Optimization of EEG Frequency Bands for Improved Diagnosis of Alzheimer Disease

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Abstract—Many clinical studies have shown that electroencephalograms (EEG) of Alzheimer patients (AD) often have an abnormal power spectrum. In this paper a frequency band analysis of AD EEG signals is presented, with the aim of improving the diagnosis of AD from EEG signals. Relative power in different EEG frequency bands is used as features to distinguish between AD patients and healthy control subjects. Many different frequency bands between 4 and 30Hz are systematically tested, besides the traditional frequency bands, e.g., theta band (4–8Hz). The discriminative power of the resulting spectral features is assessed through statistical tests (Mann–Whitney *U* test). Moreover, linear discriminant analysis is conducted with those spectral features. The optimized frequency ranges (4–7Hz, 8–15Hz, 19–24Hz) yield substantially better classification performance than the traditional frequency bands (4–8Hz, 8–12Hz, 12–30Hz); the frequency band 4–7Hz is the optimal frequency range for detecting AD, which is similar to the classical theta band. The frequency bands were also optimized as features through leave-one-out crossvalidation, resulting in error-free classification. The optimized frequency bands may improve existing EEG based diagnostic tools for AD. Additional testing on larger AD datasets is required to verify the effectiveness of the proposed approach.

I. INTRODUCTION

Alzheimer's disease (AD) is a neuro-degenerative disease, the most common form of dementia, third most expensive disease and sixth leading cause of death in the United States. It affects more than 10% of Americans over age 65, nearly 50% of people older than 85, and it is estimated that the prevalence of the disease will triple within the next 50 years [1, 2]. A promising diagnostic tool for AD

is electroencephalogram (EEG), which is obtained through specially designed electrodes located on the scalp.

Because of its non-invasive, safe, and easy-to-use properties, EEG is considered as a high potential diagnostic tool for AD that may complement some of the current traditional AD diagnostic methods. However, diagnosing AD in EEG signals remains a challenging problem as most of the existing methods do not offer reliable diagnosis [3, 4].

Several studies have applied linear and non-linear classification algorithms to discriminate between the EEG signals of AD patients and age-matched healthy control subjects. To date, the classification performance of these algorithms is about 80%–90% [5], and hence there is still significant room for improvement. A promising strategy to improve the diagnostic power of EEG for AD is to carefully design and optimise time-domain and frequency-domain EEG features [6]. We follow that approach in this paper: we investigate the use of *relative power* within different EEG frequency bands as a feature to distinguish mild AD from healthy control subjects. As a result, we provide optimal EEG frequency bands that improve the diagnosis of AD. Our approach may help to improve existing EEG based diagnostic tools for AD.

EEG is usually described in terms of its rhythmic activity, which is helpful in relating the EEG to the brain function. The rhythmic activity in EEG is commonly divided in specific frequency bands: 0.5–4Hz (delta), 4–8Hz (theta), 8–10Hz (alpha 1), 10–12Hz (alpha 2), 12–30Hz (beta), and 30–100Hz (gamma) [7]. Most of these bands are chosen arbitrarily, and have not been optimised for diagnostic purposes.

EEG signals are often corrupted by noise and artifacts: 50/60 Hz power line interference, motion and eye blinking artifacts, electromyogram (EMG) signals from muscles, and artifacts due to changes in the electrode-skin interface. Especially the gamma range (30–100Hz) has a low signal-to-noise ratio, and therefore will be excluded from our analysis. In this study, we consider the frequency range 1-30Hz, and investigate which EEG frequency band within that range maximizes the separability between mild AD patients and age-matched control subjects. As mentioned earlier, relative power of EEG frequency bands is used as a discriminative feature; more specifically, we compute the relative power of a frequency band within the range 1–30Hz (e.g. 1–5Hz) as the power of that band divided by the power of the "wide" frequency band 1–30Hz; as a consequence, relative power takes values between 0 and 1.

In the literature, different EEG frequency bands have been studied for diagnosis of AD, without systematically optimizing the EEG frequency range. Many studies consider a specific frequency band as a marker for AD:

- 4–8 Hz [3, 8-11]
- 7.8–12.87Hz [12]
- 5–14Hz [13]

Several studies use multiple frequency ranges as markers for AD:

- 1.5–6.5Hz and 6.5–8.5Hz [5, 14]
- 0.5–8Hz and 8–30Hz [6, 10]
- 1–4Hz, 4–8Hz, 8–12Hz, 12–25Hz [15]

In contrast to those studies, in this paper we systematically explore various frequency bands, with the aim of improving the diagnosis of AD from EEG. This paper is structured as follows. In the next section we discuss the EEG data that we use in this study. In Section III we explain our methodology and present our results. In Section IV we discuss our results and offer concluding remarks.

II.   EEG Dataset

We consider EEG data of mild-AD patients and age-matched control subjects. The EEG data set has been analyzed in previous studies [16-18]; the data was obtained using a strict protocol from Derriford Hospital, Plymouth, U.K., and had been collected using normal hospital practices [17]. EEGs were recorded during a resting period with various states: awake, drowsy, alert and resting states with eyes closed and open. All recording sessions and experiments proceeded after obtaining the informed consent of the subjects or the caregivers and were approved by local institutional ethics committees. EEG dataset is composed of 24 healthy control subjects (age: 69.4±11.5 years old; 10 males) and 17 patients with mild AD (age: 77.6±10.0 years old; 9 males). The patient group underwent full battery of cognitive tests (Mini Mental State Examination, Rey Auditory Verbal Learning Test, Benton Visual Retention Test, and memory recall tests). The EEG time series were recorded using 21 electrodes positioned according to Maudsley system, similar to the 10-20 international system, at a sampling frequency of 128 Hz. EEGs were band-pass filtered with digital third-order Butterworth filter (forward and reverse filtering) between 0.5 and 30 Hz.

The recordings were conducted with the subjects in an awake but resting state with eyes closed, and the length of the EEG recording was about 5 minutes, for each subject. The EEG technicians prevented the subjects from falling asleep (vigilance control). After recording, the EEG data has been carefully inspected. Indeed, EEG recordings are prone to a variety of artifacts, for example due to electronic smog, head movements, and muscular activity. For each patient, an EEG expert selected by visual inspection one segment of 20s artifact free EEG, blinded from the results of the present study. From each subject in the two data sets, one artifact-free EEG segment of 20s was extracted and analysed.

III.   Methodology

Our aim is to select EEG features for diagnosis of AD. In particular, we focus on spectral features, i.e., relative power of EEG frequency bands. Our approach consists of three steps: spectral feature extraction, separability tests, and classification.

A.   Feature Extraction

Many studies have shown that the EEG of AD patients has an abnormal spectrum [3, 6, 10, 13, 15, 19-21]. In particular, the EEG signals of AD patients tend to "slow down": they contain more power in low-frequency bands compared to healthy age-matched subjects. However, as far as we know, no study so far has systematically explored different EEG frequency bands for the purpose of diagnosing AD.

We compute the relative power in a frequency band [F:(F+W)]Hz as follows:

1) *Bandpass filter:* a bandpass filter is applied to each EEG channel to extract the EEG data in specific frequency band [F:(F+W)]Hz. We use Butterworth filters (of third order) as they offer good transition band characteristics at low coefficient orders; as a result, they can be implemented efficiently [22].

2) *Relative Power:* the relative power of a certain frequency band (extracted in the previous step) is obtained by dividing the power of this frequency band by the power of the total frequency band:

$$RP_i(F, F+W) = \frac{P_i(F, F+W)}{P_i(F_{\min}, F_{\max})}, \qquad (2)$$

where $P_i(F, F+W)$ is the power of the frequency band $[F, F+W]$ at channel i and $P_i(F_{\min}, F_{\max})$ is the power of the "wide" frequency range [1,30Hz].

3) *Average Relative Power (ARP):* the average relative power for each subject j is determined as

$$ARP_j(F, F+W) = \frac{\sum_{i=1}^{N} RP_i(F, F+W)}{N}, \qquad (3)$$

where $RP_i(F, F+W)$ is the relative power of the frequency band $[F, F+W]$ at channel i, and N is the number of EEG channels. (In our EEG data set, the number of channels is $N = 21$).

B.   Separability Test

After calculating the ARP for all subjects in certain frequency band [F:(F+W)]Hz, we compute the average ARP for AD subjects and all healthy subjects, denoted by μ_{AD} and μ_{Ctr} respectively. Likewise, we compute the standard deviation of ARP within both populations, denoted by σ_{AD} and σ_{Ctr} respectively.
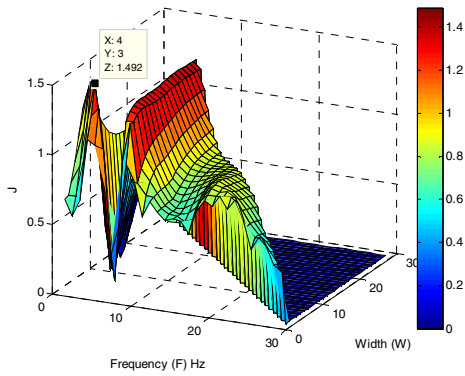
Fig. 1. The linear separation value J between Alzheimer and Control subjects, for relative power calculated over different frequency bands [F, $F+W$]. The x-axis represents the frequency F, the y-axis represents the width W, while the z-axis represents the linear separation J. For example, if the frequency F is 4Hz and the width is 3Hz, the corresponding frequency band is 4–7Hz and its $J(4,7)$ value is 1.492; this happens to be the maximum linear separation in our study. The figure shows three peaks in J (see also Fig.2).
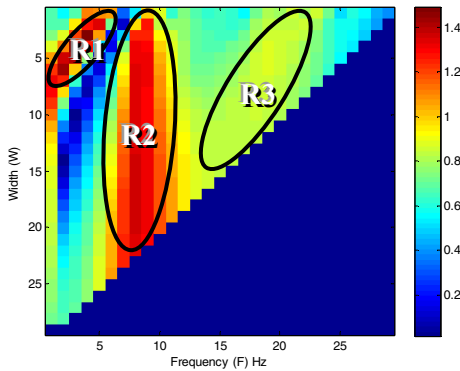

Fig. 2. This is a 2D presentation of Fig.1; it shows the regions of (F,W) values with the highest index $J(F,W)$. The x-axis represents the frequency F, the y-axis represents the width W, while the color indicates the linear separation value J. Three regions in the (F,W) plane can be distinguish with large J values. The three regions (from left to right) R1, R2, and R3 include theta, alpha, and beta bands respectively.

The linear separability criterion J is then computed:

$$J(F,F+W) = \frac{\left| \mu_{Ctr}(F,F+W) - \mu_{AD}(F,F+W) \right|}{(\sigma_{Ctr}(F,F+W) + \sigma_{AD}(F,F+W))} . \quad (4)$$

We calculate the index $J(F,F+W)$ over a range of frequency bands, i.e., $F =1, 2, …, 29$Hz and $W = 1, 2, …, 29$ Hz, corresponding to 841 different frequency bands within [1,30Hz]; we depict the value J as a function of F and W in Fig. 1 (3D) and Fig. 2 (2D). Interestingly, Fig.2 reveals three peaks in J, representing the largest linear separation J between AD and Control subjects.

Fig.2 illustrates the corresponding regions in the (F,W) plane. Fascinatingly, these regions R1, R2, and R3 contain the standard theta (4–8Hz), alpha (8–12Hz), and beta (12–30Hz) frequency bands respectively.

Region 1			Region 2			Region 3		
F	$F+W$	J	F	$F+W$	J	F	$F+W$	J
4	7	1.4917	8	25	1.3621	19	24	0.8809
3	7	1.4761	8	24	1.3613	19	25	0.8767
2	8	1.4301	8	26	1.3609	19	23	0.8717
3	8	1.4050	8	23	1.3584	21	22	0.8674
2	7	1.3629	8	27	1.3580	19	26	0.8665
			8	28	1.3540			
			8	22	1.3539			
			8	29	1.3494			
			8	21	1.3485	15	30	0.8346
			8	15	1.3450			

We sorted all 841 $J(F,W)$ values in descending order. In Table I we list largest J values for each region separately, with the corresponding frequency bands [$F,F+W$]. As can be seen from that table, the maximum separation J between AD and Control subjects occurs for the 4–7Hz band, which lies in Region 1. In Region 2 the frequency band 8–25Hz has the largest linear separability J; that band covers the classical alpha and beta band. In the same region, also the band 8–15Hz yields large J; that frequency band approximately corresponds to the standard alpha band (8–12Hz), yet yields larger J (not shown here). In Region 3 the frequency band 19-24 has the highest J value; it approximately corresponds to the standard beta band (12–30Hz).

C. Mann–Whitney U Test

The Mann-Whitney statistical test allows us to investigate whether the EEG statistics at hand (relative power of various frequency bands) take different values between the two subject populations. Low p-values indicate large difference in the medians of the two populations.

D. Linear Discriminant Analysis (LDA)

We apply linear discriminant analysis (LDA) with each spectral feature separately, with the aim of distinguishing AD patients from healthy control subjects. LDA has been used earlier for diagnosis of AD from EEG [5, 10, 15, 18, 20, 23]. We assess the classification performance of LDA through leave-one-out (LOO) cross-validation. Each learning set is created by taking all the samples except one, and the corresponding test set is the sample left out. Thus, for n samples, we have n different training sets (each yielding a coefficients vector **w**) and n different test sets. We conduct this procedure for each spectral feature.

TABLE II

TABLE II
P-VALUES AND CLASSIFICATION ERRORS ASSOCIATED WITH
STANDARD AND OPTIMIZED FREQUENCY BANDS

Measures	Traditional Frequency Bands			Optimized Frequency Bands		
	4-8Hz	8-12Hz	12-30Hz	4-7Hz	8-15Hz	19-24Hz
p-value	5.3×10^{-7}	4×10^{-7}	1.2×10^{-5}	8.4×10^{-8}	3.5×10^{-7}	1.7×10^{-5}
Error of LDA	12.2%	12.2%	24.4%	2.43%	7.3%	19.5%

TABLE III
P-VALUES AND CLASSIFICATION ERRORS FOR FREQUENCY BANDS
WITH LARGEST LINEAR SEPARABILITY J (TOP 5)

	Top Frequency Bands				
	4-7Hz	3-7Hz	2-8Hz	3-8Hz	2-7Hz
p-value	8.4×10^{-8}	8.4×10^{-8}	1.5×10^{-7}	9.7×10^{-8}	2.3×10^{-7}
Error of LDA	2.43%	4.87%	9.75%	7.31%	9.75%

Note that in this approach, the features are not selected through LOO; instead we analyze the discriminative power of each feature in terms of LDA classification error (assessed through LOO). We have also conduct feature selection through LOO, as we will discuss in the following section.

IV. DISCUSSION AND CONCLUSION

The performance of the frequency bands with largest linear separability J is displayed in Table II, where we consider the three regions separately (cf. Fig. 2); in Table III, we report results for the frequency bands with largest linear separability J overall, independent of the region; interestingly, those bands all happen to be part of Region 1.

As can be seen from Table II, the frequency band 4–7Hz (Region 1) yields the lowest *p*-value and the lowest LDA classification error; that band also has the largest separability index J. Interestingly, the band strongly resembles the classical theta band (4–8Hz), yet has vastly more discriminative power. Moreover, frequency band 8–15Hz (Region 2) achieves clearly better results as compared to 8–12Hz (alpha band). Relative power in 4–7Hz and 8–15Hz seem to be good EEG markers for AD, at least for the data set at hand.

In Region 3, the band 19–24Hz performs slightly better than 12–30Hz band (beta) in terms of classification error, but the corresponding *p*-values are comparable.

The lowest *p*-value, after testing all frequency bands, has been obtained for the 4–7Hz band, consistent with the J criterion and LDA error results.
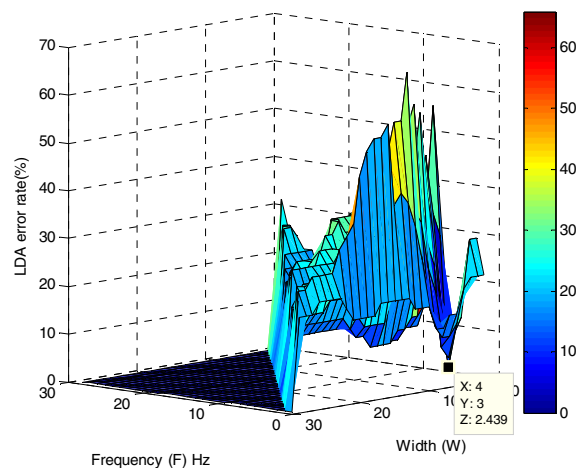

Fig. 3. Classification performance for distinguishing Alzheimer from Control subjects by means of LDA, for relative power calculated over different frequency bands [*F, F+W*]. The x-axis represents the frequency *F*, the y-axis represents the width *W*, while the z-axis represents the error scored from LDA classifier. The frequency band 4–7Hz yielded the smallest classification error, which is consistent with *J* separability result in Fig. 1.

Interestingly, the best results overall were obtained with the band 4–7Hz as shown in Fig. 3, whereas the band 4–8Hz (theta band) ranked only 46th according to the index *J,* and clearly yields lower classification performance. This shows that the discriminative power significantly varies with the choice of frequency band. So far in our discussion, we have not selected the spectral features in an automated fashion; we have simply assessed the discriminative power of each feature by means of various criteria.

TABLE IV
FREQUENCY BAND WITH THE SMALLEST LDA ERROR (COMPUTED
THROUGH LOO) FOR EVERY TRAINING SET. NOTE THAT THERE ARE IN
TOTAL 41 SUBJECTS AND HENCE THE SAME NUMBER OF TRAINING SETS.

LOO Iteration	Most Discriminative Frequency Band(s)	LDA error
1, 3, 4, 9, 10, 12, 13, 19, 20, 21, 22, 23, 24, 26, 27, 28, 29, 30, 33, 34, 35, 36, 37, 38, 39, 40, 41	4-7Hz	2.5%
7	3-7Hz	2.5%
5	4-7Hz, 3-7Hz	2.5%
32	4-7Hz, 3-7Hz	5%
6	4-7Hz, 3-8Hz	2.5%
16	4-7Hz, 5-7Hz	5%
25	4-7Hz, 5-7Hz	2.5%
8, 14, 18	4-7Hz, 3-7Hz, 3-8Hz	5%
11, 15	4-7Hz, 3-7Hz, 5-7Hz	5%
2, 17, 31	4-7Hz, 3-7Hz, 3-8Hz, 5-7Hz	5%

As a last experiment, we select the spectral features through leave-one-out crossvalidation (LOO). In each training set (containing all subjects except one), the spectral features are ranked according to LDA classification error. The latter is in turn also computed by LOO, as we did in Section 3.D; however, here we do not consider the entire data set but a training set instead (containing all subjects except one).

As a result, we obtain a table similar to Table I for every training set, which lists the classification error (instead of index J) for every spectral feature, in descending order. Next we select the spectral feature with the lowest classification error, and we conduct LDA with that feature on the training set. The resulting linear classifier (with optimized feature) is then evaluated on the remaining test sample; that procedure is repeated for every training set and corresponding test set.

It is noteworthy that every test sample happens to be *correctly* classified; in other words, the classification error obtained through LOO feature selection is *zero*.

Interestingly, again the frequency band 4–7Hz yields the lowest classification error for most training sets (see Table IV), and therefore, it seems to result in stable classifiers.

Of course, it is important to point out that the data set at hand is fairly small. A larger sample size and a more diverse data set are needed in order to generalize the findings of this study. Multiple types of dementia and other neurological disorders can also be analyzed through our technique, which may further validate our results. The ultimate objective of this line of research is to determine the most appropriate EEG frequency bands for diagnosing AD (and potentially other neurodegenerative diseases) at an early stage using scalp EEG.

V. ACKNOWLEDGEMENT

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