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Robust Alzheimer's disease Severity Classification in Compressed EEG Signal

Lekshmi G.S[1], Binu Chacko[2]

PG Student, Department of Electronics, Applied Electronics and Instrumentation,

Lourdes Matha College of Science and Technology, Kerala, India[1]

Assistant Professor, Department of Electronics, Lourdes Matha College of Science and Technology, Kerala, India[2]

Abstract: Alzheimer's disease (AD) is considered to be the most common and the fastest growing neurological disease in the world. Biomarker tools for early diagnosis and disease progression in AD remain key issues for clinical applications, sanitary systems and pharmaceutical companies. Electroencephalogram (EEG) yields, a powerful and relatively cheap way for screening of dementia and AD in their early stages. Portable EEG systems based on wireless sensors can be used for unobtrusive long term monitoring provided they can solve technological problems. Clinical applications require intensive recording of massive EEG data, raising the need for efficient and flexible compression techniques. Early diagnosis of Alzheimer's disease and its prodromal stage is very important for possible delay of the disease, and there is thus a great deal of interest in the development of new methods for earlier detection. In this thesis, a novel approach to the diagnosis of Alzheimer's disease from EEG is proposed with the use of decision tree classification algorithm combined with empirically determined regions of interest as attributes. In addition to this a model based Greedy search algorithm is used to allocate the weight value.

Keywords: Alzheimer's disease, Compressive Sensing**,** Greedy search algorithm, Decision tree classification.

I. INTRODUCTION

Electroencephalography (EEG) is a well-established modality for measuring the electrical activity generated by populations of neurons of the cerebral cortex. In scalp EEG, the bioelectric signals are recorded non-invasively through a set of electrodes placed over the head of the subject. The EEG can be considered as a multivariate signal acquired over many channels (20 to 128) with various sampling rates (from 200 to 1000 Hz) at 12-16 bits, according to the clinical application. This implies potentially many hours of wear time with discomfort of patients and the generation of lots of data to be stored and transmitted [1, 2]. A judicious reduction of those data can give more efficient storage and remote transmission. EEG is not only a key diagnostic tool for neurologists, but it is growingly used in Brain-Computer Interfaces (BCI) applications. EEG has also recently raised interest for some industrial automotive applications. There is, thus, a generalized call for innovative techniques of compressive EEG. The traditional approach to EEG signal processing is to perform Nyquist sampling on a bandlimited version of the signal.

However, wavelet methods can yield the possibility of retaining just relevant information through a suitable thresholding procedure carried out on the transformed domain coefficients. Unluckily, this approach implies the computation of all of the coefficients before discarding the ones below threshold. The compressive sensing technique allows for simultaneous sampling and compression as well as to recover the signals at a later stage (off-line) from a very limited number of samples than traditional systems. The main concepts behind this approach are sparsity and incoherence [3]. In short, the compressive sensing approach is based on the observation that the information rate of the signal may be smaller than bandwidth if the original signal is represented in a proper basis. Exploiting sparsity may guarantee to adhere to the information content of the signal while transmitting a limited number of data. Incoherence is used at the reconstruction level of the procedure: the signal is correlated with a reduced number of basis waveforms which are incoherent with the sparsifying basis. For example, noiselets are incoherent with Daubechies wavelets, and a low coherence means that fewer samples of the signals are needed.

An efficient way of compressing EEG signals can be the key to allow many clinical real time applications be technically implemented; in particular, by transmitting only relevant data thus reducing both memory and power requirements. Feature extraction techniques can be useful in this sense, but they require training, are usually signal specific and do not allow full reconstruction of the signal.

Furthermore, the nonstationarity nature of many bio-signals calls for extracting different features in separate sections of the signal. In this paper, the use of EEG compression techniques is proposed as a novel approach to the diagnosis of Alzheimer's disease (AD) from EEG. It will be shown that the EEG of AD has a super-compressibility property with respect to the EEG of

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Healthy Controls (HC). Furthermore, it is also observed that Mild Cognitive Impaired (MCI) subject, potentially converting to AD in the near future, has an intermediate behaviour in compressibility. In recent years, many researchers have observed that an EEG complexity analysis may yield possible insights regarding AD diagnosis also in the early stages [4, 5]. Having the opportunity to use non-invasive scalp EEG to make a screening of population at risk of developing AD is certainly beneficial, because of the cost of other diagnostic modalities (like PET or MRI) [2]. The use of EEG in monitoring the alterations of human brain with disease and aging in widely accepted [6, 7]. In particular, the EEG traces of AD patients typically shows three kinds of abnormalities [4, 8, 9]: 1) slowing, i.e., the increase of the relative power of the low frequency bands (delta, 0.5-4 Hz, and theta, 4-8 Hz), coupled with a reduction of the individual mean alpha frequency; 2) a reduction of complexity, i.e, an increase of regularity of the signal also measured by non linear/entropic parameters; 3) altered synchrony of the EEG channels recordings. In [10], it is clarified that EEG can be used as a tool for assessing different brain states, possibly related to the disease.

Compressibility of EEG EEG compression is achieved by exploiting correlation (redundancy) in the source data. The compressibility of EEG depends on its amplitude distribution and its power spectrum. Since the amplitude of EEG is in the order of µV, the acquisition system amplifies the signal about a million times, thus amplifying noise as well. This limits the compressibility of the signal. In this paper, only intra-channel correlations (among the adjacent samples of the signal) are considered, although the very nature of EEG suggests to take advantage of inter-channel correlations, i.e. joint sparsity. EEG is often modelled as an auto-regressive (AR) process exploiting knowledge of previous samples to predict present one. EEG is not usually considered sufficiently sparse in time or frequency domains for matching the recovery requirements of the clinical practice.

However, filtered EEG show an amplitude distribution and a frequency spectrum largely concentrated in suitable ranges. This is particularly true for slowed EEG of AD patients. In this section, the wavelet transform and the compressive sensing methods are separately analysed.

Alzheimer's disease

Alzheimer's disease (AD), also known 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 (and later named after) German psychiatrist and neuropathologist Alois Alzheimer in 1906. Most often, AD is diagnosed in people over 65 years of age, although the less-prevalent early-onset Alzheimer's can occur in much younger people. In 2006, there were 26.6 million people worldwide with AD. Alzheimer's is predicted to affect 1 in 85 individuals globally by 2050. Initial symptoms are often mistaken for 'age-related' concerns, or manifestations of stress. The most common early symptom is short term memory loss difficulty in remembering recent events. The diagnosis is usually confirmed with tests that evaluate behaviour and thinking abilities, often followed by a brain scan if available; however, examination of brain tissue is required for a conclusive diagnosis. As the disease advances, symptoms can include confusion, irritability, aggression, mood swings, trouble with language, and long-term memory loss. As the person's condition declines they often withdraw from family and society. Gradually, bodily functions are lost, ultimately leading to death. Although the speed of progression can vary, the average life expectancy following diagnosis is approximately seven years. Fewer than 3% of individuals live more than 14 years after diagnosis.

Alzheimer's disease is classified as a neurode generative disorder, the cause and progression of which are poorly understood. The disease process appears to be associated with plaques and tangles in the brain. No treatments stop or reverse its progression, though some can lessen symptoms. As of 2014, more than 1,500 clinical trials have been or are being conducted to test various treatments in AD. Mental stimulation, exercise, and a balanced diet have been suggested as ways to delay cognitive symptoms (though not brain pathology) in healthy older individuals, but there is no conclusive evidence supporting an effect.

Pre-dementia

The first symptoms are often mistakenly attributed to ageing or stress. Detailed neuropsychological testing can reveal mild cognitive difficulties up to eight years before a person fulfills the clinical criteria for diagnosis of AD. These early symptoms can affect the most complex daily living activities. The most noticeable deficit is memory loss, which shows up as difficulty in remembering recently learned facts and inability to acquire new information.

EEG

Electroencephalography (EEG) is the recording of electrical activity along the scalp. EEG measures voltage fluctuations resulting from ionic current flows within the neurons of the brain. In clinical contexts, EEG refers to the recording of the brain's spontaneous electrical activity over a short period of time, usually 20–40 minutes, as recorded from multiple electrodes placed on the scalp. Diagnostic applications generally focus on the spectral content of EEG, that is, the type of neural oscillations that can be observed in EEG signals.

The brain's electrical charge is maintained by billions of neurons. Neurons are electrically charged (or "polarized") by membrane transport proteins that pump ions across their membranes. Neurons are constantly exchanging ions with the extracellular milieu, for example

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to maintain resting potential and to propagate action potentials. Ions of similar charge repel each other, and when many ions are pushed out of many neurons at the same time, they can push their neighbours, who push their neighbours, and so on, in a wave. This process is known as volume conduction. When the wave of ions reaches the electrodes on the scalp, they can push or pull electrons on the metal on the electrodes. Since metal conducts the push and pull of electrons easily, the difference in push or pull voltages between any two electrodes can be measured by a voltmeter. Recording these voltages over time gives us the EEG.

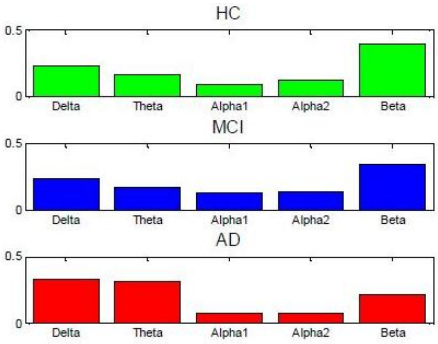

Fig. 1. Relative power content of the frequency bands for three different groups of subjects (HC, MCI, AD), averaged on all the 19 referential electrodes.

The electric potential generated by an individual neuron is far too small to be picked up by EEG or MEG. EEG activity therefore always reflects the summation of the synchronous activity of thousands or millions of neurons that have similar spatial orientation. If the cells do not have similar spatial orientation, their ions do not line up and create waves to be detected. Pyramidal neurons of the cortex are thought to produce the most EEG signal because they are well-aligned and fire together. Because voltage fields fall off with the square of distance, activity from deep sources is more difficult to detect than currents near the skull.

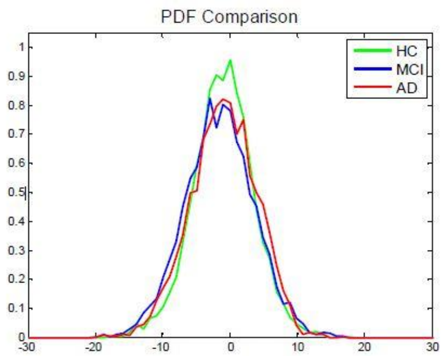

Fig. 2. Amplitude distributions (normalized frequency of occurrence) of EEG signals (abscissa axis is quoted in μV).

Scalp EEG activity shows oscillations at a variety of frequencies. Several of these oscillations have characteristic frequency ranges, spatial distributions and are associated with different states of brain functioning (e.g., waking and the various sleep stages). These oscillations represent synchronized activity over a network of neurons. The neuronal networks underlying some of these oscillations are understood (e.g., the thalamocortical resonance underlying sleep spindles), while many others are not (e.g., the system that generates the posterior basic rhythm). Research that measures both EEG and neuron spiking finds the relationship between the two is complex, with a combination of EEG power in the gamma band and phase in the delta band relating most strongly to neuron spike activity.

Wavelet transform-based EEG compression

In the wavelet approach, the EEG signal, as a sequence of N signal samples, i.e., as an N-dimensional vector, is transformed in the wavelet domain through an orthogonal transformation. The continuous wavelet transform can be computed in different ways by introducing a translation and a dilation (scale) operators on L2 (R). This integral transform is able to analyze signals in both time/space and scale. Moreover, signals can be recovered from their CWT if an admissible wavelet is used. CWT can be digitized thus generating the Discrete wavelet Transform (DWT). The wavelet transform of a signal e(t) can be calculate efficiently and the signal can be reconstructed from the transform coefficients under some necessary and sufficient conditions given by Daubechies. Since relatively few wavelet coefficients capture most of the signal energy, it is possible to make a lossy reconstruction of the original signal by zeroing out all the coefficients in the wavelet expansion but the largest ones before inverse transforming. The amount of energy concentrated in low frequency bands is a measure of signal's smoothness, and, ultimately of good compressibility. In principle, the slowing effect noted in EEG of AD patients implies a smoothness filtering of the signal.

Compressive sensing theory

Compressive sensing (CS) is an emerging lossy compression scheme that exploits signal structure to acquire data at a rate proportional to the true information rate rather than to the Nyquist rate. In so doing, the effective sampling rate is basically lowered. The inherent redundancy in specific types of signals allows, in principle, compression while sampling.

Compression process

Compressive sensing theory is based on the recent understanding that a small set of non-adaptive linear measurements of a compressible (sparse) signal contain sufficient information for reconstruction. In EEG processing, the electrical potential samples are collected in vectors (one per channel) with elements x (n), with n=1,2, …, N. Usually, N is very large and thus, in several real time monitoring applications, the signal should be compressed through a coding process. A vector, of length

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N, is K sparse if it has K non-zero entries and the remaining (N − K) entries are zero. If these coefficients are not exactly zero, but are below a prescribed threshold, the signal is said approximately sparse. In this case, these coefficients are forced to zero in the course of the coding procedure. A single-channel of digitized EEG data, e(t), is an (N × 1) vector. It is coded in terms of a set of coefficients Then assume that this signal can be represented by its projection onto a different basis set:

$$e = \sum_{i=1}^{N} \upsilon_i \Psi_i; \quad \underline{e} = \underline{\underline{\Psi}}\,\underline{\upsilon}$$

where υ is an (N ×1) vector and **Ψ** is an (N ×N) basis matrix. This matrix is formed by stacking the vectors {Ψi} as colomns.

$$\underline{\underline{\Psi}} = [\underline{\Psi}_1 \,|\, \underline{\Psi}_2 \,|\, \ldots \,|\, \underline{\Psi}_N]$$

The vector υ is given by the inner product of e and Ψ, and the entries in Ψ are known as the dictionary functions. As an example, smooth signals are sparse in the Fourier basis, and piecewise smooth signals are sparse in a wavelet basis .Both υ and e represent the signal equivalently, but in different domains. Compressive sensing aims to find a basis Ψ where the coefficient υi is sparse (i.e., where only k<<N coefficients are non zero). Different choices for Ψ are available leading to different ways for exploiting the sparsity of EEG signal. The JPEG and JPEG-2000 compression standards are based on a wavelet transform coding. However, the wavelet approach requires to start with a large (N) number of samples and to compute all the N coefficients before discarding all but K of them. Finally, also the locations of the large coefficients must be encoded.CS bypasses the sampling process and directly acquires a reduced representation of the signal using M < N linear measurements between e and a collection of functions Φ,(formula 3). **e** is thus related to another signal:

$$\underline{\underline{\Phi}} = \{\Phi_m\}_{m=1}^{M} \qquad y(m) = \langle \underline{e}, \Phi_m \rangle$$

$$\underline{y} = \underline{\underline{\Phi}}\,\underline{e} = \underline{\underline{\Phi}}\,\underline{\underline{\Psi}}\,\underline{\upsilon}; \qquad \underline{e} \in R^N : y \in R^M$$

where Φ is a measurement matrix of dimensions (M×N), with M~K and y is the compressively sensed version of e. y has dimensions (M×1) and if M < N, data compression is achieved. Provided that Φ is correctly chosen, exact reconstruction of e from y even with a sampling at a subNyquist rate. The effective sampling rate has thus been lowered. It can be shown that this technique is possible if Φ and Ψ are incoherent; that is if the elements of Φ and Ψ have low correlation [3]. Incoherence basically means that no element of one basis has a sparse representation in terms of the other basis. In general, to satisfy this condition Φ is chosen as a random matrix following a given probability distribution. Multiple choices for Φ are also available.

Analysis of the EEG database The above described compression techniques were tested by analyzing EEG of three different groups of subjects (male and aged between 60–75 years): MCI patients, AD patients and age-matched healthy elderly control (HC). In Fig. 1, the distribution of the power spectral density for the subjects belonging to the different categories (HC, MCI, AD),within the bands of interest is reported. It is evident the effect of "slowing" of the signals in the case of AD patients. The differences between HC and MCI categories are mainly related to the redistribution of power in the sub-bands alpha1 and alpha2. Theta relative power is usually larger in MCI patients compared to reference subjects, whereas beta power is significantly smaller.

In the AD patients the perturbations on EEG relative power are stronger: delta and theta relative power is significantly larger than in the reference subjects, whereas alpha and beta power is significantly smaller. In other words, slowing occurs in both the MCI and AD patients at different levels, which is in agreement with earlier studies. It was decided to report in Fig. 1 data averaged on all the subjects and on all the electrodes in order to avoid a "driven" choice of the "best" channels for compression with respect to the problem at hand, and, accordingly, not to raise perplexity on the electrodes' choice. It is also possible to improve the compression results by extracting specific bands from the signal; however, this would rather be in contrast with the final objective of making real-time on line sensing.

In Fig. 2, the amplitude distribution of the EEG values is reported. It is clear that the categories are hardly discriminated by only inspecting the EEG in time. The slowing effect can also be observed in the (normalized) EEG spectra, shown in the subplot of Figs. 3-5. In particular, the effect of slowing in the AD subjects is very clear observing frequency distribution: power is more concentrated in theta band in AD patients than in the agematched control subjects.

B. Time-frequency (wavelet) analysis

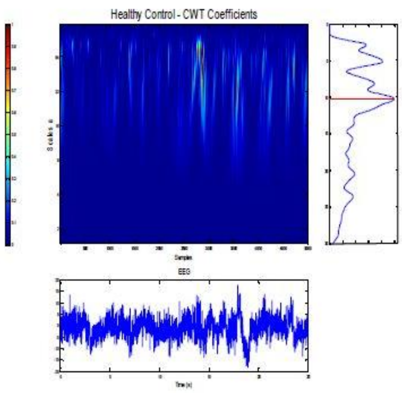

Fig. 3. Time-frequency plots for a segment of EEG signal recording (HC).

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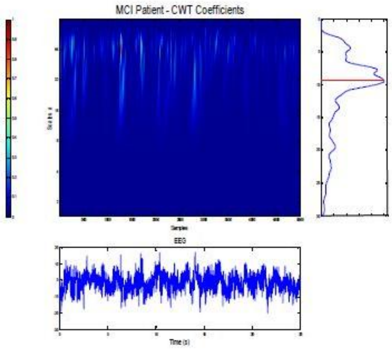

Fig. 4: Time-frequency plots for a segment of EEG signal recording (MCI).

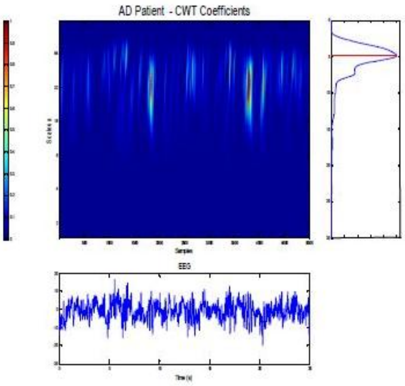

Fig. 5. Time-frequency plots for a segment of EEG signal recording (AD).

Figs. 3-5 illustrate the time-frequency distribution of the wavelet coefficients for representative cases in the three categories. Each figure reports below the time evolution of a segment of 25 s of the original EEG signal for one selected electrode (F3, frontal area). The box-plot on the right reports the filtered Power Spectral Density (PSD) of the Fourier transformed signal. The horizontal line indicates the estimated Instantaneous Peak Frequency (IPF) for the alpha band. It is easily seen the effect of slowing within the band, i.e. the reduction of the IPF both for MCI and AD. The central subplot of the figures shows the distribution and power of the wavelet coefficients. In detail, the Continuous Wavelet Transform (CWT) of the signals is computed, by using the Daubechies 4 wavelet, and its modulus is depicted in the scale-time 2D plot. In the case of AD, most of the power is concentrated in the low-frequency bands and it is highlighted the presence of characteristic “bumps”, as suggested by [10]. The number of significant coefficients appears reduced in the AD patient. This effect is then quantified by the following analysis: by using the classical denoising procedure, the coefficients under threshold are zeroed. Then, an inverse transform is carried out in order to reconstruct the original signal from the remaining coefficients. Usually, the denoising algorithms compute an adaptive threshold related to the standard deviation of the amplitudes; however, in order to correctly compare the performance of the three different cases in terms of compression rate, a fixed reconstruction error is here assumed (1x10-2 μV). Table I reports the derived thresholds and the number of coefficients under threshold for the three categories. The samples of the time signal are 5000 (25 s of signal at the sampling rate of 200 Hz); the related wavelet coefficients correspond to a reduction of 15%, 18%, and 29%, respectively. Thus, as hypothesized, the compressibility of the EEG channel largely varies with the progression of the disease. In the case of the AD patients, a good reconstruction can be already achieved with a 50% reduction of the needed samples. The differentiation is subtle between HC and MCI, as also measured by other markers [4, 8]. It is also predictable that a joint use of different channels could further improve the compressibility, particularly for the AD case; indeed, the disease is also known to be responsible of a perturbed synchrony among channels, more relevant for electrodes covering neighboring areas of the scalp.

Denoising of EEG signals through wavelet approach (thresholds are computed at a fixed RMS reconstruction error).

	Threshold	Under Threshold Coefficients
HC	0.42	763
MCI	0.40	889
AD	0.30	1406

Decision tree

A decision tree is a decision support tool that uses a tree-like graph or model of decisions and their possible consequences, including chance event outcomes, resource costs, and utility. It is one way to display an algorithm.A decision tree is a flowchart-like structure in which each internal node represents a "test" on an attribute (e.g. whether a coin flip comes up heads or tails), each branch represents the outcome of the test and each leaf node represents a class label (decision taken after computing all attributes). The path from root to leaf represents classification rules.

In decision analysis a decision tree and the closely related influence diagram are used as a visual and analytical decision support tool, where the expected values (or expected utility) of competing alternatives are calculated.

A decision tree consists of 3 types of nodes:
1. Decision nodes - commonly represented by squares
2. Chance nodes - represented by circles
3. End nodes - represented by triangles

Decision trees are commonly used in operations research, specifically in decision analysis, to help identify a strategy most likely to reach a goal. If in practice decisions have to be taken online with no recall under incomplete knowledge, a decision tree should be paralleled by a probability model as a best choice model or online selection model algorithm. Another use of decision trees is as a descriptive means for calculating conditional

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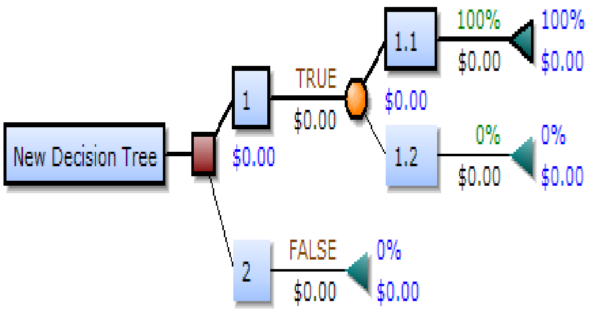
probabilities. Decision trees, influence diagrams, utility functions, and other decision analysis tools and methods are taught to undergraduate students in schools of business, health economics, and public health, and are examples of operations research or management science methods.

Decision tree building blocks

1) Decision tree elements



Drawn from left to right, a decision tree has only burst nodes (splitting paths) but no sink nodes (converging paths). Therefore, used manually, they can grow very big and are then often hard to draw fully by hand. Traditionally, decision trees have been created manually - as the aside example shows - although increasingly, specialized software is employed.

Types of decision trees

1) Simple decision tree

The model in which every decision is based on the comparison of two numbers within constant time is called simply a decision tree model. It was introduced to establish computational complexity of sorting and searching

The simplest illustration of this lower bound technique is for the problem of finding the smallest number among n numbers using only comparisons. In this case the decision tree model is a binary tree. Algorithms for this searching problem may result in n different outcomes (since any of the n given numbers may turn out to be the smallest one).

2) Linear decision tree

Linear decision trees, just like the simple decision trees, make a branching decision based on a set of values as input. As opposed to binary decision trees, linear decision trees have three output branches. A linear function $f(x_1, \ldots, x_i)$ is being tested and branching decisions are made based on the sign of the function (negative, positive, or 0).

3) Algebraic decision tree

Algebraic decision trees are a generalization of linear decision trees to allow test functions to be polynomials of degree d. geometrically; the space is divided into semi-algebraic sets (a generalization of hyperplane). The evaluation of the complexity is more difficult.

Decision tree classifier

A decision tree is a sequence of binary splits of data. Several popular indexes are proposed to determine the best variable and best place on which to split a node in learning decision tree. Decision tree classifier is powerful for automatic feature selection. But one decision tree is unstable and only provides limited modeling of the joint statistics of data. The ends of training, all weak learners are combined with different weights to make decision.

Greedy search

Greedy search is the logical extreme of weighted A*. Rather than scaling h relative to g, greedy search ignores g completely. As a result, there is no way to request a fixed quality solution from greedy search; the quality of the solution returned may be determined after the fact by comparing its cost with a lower bound on the optimal solution cost for the problem which can either be derived from the initial state or a linear scan of all the nodes on the open list when the goal was returned. The open list of A∗ sorts nodes as they would be by A*. It uses the open list to form a subset of nodes to consider for expansion called the focal list. The focal list contains all nodes such that f (n) ≤ w · In some sense it behaves much like a greedy search on d, but rather than comparing all of the d values globally, it singles out a subset of the nodes to be considered.

CONCLUSION

The recently introduced compressive sensing (CS) methodology has been shown to be applicable in EEG analysis for discriminating among different, possibly pathological, brain states. In particular, CS can be seen as an evolution of other compression techniques, like wavelet decomposition denoising that has been also observed to increasingly compress EEG recordings from AD patients. CS, in addition, allows indeed to sampling while sensing, thus yielding clear advantages for wireless, also smartphone-based, EEG monitoring systems. This can be useful to monitor patients at home while following the evolution of the disease and the effect of drugs.

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BIOGRAPHY

Lekshmi G S has completed her Bachelor's degree in engineering in Electronics and Communication from Udaya School of Engineering, Nagarcoil (2013) and presently pursuing Master of Technology in the department of Applied Electronics and Instrumentation Engineering in Lourdes Matha College of Science and technology, Kerala, India.