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Linear and Nonlinear Approaches in Processing Of Neurophysiological Data: Biomedical and Mathematical Principles

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Abstract The diagnostic relevance and practical utility of traditional ways related to biomedical signal processing is often questionable. Traditional power spectral analysis was not designed for complex nonstationary EEG and other neurophysiological recordings with nonlinear nature. As brain activity is a highly complex and irregular system, we highlight a more suitable measures of multiple time-frequency resolution, especially the wavelet analysis, chaos theory and methods of nonlinear dynamics. Those non-conventional approaches proved a high sensitivity for the diagnosis of different neurophysiological stages. In this paper, we present algorithms to quantify the neurophysiological data complexity and discuss their practical relevance and diagnostic potential.

***Keywords*:** neurophysiological data, wavelet analysis, entropic brain, spectrum, modern diagnostics

1. Introduction

Neuroscience, as a previously essentially biological discipline, quickly developed a novel level of understanding brain processes using conceptual backgrounds from mathematics and physics. Each neurophysiological signal, such as EEG, ENG or EMG represents the result of complex mechanisms, including multiple feedback and coupling interactions and inputs from internal and external sources. Therefore, the basic traditional algorithms resulting from linear approaches showed to be insufficient and often fail as a potential diagnostic tool [1].

On the other hand, modern mathematical algorithms based on multiple time-frequency resolution [2] or non-linear dynamics [3] showed potential to unravel hidden pathophysiological mechanisms from the appropriate biosignal patterns. In this paper, the chosen analytical methods are presented, including the wavelet transformation or the calculations of approximate and sample entropy, nonlinear complexity metrices.

2. Linear approaches in neuroscience

Neurophysiological data are characterised by a high degree of non-stationary processes. Their time – frequency features are characterised by a high variability. Analysis of such a signal requires adequate methodology with multiple time – frequency resolution during analysis. The wavelet transformation, contrary to the traditional analytical tools based on Fourier analysis, enables to change the time – frequency resolution by transition and shifting and scaling the window function, called mother wavelet. In this way, lower frequencies are better distinguishable in the frequency domain. On the contrary, higher frequencies reach better resolution in time. The wavelet coefficients, functions of a function of time and wavelet scale, could be obtained by the following formula of continuous wavelet transformation.

$$W(s,p)=\int_{-\infty}^{\infty}x(t)\psi_{s,\nu}(t)dt=\frac{1}{\sqrt{s}}\int_{-\infty}^{\infty}x(t)\psi^{*}\left(\frac{t-\nu}{s}\right)dt \tag{1}$$

where x(t) is a time representation of analyzed signal, ψ is the transforming function called the mother wavelet**,** ν is the wavelet translation, *s* is the wavelet scale.

Higher frequencies are expressed by lower wavelet scales, a vice versa.

$$F_a \equiv \frac{F_c}{sT_s} \tag{2}$$

where s is a wavelet scale, T_s is the sampling period, F_c is the centroid frequency of the wavelet function calculated by approximation.

The algorithm of discrete wavelet transformation is based on passing the original signal though a series of two kinds of filters. The low-pass filter separates the approximate coefficients and the high pass filter separate the detail coefficients from the original neurophysiological recording. The process could be repeated to obtain approximation or detail coefficient at higher level. This algorithm was effectively used to distinguish typical EEG waves and derive further quantitative parameters related to different neuropsychiatric diseases.

Mathematically, discrete wavelet transformation could be defined as:

$$\psi_{m,n}(\nu) = \frac{1}{\sqrt{2^m}} \psi\left(\frac{\nu - 2^m.n}{2^m}\right) \tag{3}$$

where ψ is the mother wavelet, m is a wavelet scale and n is a time position.

$$s = 2^m \; and$$
$$\tau = 2^m.n$$
$$where \qquad m, n \in Z$$

When considering the decomposition as

$$x(t) = \sum_{k=1} A_j(k)\psi_{j,k}(t) + \sum_j \sum_k c_j(k)\psi_{j,k}(t) \tag{4}$$

where where ψ is the mother wavelet, $c_j(k)$ are the discrete wavelet transform coefficients at resolution level *j* and time k, it is possible to define the wavelet energy and wavelet entropy measures.

The energy at the at each resolution level j is

$$E(j) = \sum_k |c_j(k)|^2 \tag{5}$$

where $c_j(k)$ are the discrete wavelet transform coefficients at resolution level *j* and time k.

And the total energy is

$$E_{tot} = \sum_j E_j. \tag{6}$$

The relative energy is understood as a probability distribution of energy across different decomposition levels.

$$p_j = \frac{E_j}{E_{tot}} \tag{7}$$

Finally, the wavelet entropy is defined as

$$WE(p) = -\sum_j p_j \,.\, ln[p_j] \tag{8}$$

where p_j is a relative wavelet wavelet energy.

3. Nonlinear approaches in neuroscience

Many different algorithms developed to assess the nonlinear nature of neurophysiological data. The correlation dimension, fractal dimension, largest Lyapunov exponent, Lempel-Ziv complexity, approximate entropy, sample entropy, permutation entropy or Hurst exponent are few of them. The following text deals with an approximate entropy (ApEn) and sample entropy (SampEn) in more detail.

The approximate entropy is often described as a measure of signal complexity and reflects the level of new signal pattern generation. This dimensionless number is reflecting the degree of disorder in the analysed system. Low values of

approximate entropy are associated with a high degree of regularity and predictability, thus a lower system complexity. The approximate entropy value increases when the system is characterised by high disorder and irregularity.

Let us consider data time series x(n) = x(1), x(2), ...,x(N), where N is a number of data samples, and SD is a standard deviation of the analyzed signal.

$$SD_x = \sqrt{\frac{1}{N-1}\sum_{n=1}^{N}[x(n) - \frac{1}{N}\sum_{n=1}^{N} x(n)]^2} \tag{9}$$

The algorithm of ApEn calculation begins with an estimation of vectors X(i) defined

$$X(i) = [x(i), x(i+1), \ldots, x(i+m-1)] \tag{10}$$

for i=1, N-m+1.

The difference between X(i) and X (j), d[X(i),X(j)] is estimated as a maximum absolute difference between their related scalar components

$$d[X(i), X(j)] = max_{k=0,m-1}[\,|x(i+k) - x(j+k)|] \leq r \tag{11}$$

where r is a threshold level.

Next, the number of differences d[X(i),X(j)], for j =1, N-m+1 that is smaller or equal than the threshold *r* is calculated and the ratio of this number to the total number of m-vectors (N-m+1) must be assessed.

If $N_r^m(i)$ is number of d[X(i), X(j)] $\leq r$, then

$$C_r^m(i) = N_r^m(i)/(N-m+1) \tag{12}$$

This step is repeated for any i, where i=1,...,N-m+1. Averaged value of $C_r^m(i)$ natural logarithm is calculated as

$$\Phi^m(r) = \sum_{i=1}^{N-m+1} ln\, C_r^m(i)/(N-m+1) \tag{13}$$

The embedding dimension m is increased to m+1 and all the algorithm is repeated. The value of $C_r^m(i)$ and $\Phi^{m+1}(r)$ is estimated. Finally, ApEn is theoretically defined as

$$ApEn(m,r) = \lim_{N\to\infty}[\Phi^m(r) - \Phi^{m+1}(r)] \tag{14}$$

Practically, parameter ApEn is expressed as

$$ApEn(m,r,N) = [\Phi^m(r) - \Phi^{m+1}(r)] \tag{15}$$

The algorithm of sample entropy is a comparable metrics with an advantage that it does not include itself when it is counted. The ratio of the number of d[X(i),X(j)] less than r to the total distance N-m is recorded as $B_i^m(r)$ and the average value of $B_i^m(r)$ is than calculated as

$$B^m(r) = (N-m+1)^{-1}\sum_{i=1}^{N-m+1} B_i^m(r) \tag{16}$$

where m is an embedding dimension and r is a threshold level.

The whole procedure is repeated, and the $B_i^{m+1}(r)$ is calculated for m+1 dimensions. The sample entropy of the original data sequence is then calculated as

$$SampEn(m,r) = \lim_{N\to\infty}\left[-\ln\frac{B^{m+1}(r)}{B^m(r)}\right] \tag{19}$$

Practically, when N is a finite number, the sample entropy finally is

$$SampEn(m,r,N) = \ln B^m(r) - \ln B^{m+1}(r) \tag{20}$$

3. Results and discussion

Although most of spectral characteristics of neurophysiological data are still analysed by commonly used Fast Fourrier transformation with a limited effect, the wavelet algorithm brings novel view on their varying time-frequency characteristics.

In neuroscience, the wavelet transform has many different applications. For example, multiresolution analysis was used effectively used to diagnose different neuropsychiatric diseases. Patients suffering from schizophrenia were effectively diagnosed by EEG by an algorithm based on the orthogonal wavelets filter. Subsequently, authors declare the accuracy of 99.21% and 97.2% using K-nearest neighbour classifiers with ten-fold and leave-one-subject-out cross-validations [4]. The wavelet transform is very sensitive to emotional stability. The higher wavelet entropy observed in the EEG of depressive patients was found in the prefrontal region, especially in the right hemisphere [5].
Puthankattil and Joseph (2014) [6] found a higher relative wavelet entropy in the delta frequency band (0.5 2 Hz) and associated it a quantitative biomarker that characterises major depressive disorder [6].
However, wavelet analysis was also effectively used to study the mechanisms of vital condition, which were still not fully understood. Respiratory activity in anaesthetized animals was analysed by wavelet analysis applied to recordings from respiratory muscles and the phrenic nerve [7, 8]. The results showed that cough and eupnoeic inspiration are generated by similar neuronal structures [7]. Moreover, the stable specific way of information processing during generation of the aspiration reflex was proved. It was characterised by stable time–frequency energy distribution, regardless of the type of anaesthetic used, contrary to othe respiratory reflexes [8]. Benzy et al. used wavelet entropy together with an approximate entropy measure to assess the dept of anaesthesia [9].

The complexity of EEG and other neurophysiological signals is underlying alterations related to pathologically altered neurodynamics. EEG signals from depressed patients are found more regular and predictable [10]. The correct classification of emotional state reaches a classification accuracy according to Hosseini et al. using wavelet and approximate entropy as a very sensitive tool of mood alteration [11]. Shou-Zen Fan et al. [12] found that ApEn parameter responds more rapidly to recovery from inhalational general anaesthesia than does a bispectral index. This is not surprising since the bispectral index is derived from basic linear tools to monitor the anaesthetic depth and thus does not reflect the non-linear nature of EEG.

Non-linear dynamics-based biomarkers bring interesting results in sleep research and ageing. The conclusions show that the sample entropy reflects the balance between the sleep-promoting and alertness-promoting mechanisms. The value of sample entropy was higher for older patients mainly during REM sleep, which may suggest that the cortical state is moved towards alertness in elderly subjects [13]. The other study found a direct correlation between deep sleep and the sample entropy value of the sample [14]. Keshmiri [15] made interesting conclusions in the field of comparison of entropic state and level of consciousness, which plays role in the capacity for adaptation.

4. Conclusion

The analysis of neurophysiological data requires appropriate quantitative tools to unravel the biological complexity behind different physiological and pathophysiological processes. Analytical methods based on multiresolution analysis and nonlinear dynamics have repeatedly been shown to serve as objective and reliable biomarkers with the potential for prompt and effective diagnostics and effective therapeutic approach.

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