



# Identification of amyotrophic lateral sclerosis disease based on nonlinear analysis of gait signal and fusion in intelligent classifiers

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## Abstract

Neurodegenerative diseases (NDD) including Amyotrophic Lateral Sclerosis (ALS), Parkinson's disease (PD) and Huntington disease (HD) can be defined as the degeneration in the structure of neurons in human body. It is mentioned in the related literature that NDD may cause various clinical symptoms disrupting gait dynamics. The characterization of gait analysis is crucial for early diagnosis, efficient treatment planning and monitoring of ALS progression and other NDD. The database consisting of 64 five-minute recordings of Compound Force Signal (CFS) obtained from 13 ALS, 15 PD, 20 HD and 16 healthy subjects was used in the study. a five-stage structure is used. In the first step, a data group recorded by force sensitive sensors was used to analyze the walking dynamics that is underneath. In the second step, the signal filtered by the filter bank of wavelet transform with the default coefficients of the noise reduction and improve it. In third Step a set of feature is extracted from recorded data. In the fourth step, the extracted features are considered as inputs of a feature dimension reduction structure. The reduced dimensional attributes are considered as inputs of linear classification structures (SVM) and nonlinear (KNN, D-Tree and MLP). The goal of finding a grade tag is the type of disease based on walking signal analysis. All simulations were implemented under MATLAB software and validation of the proposed method was done by analyzing the confusion matrix and calculating the accuracy, sensitivity and specificity index. The results of the simulation showed that the perceptron multi-layered neural network has a precision accuracy of 92% higher in the diagnosis of neurodegenerative complication based on dynamic walking analysis.

**Keywords:** Neurodegenerative, ICA, Genetic algorithm, AdaBoost, fractal.

## 1-INTRODUCTION

Neurodegenerative diseases refer to the dysfunction of muscular and nervous system control. Since lower extremity flexion and extension movements are controlled by the central nervous

system, the gait is always abnormal in a patients with neurodegenerative disease. This is caused by the loss of motor neurons. These diseases include Parkinson's disease, amyotrophic lateral sclerosis, and Huntington's disease. Since neurons of the basal ganglia are involved in neuromuscular control (e.g. balance and sequential movements), neurodegenerative diseases are expected to disturb gait cycles and dynamics . Amyotrophic lateral sclerosis (ALS) is a primary neurodegenerative disease characterized by progressive muscular paralysis reflecting degeneration of motor neurons in the primary motor cortex, brainstem, and spinal cord. Parkinson's and Huntington's diseases are common disorders affecting the basal ganglia that lead to problems with movement timing and rhythm. The data from gait analysis are widely used for kinematic studies in order to investigate motor diseases and disorders. Gait signal analysis is used for better recognition of mechanisms of motor disorders. It is a high-potential non-invasive method based on walking dynamics for diagnosis of various types of neurodegenerative disorders (NDD). Gait dynamics is controlled by mixed nerves. It appears that the feedback loops that control the physiological systems should receive a set of spatial and temporal scales to adapt to any environmental changes. Therefore, walk/stop/turn time series affect the spatial and temporal scales.

Extensive studies have been conducted in recent years with the help of computer tools to measure the parameters of walking distance in healthy adult human models and characteristics of the gait signal in neurodegenerative diseases. Scafetta et al. [1] used a central pattern generator model to simulate the dynamics of human walking. He also discussed random and fractal characteristics of walking signals in three categories of the disease. Liao et al. proposed a method for measuring the signal of gait asymmetry to diagnose NDD using the multi-resolution entropy analysis of stance time fluctuations. The results of this study showed that gait symmetry signal in subjects with NDD, especially with ALS, is significantly disturbed. Daliri presented a method for diagnosing neurodegenerative diseases based on gait analysis[2]. He used the data from a time series of stride intervals, swing intervals, stance intervals and double support intervals of stride-to-stride measures of footfall contact times[3]. The support vector machines using different kernels were examined for the diagnosis.

Aziz and Arif converted stride time series to a symbolic sequence and proposed a threshold based on the symbolic entropy method for analysis of the complexity of gait signal. They showed that normalized corrected Shannon entropy (NCSE) of walking decreases in various values of small threshold of Shannon entropy in ALS cases[4]. Wu and Shi [5] proposed an analytical statistic to classify healthy and ALS cases. In the former study, the probability density functions (PDFs) were estimated using the nonparametric Parzen-window approach. The Kullback–Leibler divergence (MKLD) was then extracted. This method can effectively separate the stride patterns between the groups of healthy controls and ALS patients with an overall accuracy rate of 82.2%. In a similar study, it was assumed that the number of swing intervals in patients with ALS may be different from healthy controls. Patterns of walking in ALS patients were classified using this parameter and linear and nonlinear structures[6]. The results of this study showed that this parameter along with the mean intervals of strides can be used to differentiate walking patterns in healthy and ALS cases with an accuracy of 89.66%.

Wavelet-Based Multi-Scale Entropy and non-static analysis based on statistical methods and frequency-time analysis were proposed in various papers to investigate the relationship between walking signal and NDD. Sarbaz et al. [7] used spectral analysis to classify the patients with Huntington's disease and normal cases. Sang-hong et al. [8] presented a method to classify the patients with Parkinson's disease using wavelet transform based feature. extraction of gait characteristics. Hausdroff et al compared the stride intervals in walking signal between healthy individuals and the patients with Huntington's disease [9]. They calculated the correlation between stride intervals in comparison to previous and next intervals of walking. The results of this study showed that walking pattern in Huntington's cases is more random than healthy individuals. Zheng categorized healthy individuals from patients with Parkinson's disease using a statistical method [10].

Sugavanes waran et al. offered a method for classifying healthy individuals from ALS cases based on time-frequency analysis. Baratian et al. presented a diagnostic support method for classifying healthy individuals and ALS cases based on an unbiased cross-validation strategy

[11]. This paper presents a six-step algorithm for classifying neurodegenerative diseases. In the first step, a set of gait signals is collected from the physionet database [9, 12]. In the second step, a wavelet-based waveform pre-processing algorithm and sub-band analysis are used. In the third step, independent component analysis is performed to extract the optimal band signal. In the fourth step, chaotic and fractal nonlinear features of each sub-band are extracted. In the fifth step genetic algorithms are used to reduce space and select the best features. In the sixth step, structures of linear and nonlinear classification are used to diagnose and distinguish healthy individuals from patients with neurodegenerative diseases. The structure of the presentation of these concepts in this article is as follows. Data collection methods and used databases, the methods used to extract preprocessing and processing features, space reduction methods, characteristic selection and classification structures are discussed in the section of techniques. The accuracy, sensitivity and specificity parameters of used methods are calculated and compared in the results section. In conclusion, an optimal and superior technique is introduced and several recommendations are given for its use in future studies.

## 2-TECHNIQUE AND METHODS

### 2-1-DATA COLLECTION

This paper used Physionet database [9, 12], which included gait signal recording in four groups: ALS, Huntington, Parkinson's, and control (healthy people). This database has 13 records from ALS patients, 20 from Huntington's patients, 15 from Parkinson's patients, and 20 from the control group (healthy state). The data were measured using force-sensitive resistance sensors placed under the foot that measured the force according to the steps of the right and left legs. Each record contains two sample columns, each of which is dedicated to the sensor output embedded below the right and left foot. The recorder was a 12-bit converter with a sampling frequency of 300 Hz, with a record length of 5 minutes and a total of 90,000 samples.

#### A.PREPROCESSING

A discrete wavelet transform (DWT) was used for preprocessing raw data. Wavelet transform is a time-domain frequency converter that besides maintaining frequency components it is capable of retaining the time components. Wavelet transform utilizes a sliding window scaled according to the signal changes. In other words, while preserving temporal resolution, it provides a proper resolution in frequency by applying comparative scales in the mother wavelet. Wavelet transform utilizes a filter bank structure (FBS) and analyzes the signal based on FBS and the number of user-specified levels. At each level of decomposition, signal sample is reduced, and the sparse output is considered as high-pass and low-pass filter input. High-pass filter output is called details, which contains components of a higher-frequency signal. Therefore, by deleting one of the sample lengths the signal is lost without information. A similar process is performed using a digital half-band pass filter with a  $g[n]$  impact response. As a result, the output of the first stage of using the wavelet converter, two versions, another high pass and low pass, is obtained by reducing (half) the main signal as follows:

$$y_{\text{high}}[k]=\sum_n x[n].h[2k-n] \quad (1)$$

$$y_{\text{low}}[k]=\sum_n x[n].g[2k-n] \quad (2)$$

Where  $h[n]$  is the high-pass filter (HPF) and  $g[n]$  is the low pass filter (LPF),  $y_{\text{high}}$  is the output of HPF  $y_{\text{low}}$  is the output of LPF and  $x[n]$  is the input signal. The output of HPF is again redirected to the sample decimation block and high-pass and low-pass filter to form FBS based on the number of user-defined levels. This paper used wavelet-transform to remove the signal noise by matching mother wavelet with daughter signal. For this purpose, the default coefficients of MATLAB software were used for FBS using Daubechies4 mother wavelet.

## B. PROCESSING

Independent component analysis was used to process noise-reduced data. In this method, it is assumed that a signal is a linear combination of its sources and statistically independent (ICA). Thus, this method can be used to decompose the input signal and extraction of independent sources whose numbers are equal to the signal dimension. If we assume that a signal is a linear combination of its sources, we can write:

$$S = WX \quad (3)$$

Where  $x$  is a multi-dimensional signal and  $s$  is the independent sources.

Kurtosis is used to extract the best independent component, which is defined as follows.

$$\text{Kurt}(s) = E\{s^4\} - 3(E\{s^2\})^2 \quad (4)$$

Where  $E\{\}$  is Operator of expected value and  $s$  is the source component.

If the kurtosis approaches zero, data distribution approaches Gaussian, otherwise it distances from normal distribution. Therefore, in order to extract the optimal independent component in the gate signal, selection criterion is the largest kurtosis value between the components. This paper used 8-level independent component analysis (ICA) for each sensor of the left and right feet and for each sensor; a component with the largest kurtosis value was selected. It appeared that the use of ICA is effective in signal improvement and noise reduction.

## C. FEATURE EXTRACTION

Non-linear dynamic features based on chaos concepts were used to model the nonlinear behavior of the gait signal. The signal analysis seems to reflect the valuable information of the signal in the form of the feature in the case where its stable behavior is important. However, the use of non-linear features paves the ground for making feature extraction process resistant to noise (it compensates for the defect of time domain features). We dealt with the features extracted in this paper as outlined below.

### 3- LYAPUNOV EXPONENT

The rate of separation can be different for different orientations of initial separation vector. Thus, there is a spectrum of Lyapunov exponents equal in number to the dimensionality of the phase space. It is common to refer to the largest one as the maximal Lyapunov exponent, because it determines a notion of predictability for a dynamical system. One index of chaotic systems to show the sensitivity of the system response to small stimuli was evaluated through this quantity. For a one-dimensional map, this quantity measures the divergence rate of the response to the initial conditions close to each other. This means that if we have two initial conditions close to each other, such as  $x_0, x_0 + dx_0$ , and apply map  $M$  to them after  $n$  consecutive times, we will have:

$$dx_n \approx e^{hn} dx_0 \quad (5)$$

$h$  is Lyapunov exponent for this map, so one can write:

$$h = \lim_{T \rightarrow \infty} \frac{1}{T} \ln \left| \frac{dx_T}{dx_0} \right| \quad (6)$$

$$\frac{dx_T}{dx_0} = \frac{dx_T}{dx_{T-1}} \frac{dx_{T-1}}{dx_{T-2}} \dots \frac{dx_1}{dx_0} \quad (7)$$

$$M'(x_{T-1})M'(x_{T-2}) \dots M'(x_0) \quad (8)$$

Thus, we will have:

$$h = \lim_{T \rightarrow \infty} \frac{1}{T} \sum_{n=0}^{T-1} \ln |M'(x_n)| \quad (9)$$

Given the natural boundary discussion for a set,  $h$  can be also shown as follows:

$$h = \int \ln |M'(x_n)| d\mu(x) \quad (10)$$

In most applications, calculating only the largest Lyapunov coefficient is enough. Lyapunov exponent of an  $n$ -dimensional system is as  $\lambda_1 \geq \lambda_2 \geq \dots \geq \lambda_n$ , where  $\lambda_1$  is the largest Lyapunov coefficient and considered as a feature in this study.

#### 4- DETRENDED FLUCTUATION ANALYSIS (DFA)

DFA measures the intra-signal correlation, which is not only resistant to non-stationary, but can also systematically eliminate various timescale deviations caused by noise from time series. The main idea of DFA to calculate the root mean square is the time series fluctuations where  $(X)_{\bar{j}}$  denotes the mean value of the time series.  $S_j$  is called cumulative sum or profile. Finally, this process of detrending followed by fluctuation measurement is repeated over a range of different window sizes  $N$ :

$$Y(k) = \sum_{j=1}^k (X_j - \bar{X}), \quad k = 1, \dots, N \quad (11)$$

$\bar{X}$  represents the mean of time samples. The summed up series is then divided into parts of equal length  $n$ . In each section, the data are estimated with the least square error line that displays trend in that window.  $Y_n(k)$  shows these regression lines. The summed up series  $Y(k)$  is then detrended in each window. Thus, the square root of the mean square oscillation is summed up and  $Y_n(k)$  is calculated. This calculation is repeated on all time scales (window sizes) to obtain the relation between  $F(n)$  and the size of window  $n$ .  $F(n)$  increases with window size.

$$F(n) = \sqrt{\frac{1}{N} \sum_{k=1}^N (y(k) - y_n(k))^2} \quad (12)$$

The oscillation in small windows is related to oscillations that can be expressed by auto-similarity factor, and  $\alpha$ , which is called scaling exponent, is the line slope of  $\log f(n)$  relative to  $\log(n)$ . In general,  $\alpha$  can be considered as a sign of the unevenness of the original time series.

#### 5- TIME REVERSIBILITY (TR)

A time series is called TR only if its possible characteristics are constant with TR. A test was suggested for zero assumption that a time series is reversible. A deterministic process is time-reversible if the time-reversed process satisfies the same dynamic equations as the original process; in other words, the equations are invariant or symmetrical under a change in the sign of time. A stochastic process is reversible if the statistical properties of the process are the same as the statistical properties for time-reversed data from the same process. The rejection of the zero hypothesis shows that the time series cannot be described by a random Gaussian linear process. Thus, TR can be used as a strong reason for non-linearity. In this study we used a simple method that calculates TR for signal  $s$ :

$$Tr(\tau) = \frac{1}{N - \tau} \sum_{n=\tau+1}^N (S_n - S_{n-\tau})^3 \quad (13)$$

Where  $N$  is the length of the signal and this study used  $\tau = 1$ .

#### 6- FRACTAL DIMENSION (FD)

Fractal dimension is a ratio providing a statistical index of complexity comparing how detail in a pattern (strictly speaking, a fractal pattern) changes with the scale at which it is measured. It has also been characterized as a measure of the space-filling capacity of a pattern that tells how a fractal scales differently from the space it is embedded in; a fractal dimension does not have

to be an integer. This method divides the waveform into  $N_0 = N-1$  separate sections, and then calculates the fractal with respect to the Kutz equation below:

$$D = \frac{\log_{10}(N')}{\log_{10}\left(\frac{d}{L}\right) + \log_{10}(N')} \quad (14)$$

Where  $d$  is the flatness of the curve and  $L$  is the curve length, both of which are defined as:

$$d = \max(\text{distance}(1, i)) \quad (15)$$

$$L = \sum_{i=1}^{N'} \text{dist}(i, i + 1) \quad (16)$$

Dist ( $i, j$ ) is the distance between the points  $i$  and  $j$  from the curve. Several authors used this algorithm to analyze biological signals. FDs show the geometric properties of the absorbent bed, but have a high computational speed.

### 7- PETROSIAN FRACTAL DIMENSION (PFD)

PFD method is a very simple and fast way to calculate the dimension. This dimension is calculated as follows:

$$D = \frac{\log_{10}(N)}{\log_{10}(N) + \log_{10}\left(\frac{N}{N+0.4N\Delta}\right)} \quad (17)$$

Where  $N$  is the length of the time series and  $N\Delta$  is the number of changes in the signal in the derivative of the signal. Since the signal is discrete, the sequential difference of the time series elements is calculated. In comparing FDs, it should be noted that the correlation method requires a large number of samples to calculate higher dimensions over a time series. This method is not suitable for signals that do not have a stationary condition over time.

### A. FEATURE SPACE REDUCTION

Genetic Algorithm has been used to improve the accuracy of the classification and selection of optimal features. This is a optimization algorithm that can be used for optimal feature selection. Each gene from a chromosome assumes zero and one, which shows the value one in existence of this feature in the optimal feature space and zero in its absence. Thus, the position of a feature in the selected space is coded with zero (non-existence) and one (existence) as binary.

Step 1: Entering feature matrix

Step 2: Generation of the initial population: to generate a population, several binary chromosomes whose number of genes is equal to the number of features are randomly created.

Step 3: The fitness function is determined by increasing the accuracy in AdaBoost Algorithm.

Step 4: Given the fitness level of each chromosome, a new population is created

A. crossover: Two parent chromosomes are crossover by XOR function and a new population is created.

B) Mutation: A random number is selected at the length of the chromosome (feature) and the value of that gene is mutated.

Step 5: Selecting optimal population according to fitness function

Step 6: Checking the termination terms

A. Not satisfied: return to step 4

B. Satisfied: The announcement of the optimal chromosome end.

### B. CLASSIFICATION AND DIAGNOSIS

Ada Boost was used to classify the extracted features. The input of classification structure is extracted, considered once after the application of reducing feature space, and once after the reduction of feature space as the input of the classification structure. The output of the classification structure is the label of disease class.

## 8-RESULT

In the first step of simulation, raw data is collected from the physionet database for neurodegenerative diseases. Each data consists of two columns, one for the right and the other for the left foot. Data was stored in four separate folders, and each record was about five minutes, and was used for this article. In the second step, 1D wavelet transform toolbox was used to reduce the noise of raw signals.

To accomplish this, the `ddencmp` MATLAB function was used to achieve this goal. This command eliminates the signal noise with the default coefficient while maintaining the approximation coefficients and reduce the noise.

In step 3, the independent components were extracted from the clean signal that was extracted after the wavelet reconstruction. For this purpose, the Fast ICA was used to compute the independent components.

The number of independent components was considered 8, and the critter of kurtosis was used to select the independent components for the recorded data. The component with the highest value of kurtosis was selected as an independent component. Thus, for each record two independent components were calculated one for the right foot and the other for the left foot. In the fifth step, a set of features that were addressed in the technique and methods section, was extracted from optimal component.

These features are calculated for each registry for two independent components. In the sixth step, the optimal features of the extracted features were selected using the genetic algorithm.

The results of simulation showed that DFA, FD PFD are the best features that are selected by genetic algorithm. The attributes before and after feature selection are considered as inputs of the AdaBoost classification structure. The results of the simulations are presented in Table 1. These results showed that the use of the genetic algorithm in the selection of optimal features improved the classification indexes.

TABLE 1-CLASSIFICATION EFFICIENCY EVALUATION

Features type	sensitivity	accuracy	specificity
All features	86.54±3.7%	87.27±3.2%	88.38±3.3%
Selected features	93.34±1.7%	92.34±2.1%	91.34±1.1%

## 9- CONCLUSION

In this paper, a novel method for diagnosis of neurodegenerative diseases based on the extraction of chaotic and fractal features is presented. The results of the simulation showed that the fractal features provide a basis for classifying different disease types. Also, the results showed that the application of the genetic algorithm in the selection of features could improve the classification indexes. However, this technique is still a challenge in terms of time to solve the optimization problems. The characterization of gait analysis is crucial for early diagnosis, efficient treatment planning and monitoring of ALS progression and other NDD. The database consisting of 64 five-minute recordings of Compound Force Signal (CFS) obtained from 13 ALS, 15 PD, 20 HD and 16 healthy subjects was used in the study. a five-stage structure is used. In the first step, a data group recorded by force sensitive sensors was used to analyze the walking dynamics that is underneath. In the second step, the signal filtered by the filter bank of wavelet transform with the default coefficients of the noise reduction and improve it. In third Step a set of feature is extracted from recorded data. In the fourth step, the extracted features are considered as inputs of a feature dimension reduction structure (principal component analysis). The reduced dimensional attributes are considered as inputs of linear classification structures (SVM) and nonlinear (KNN, D-Tree and MLP). The goal of finding a grade tag is the type of disease based on walking signal analysis. All simulations were implemented under MATLAB software and

validation of the proposed method was done by analyzing the confusion matrix and calculating the accuracy, sensitivity and specificity index. The results of the simulation showed that the perceptron multi-layered neural network has a precision accuracy of 92% higher in the diagnosis of neurodegenerative complication based on dynamic walking analysis.

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