Modeling of evoked potentials of electroencephalograms: An overview

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Abstract

Electroencephalograms (EEGs) are brain waves, which are recorded using scalp electrodes. Generally, signal attenuate on recording and amplitude of the evoked potentials (EPs) are low when merged with the base brain waves. Therefore, mathematical tools are needed to analyse the time series (EEGs) to discover the EPs in the base EEGs. This paper reviews spectral analysis based on periodic amplitude analysis (PAA), wavelet transform (WT), fast Fourier transform (FFT), and fractal dimension (FD) of EEGs to predict the evoked potentials.

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1. Introduction

Revolutionary developments have taken place in neuro-imaging techniques such as magnetic resonance imaging (MRI), positron emission tomography (PET), and computerized axial tomography (CAT). However, EEGs continue to be used as a noninvasive clinical tool to evaluate brain function, especially for patients suffering from epilepsy, sleeping disorder, etc. From the frequency distribution of brain waves the function of an organ can be identified or diseases recognized, while, the morphology or amplitude of the waves provide less significant information to detect the disease or identify the function of an organ.

A detailed summary of different frequencies of brain waves (EEGs) observed in human and animal subjects are given in Table 1 and are shown in Fig. 1 [1–8]. Amplitude of the EEGs vary up to a maximum of 200 micro volts (µV), usually 40–70 µV amplitudes are seen when EEGs are recorded on the scalp.

EEG recorded from the scalp is considered to be generated within the pyramidal cells of the outer layer in the cerebral cortex (grey matter) [1]. To be precise, it is considered to reflect extra cellular current flow related to post synaptic activity. A relatively wide spread synchronization of potentials within cortical areas which are mutually interconnected by associated fibers (callosal fibers in both hemispheres) lead to brain waves. However, contributions to the desynchronized EEGs are from cellular excitability in the thalamo-cortical area, which are reflected in cortical activation as low voltage irregular potentials [1]. The post synaptic excitatory potentials from fiber synapse to the
<table>
<thead>
<tr>
<th>Waveform</th>
<th>Frequency (Hz)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow alpha wave</td>
<td>0.5–1.5</td>
<td>–</td>
</tr>
<tr>
<td>Spike</td>
<td>1.7</td>
<td>Odorant effects seen in rat</td>
</tr>
<tr>
<td>Delta wave</td>
<td>1–4</td>
<td>Normal sleep, 75 µV</td>
</tr>
<tr>
<td>Spike</td>
<td>3</td>
<td>Sharp wave (example: epilepsy)</td>
</tr>
<tr>
<td>Theta</td>
<td>3–7</td>
<td>Occurs in parietal-temporal lobes and low in voltage. Observed during stage-1 sleep activity, waking and drowsiness state-1 activity</td>
</tr>
<tr>
<td>Alpha</td>
<td>8–13</td>
<td>Seen in parietal-occipital lobes, for eyes close and relax states as well as waking conditions</td>
</tr>
<tr>
<td>Mu</td>
<td>8–12</td>
<td>Dominant in central lobe, similar to half sinusoidal wave usually blocked by alpha and beta waves</td>
</tr>
<tr>
<td>Sigma (sleep spindle)</td>
<td>12–14</td>
<td>Waxing and waning of sinusoidal wave, alike spindle seen during sleep</td>
</tr>
<tr>
<td>Beta</td>
<td>18–30</td>
<td>Observed in frontal-parietal lobes</td>
</tr>
<tr>
<td>Lambda</td>
<td>Transient</td>
<td>Potential arise in occipital lobe, during reading and due to saccadic eye movements</td>
</tr>
<tr>
<td>V-wave (vertex wave)</td>
<td>14 (transient)</td>
<td>Occurs during stage-2 phase of sleep</td>
</tr>
<tr>
<td>K-complex</td>
<td>Transient</td>
<td>Prolonged V-wave and super imposed with sleep spindles. Also, arise during sleep and responding to auditory</td>
</tr>
<tr>
<td>Grand mal epilepsy</td>
<td>High</td>
<td>Irregular high voltage fast waves (100 µV)</td>
</tr>
<tr>
<td>Petit mal epilepsy (focal epilepsy, psychomotor, seizure, ictal)</td>
<td>Low</td>
<td>Irregular high voltage slow waves (50 µV)</td>
</tr>
<tr>
<td>Irregular waves (desynchronized EEG)</td>
<td>8</td>
<td>Occur as active mental activity, alert eye open waking state and REM sleep</td>
</tr>
<tr>
<td>saw tooth waves</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast rhythmic waves</td>
<td>40</td>
<td>Observed in cats and monkeys cortical area</td>
</tr>
<tr>
<td>Quasi-sinusoidal waves</td>
<td>40</td>
<td>Waves are generated from auditory cortex of human</td>
</tr>
<tr>
<td>Fast rhythmic waves (evoked potential)</td>
<td>35–55, 55–75</td>
<td>Observed in rabbits and cats of auditory and/or odor responses</td>
</tr>
<tr>
<td>Gamma</td>
<td>20–80</td>
<td>Neural synchronization or phase lock of firing activities, for example, visual, sound, linguistic, attention, working memory, object recognition, etc., observed for animal and human subjects</td>
</tr>
<tr>
<td>Very high frequency rhythmic waves</td>
<td>&gt; 50 up to 120</td>
<td>Frontal intra cerebral records show these waves</td>
</tr>
<tr>
<td>Bursting pattern</td>
<td>250–400</td>
<td>Found during experimentation with animals; firing patterns of thalamo-cortical neurons associated with hyper-polarization of the cell membrane observed during alpha rhythm</td>
</tr>
<tr>
<td>Evoked potential</td>
<td>200–2200</td>
<td>Corresponds to visual activities</td>
</tr>
<tr>
<td>Head size (brain size)</td>
<td>–</td>
<td>Wider the frequency change lower the alpha frequency</td>
</tr>
<tr>
<td>Oxygen intake</td>
<td>–</td>
<td>Strong correlation is observed in case of gray matter (cerebral cortex)</td>
</tr>
<tr>
<td>Oxygen intake</td>
<td>–</td>
<td>Weak correlation is seen with white matter</td>
</tr>
</tbody>
</table>

Table 1
EEG waveforms in human and animal subjects [1–8]

2. Evoked potentials, for instance, olfactory stimulus

Evoked potentials (action potential) are generated associated with the functions of various body parts such as eye, ears, nose, muscular movements, etc. The present paper focuses on olfactory stimuli as an example of EPs in EEGs. Vickers et al. [6] recorded the neuron activity of male moths due to odor stimuli, and its changes occurring in the millisecond time-frame using electro-antennograms (EAG). The review [7] extensively discusses on the sense of smell in tiger salamander related to chemical detection system, stimuli translation, odor-coding, neural function, etc.
Fig. 1. Typical brain waves of normal and abnormal patients [1–8].
An investigation [8] on the properties of olfactory receptor neurons (ORN) in rats showed spontaneous ORN active firing more than 100 spikes per minute (1.7 Hz) when the animals were exposed to odorants. Electro-olfactogram (EOG) was used to record the trans-epithelial potential which results from a summation of the activities of numerous ORNs. Camphor, limonene, anisole, aceto-phenone, iso-amyl acetate, methyl amyl ketone odorants were used in the study. Variation of the concentration of the odorants also affected the number of evoked spikes per second.

Based on the information obtained from the olfactory bulbs of the mouse, Mori et al. [9] enumerated, the coding and processing of odor molecules. Axonal connection is precisely organized such that signals from 1000 different types of odorant receptors are sorted out in 1800 glomeruli in the bulb. Still the knowledge on cortex related to olfactory is to be understood in detail. Wilson et al. [10] also investigated transformation of olfactory representations and stated that major interaction occurs within the antennal lobe in drosophila. Recent research work [11] suggests that metal ions play an important role in the sense of smell, where olfactory receptors are metalloproteins. It is evident from these studies that evoked potentials in EEGs represent the function of body parts similar to olfactory stimuli, besides identifying the diseases in the body.

3. Modeling of EEGs, at a glance

To model EEG results, a signal from the brain, the black box, is considered as a series of sine and cosine waves of constant amplitude for the duration of the segment of the signal analyzed. For the first time, Billionon came up with a mathematical model of alpha rhythm as a sine wave [1]. Walter showed that a combination of constant amplitude sine waves could be summated to yield the original wave [1]. Several lumped models were reported as an assembly of neural activities. They found similarities between summated excitation nerve networks with alpha irregular EEG activities. The Wilson–Cowan model employed coupled nonlinear integro-differential equations to characterize dynamic neuron network activities. Zhadin also modeled the post synaptic potentials of neocortical as well as cortex pyramidal cells by integro-differential equation [1]. The Frolov model showed that the strength of the interconnections is more important than the excitability of the summed postsynaptic potentials [1]. In the Ingber model it is believed that the inhibitory synapses play a more significant role than excitability [1]. The dual-oscillatory model can be used to stimulate various types of EEG patterns. These generated waves are very much similar to alpha waves [1].

Many researchers have modeled EEG using nonlinear dynamics (chaos) to determine whether it is truly random (stochastic) or pseudo-random (deterministic chaos). Basar et al. suggested a correlation dimension $D_2$ (a quantitative measure of degree of chaos) of a given EEG is 9.0, indicating truly random, while a value of 2–3 explains deterministic chaos [1]. Higher dimensions are attributed to eye opening, stage-4 sleep, the Creutzfeldt–Jacob disease, etc. The Freeman model showed that the potential rhythm of the olfactory cortex was based on a linear system approach with a regular basal activity and an irregular activity as filtered noise [1]. Since the EEG pattern varied for different odors, they considered it as a different chaotic attractor. They simulated EEG as a solution coupling to nonlinear ordinary differential equation. In order to distinguish the classes of time series (EEG), which correlate to brain activities, it is a general practice to find its fast Fourier transform (FFT), wavelet transform (CWT), and/or fractal dimension (FD). Section 4 overviews the mathematical analysis of EEGs and studies on the prediction of stimuli of animal and human subjects.

4. Fast Fourier transform of EEGs

For $N$ equally spaced samples (length of $N$ sequence, $(f(t))$ the discrete Fourier transform (Eq. (1)) of the sequence is sufficient to describe the frequency-domain $(f(\nu))$ representation of the sequence [12]. The power spectrum (Eq. (2)) is the sequence of squares of the amplitudes of its Fourier coefficients, which represents the “energy” associated with each frequency. Thus, the generally used technique for analyzing spontaneous EEG is the Fourier power spectrum (FFT power spectrum).

$$f(\nu) = \mathcal{F}_t[f(t)](\nu) = \int_{-\infty}^{\infty} f(t)e^{-2\pi i \nu t} dt,$$

$$f(\nu) = \mathcal{F}_t[f(t)](\nu) = \int_{-\infty}^{\infty} f(t)e^{-2\pi i \nu t} dt$$
Fig. 2. FFT power spectra of FP1-F7 and Oz-C3’ channels of a patient on inhalation of jasmine, English rose, lemon orange, rose garden, and sandalwood odors and on normal breathing.

\[
\text{power} = \frac{V \times (\text{conj}V)}{N}.
\]  

(2)

Ferree and Hwa [13] computed the Fourier power spectrum for the time series of the EEG. For linear amplitude and frequencies, a peak was evident near 10 Hz, and at frequency greater than 10 Hz erratic results were observed. De-trended fluctuation analysis (DFA) showed how power-law scaling behavior was evident in two distinct temporal ranges. Vickers et al. [6] found that high amplitude activity at 2.2 Hz frequencies of odor dynamics (evoked potential) occur in male moths. Blanke et al. [14] reported frequency domain (FFT approximation) analysis have been reliably used to detect pathological activity of seizure.

Braga et al. [15] found FFT based quantitative analysis revealed differences in 23 children out of 39 normal children with rolandic spikes and the observations agreed with other evidence. Hadjiyannakis et al. [16] studied the EEG power density (FFT analysis) of stage-2 REM sleep transition in narcoleptic patients and normal sleepers. They found evidence of delta, theta, alpha, and sigma waves. Both patients revealed similar behaviors and changes of the frequencies were continuous and unremarkable. Muthuswamy and Thakor [17] mentioned that FFT spectral estimation was a useful technique to analyze neurological signals because of its computational simplicity.

Blanco et al. [18] plotted the time–frequency curve from an EEG signal using the Gabor transform. By this method, dynamic changes during an epileptic seizure such as: pre-seizure (0–7 s), start of the seizure (14–21 s), full development of the seizure (31–38 s), and end of the seizure (45–52 s) were identified via the phase portrait plots.

Kramarenko and Tan [2] analyzed the EEG using FFT, to find the cognitive ability of the brain dynamics. Indeed, the two systems are of different nature, where the brain is a nonlinear complex system, while FFT analysis is a linear system based approach. Therefore, discrepancies between the two systems and inaccuracies are possible when EPs are subjected to Fourier spectral analysis. They concluded that the FFT spectral analysis might mislead neuro-researchers, even though, it is largely used as a clinical tool.

Murali and Kulish [19] reported that FFT power spectra could not predict (Fig. 2) evoked potentials in the base EEGs stimulated on inhalation of six different odors. The EEGs were recorded using scalp electrodes for three patients (human subjects) on relaxing and keeping the eye open and closed modes. The results showed no noticeable differences between normal breathing and the inhalation of six concentrates one at a time (Fig. 2).
5. Wavelet transform of EEGs

The continuous wavelet transform (CWT) is calculated [20–22] using the formula

$$\text{CWT}(a,b) = \int x(t)\psi^*_{a,b}(t)\,dt,$$

where $\ast$ denotes the complex conjugate, $a \in R^+$ represents the scale parameter, and $b \in R^+$ represents the translation. Akin [21] compared the wavelet transform (WT) and FFT of EEGs and found that the wavelet transform method is better at detecting brain disease than FFT. One can also observe sub-spectral components of the wavelet transform of the EEG signal in the time domain (Fig. 3). Latka and Was [22] also demonstrated the behavior of wavelet transforms of epileptic spikes and mentioned that CWT is a relatively simple computing method yet an effective detection algorithm.

6. Period amplitude analysis of EEGs

Uchida et al. [23] compared human sleep EEGs using period amplitude analysis (PAA) and FFT spectral analysis. The PAA detected by the two approaches (a) interval between two successive zero voltages (zero cross) and (b) interval between two successive first-derivative zero values (Fig. 4). Both were able to detect low frequency signals (0.5–2 Hz), however, FFT was better at detecting the EEGs over a wider range of frequencies such as 0.3–40 Hz and higher.

7. Fractal analysis of EEGs

In fractal geometry, self-similarity is an important concept [24–26], nerve cells, arteries and veins in the retina and airways in lungs are statistically self-similar in space. Concurrently, electrical voltage across the cell membrane of a T-lymphocyte cell is an example of statistical self-similar in time. A quantitative measure of self-similarity is the
Correlation dimension and information dimension are methods used to quantify fractals, referred to as fractal dimension (FD) [24–28]. A fractal or correlation dimension is defined using the slope of the $\ln(C) - \ln(r)$ curve such as

$$d_G = \lim_{r \to 0} \frac{\log C(r)}{\log r}. \quad (4)$$

Two general forms of the fractal dimensions are capacity and Hausdorff–Besicovitch. Some biological examples [24] where fractal dimension are computed and studied are: surface of proteins, surface of cell membrane, dendrites of neurons, blood vessels in the eye, heart and lung, blood flow in the heart, textures of X-rays of bone and teeth, action potentials from nerve fibers, opening and closing of ion channels, etc.

Pereda et al. [29] found in their study on human EEG (awake and sleep stages of the patient) that EEG exhibits random fractal structure with $1/f^{-\beta}$ spectrum, where the $\beta$ exponent was between 1 and 3. More than the correlation dimension ($D_2$), $\beta$ exponent is appropriate to correlate with the behavior of EEG waves. The fractal exponent is calculated based on coarse graining spectral analysis (CGSA). Arle and Simon [30] showed that the fractal dimension (FD) of transient deterministic data in the EEG were different from quasi-random background EEGs. Using this technique, it was desirable to identify seizures, spikes, evoked potentials, and other transients in the EEGs.

Bullmore et al. [31] reported that FD of arrhythmic EEGs correlate with increase in the FD value, while rhythmic EEGs correlate with a decrease in FD value. They used the Frameshift–Richardson analysis to calculate the FD of EEG. Woyshville and Calabrese [32] used fractal dimension in their studies on quantification of occipital EEG with respect to the Alzheimer disease (AD) for the three conditions defined as (1) controls, (2) probable AD, and (3) autopsy-confirmed AD. They concluded that fractal dimensions clearly describe the EEG pathology and suggested that they have a potential clinical utility.

In another investigation, Bullmore et al. [33] reported fractal analysis describing 100 stereo-electroencephalogram (SEED) data points in terms of fractal dimensions. It was shown that the methodology defines ictal onset in terms of increased FD across several channels consistently. From the intense change in the FD, clinically they could characterize severe seizures from the less severe seizures.

Bullmore et al. [34] clearly demonstrated that FD provides information on brain activities, a well-delineated phase with increased FD and slow wave activity with decreased FD were noticed.

Yao and Freeman [7] described computer simulation of the dynamics of a distributed model of the olfactory system to understand the role of chaos in biological pattern recognition. The central part of the attractor is its basal chaotic activity, which simulates the EEG activity from the olfactory system. Pattern recognition and computer simulation identifies the transition from one section to another. The fractal dimension of the EEG reflects which section of the system is placed by the input (inhalation).

Gangadhar et al. [35] measured EEG seizure using FD. FD was computed for early, middle and post seizure phases of the ictal EEG. They concluded that the post seizure FD computation might be proposed as a novel measure of
Fig. 5. Fractal spectra of FP1-F7 channel of a patient on normal breathing (—) and inhalation of jasmine odor (−−−).

seizure and can be used as a predictor of treatment response. Klonowski [36] in his fractal analysis of EEG mentioned that FD calculated using the Higuchi algorithm appeared to be the simplest method, and the methodology helps to identify “the signatures” of different physiological and pathological states of a patient.

Watters and Martin [37] suggested a new technique for analyzing the EEGs by zero crossing segmentation using detrended fluctuation analysis (DFA). This method showed no paradoxical combination of short and long-term scale invariance in the EEGs. A scaling exponent of $\alpha = 0.67$ was observed for all subjects and sites. Hence, they suggested that the zero crossing method can be used to study the fractal nature of the EEG.

Accardo et al. [38] mentioned in their study of FD on EEG signals that the nonlinear measures provide additional information to conventional spectral analysis. In general the FD measured of the EEG distinguished different pathophysiological states. Changes in the FD value appeared to reflect the degree of EEG desynchronization and thus may be a measure of cortical activation. However, further investigations are needed to define how correct it is to consider the systems of control parameters on the nonlinear cortical dynamics.

Jing and Takigawa [39] reported for epileptic patients that the correlation dimension estimated for different neurological states and frequency components vary. Furthermore, the alpha and theta components revealed close dimension estimates, hence they may cause similar dynamic processes.

Kulish et al. [40] in their study on nonlinear spectral analysis of human EEG use Rényi entropy of a given probability distribution and obtain the fractal spectrum. The generalized FDs of a given time series with the known probability distribution were defined [40] as

$$D_q = \lim_{\delta V \to 0} \frac{1}{q - 1} \log \frac{\sum_{i=1}^{N} p_i^q}{\log \delta V},$$

where moments of the order $q$ ranges from $-\infty$ to $\infty$, of the probability $p_i$, and $\delta V$ represents the sensitivity of the measuring device. They stated that the fractal spectrum contains information related to both frequency and amplitude characteristics of the EEG signals.

Murali [5] has experimented with three patients on inhaling six different odors one at a time, on relaxing and keeping the eye open or closed modes. FFT spectra analysis of the recorded EEGs could not predict the evoked potential due to odor inhalation. However, fractal spectra analysis predicted (Fig. 5) higher FD values for EEGs recorded during odor inhalation than when breathing normally. They concluded that the fractal spectra analysis was sufficiently sensitive to predict the odor evoked potentials and recommend further for an elaborate investigation on the fractal spectra analysis to apply as a diagnostic method.

Thakor and Tong [41] have reviewed advances in EEG spectrum analysis. The paper deals with EEG recording, properties, methodology, functional imaging, etc. Even though EEG is a signal vary for time, the analysis consider an epoch of the recorded wave which is stationary. The spectrum analysis was generally classified into linear or nonlinear approaches. Time domain, frequency analysis, time–frequency analysis derived from fast Fourier transform, wavelet transform, autoregressive model were studied in linear methodology. In addition, a nonparametric model based on signal amplitude was also investigated. With regard to nonlinearity, the EEG signals were analyzed based on higher order statistics, chaotic measures, information theory derived from entropy measures, fractal dimension, etc. Entropy, the method quantify the order/disorder of the time series. It was calculated from the distribution of signal parameters
from amplitude, power, time, frequency, etc. For spatial resolution, clinical studies combined EEG analysis along with medical imaging techniques.

8. Conclusions

Commonly, four EEG spectral analysis methods are studied such as FFT, WT, PAA, and FD. PAA analysis has limitations when applied to EEG analysis for frequencies greater than 2 Hz. FFT gives useful information on the frequency of the EEG waves, but researchers highlight that discrepancies were possible between linear FFT analysis and the nonlinear brain system. A study mentions that WT spectra give more information than FFT. However, similar to FFT analysis, WT is also a linear approach analysis and contradictions are anticipated. Recently, many reports on fractal dimension and fractal spectra analysis predicted the brain activities more precisely than FFT. Even fractal spectra analysis has limitations in analyzing stationary brain waves, multiple brain activities, etc. If in the future dynamic FD analysis of EEGs are developed, it may strongly attract clinicians to use such a technique. However, from the present review it is recommended that for better understanding of the EEGs, all FFT, WT, and FD computations are important to predict the brain activities. Therefore, elaborate research on fractal spectra analysis is called for, to use the analysis as a diagnostic tool in future.

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References

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Vladimir V. Kulish was born in 1966 in Mariupol, Ukraine. In 1992, Dr. Kulish received the Dr.Sc. degree in physics and mathematics from the Russian Academy of Sciences and, in 1999, the Ph.D. degree in mechanical engineering from the Southern Methodist University (Dallas, TX). In 2002, Dr. Kulish was awarded an Honorary Doctor of Divinity by the Universal Life Church (Modesto, CA). At present, Vladimir V. Kulish is an Associate Professor of the School of Mechanical and Aerospace Engineering at Nanyang Technological University in Singapore. Professor Kulish’s main research interest is in the area of mathematical modeling of energy-informational transport processes and transport phenomena in biological systems. The author of six books and more than seventy publications in professional journals and peer-reviewed conference proceedings, Professor Kulish is a holder of several prestigious awards for his scientific achievements. His name was included in 2000 outstanding scientists of the 21st century by the International Biographical Institute, Cambridge, UK, for outstanding achievements in biomedical engineering. The American Biographical Institute selected Professor Kulish a Man of the Year 2003. On April 26, 2004, Professor Kulish was elected a corresponding member of the International Academy of Sciences “Collegium.” At the same time, Professor Kulish is the Founding Editor-in-Chief of the international journal Works of the International Academy of Sciences “Collegium.”

In September 2005, Professor Kulish has been awarded the Tan Chin Tuan Fellowship and will be a visiting scholar to the Department of Physics at Stanford University from August to November 2006.