use in this analysis, as it imposes trilinearity conditions. Future work should include the comparison of the accuracy of other models such as PARAFAC2 [16], Tucker3 [17], or the nonnegative tensor factorization method [15]-[18] and its constrained model on sparsity [19].

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