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Comparison of Different Methods of Time Shift Measurement in EEG

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Summary

Digital signal processing techniques are often used for measurement of small time shifts between EEG signals. In our work we tested properties of linear cross-correlation and phase/coherence method. The last mentioned method was used in two versions. The first version used fast Fourier transform (FFT) algorithm and the second was based on autoregressive modeling with fixed or adaptive model order. Methods were compared on several testing signals mimicking real EEG signals. The accuracy index for each method was computed. Results showed that for long signal segments all methods bring comparably good results. Accuracy of FFT phase/coherence method significantly decreased when very short segments were used and also decreased with an increasing level of the additive noise. The best results were obtained with autoregressive version of phase/coherence. This method is more reliable and may be used with high accuracy even in very short signals segments and it is also resistant to additive noise.

Key words

EEG • Time shift • Signal processing • Cross-correlation • Phase/coherence

Introduction

Methods of time shift measurements are often used in analysis of EEG signals and especially in analysis of epileptic discharges and seizure spread. Numerous reports were published using linear cross-correlation (Cohn and Leader 1967, Tharp 1971, Matsuzaka *et al.* 1993, Medvedev *et al.* 1996), phase/coherence (Gotman 1981, 1983, Kobayashi *et al.* 1992, Medvedev *et al.* 1996), a non-linear correlation coefficient (Lopes da Silva *et al.* 1989, Meeren *et al.* 2002), averaged amount of mutual information (Mars and Lopes da Silva 1983, Mars *et al.* 1985) and other techniques in the analysis of epileptiform discharges. These methods are advantageous for the analysis of signals with complicated morphology, in which classic methods of time shift measurements (e.g. delay between peaks of spikes) usually fail.

Method of phase/coherence based on fast Fourier transform (FFT) was used by Brazier (1972) in the analysis of spontaneous seizures in human patients with epilepsy. An attempt was made to detect the seizure onset zone that drives the abnormal activity and to trace

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the spread of seizures. This method as modified by Gotman (1981, 1983) became very popular. Gotman as the first applied this technique for analysis of the time shift between bilateral synchronous discharges. His method underwent several modifications. One of them concerns the autoregressive version of phase/coherence developed and applied to epileptiform discharges by Kobayashi *et al.* (1992).

However, these methods were usually tested and compared on real signals obtained from patients with epilepsy or from animal models of epilepsy. The exact time delay in these signals is not defined. In our work we tested the properties and accuracy of three commonly used methods of time shift measurements in signals with a known delay. Therefore we can define conditions of using these methods and to optimize them for selected cases.

Material and Methods

Testing signals

All methods were tested on three different signals modelling epileptiform EEG. All the used testing signals had a sampling frequency 500 Hz and values of set time delay were 0-20 ms.

The first type of signal was fully artificial (Fig. 1). Other testing signals were modifications of real signals, which were obtained from a model of bilateral symmetric epileptic foci in rats (Jiruška *et al*. 2004) to be published in extenso. Signals were recorded from electrodes placed over the left and right frontal cortex just above the epileptic foci. Both signals were referred to an electrode placed in the nasal bone. Then signals were filtered between 0.5-70 Hz and digitized at a sampling frequency of 500 Hz.

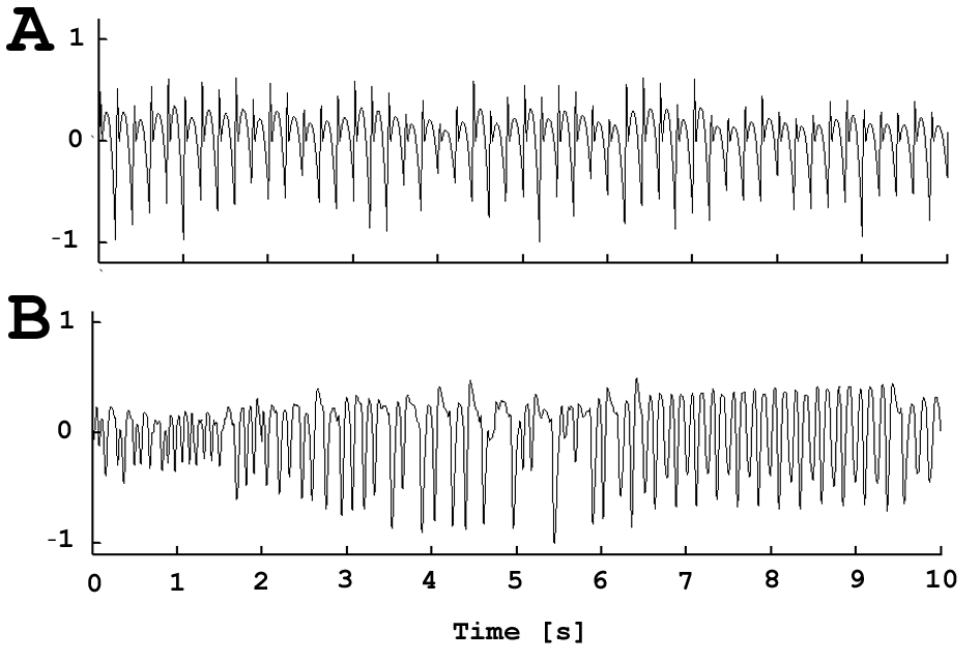

Fig. 1. Examples of signal simulation. Abscissa - time in seconds. Ordinate - amplitude of signals, which are normalized. A: Signal type I. B: Signal type III.

The artificial type I signal was a polynomial model, which combines linear and parabolic curves, so that the resulting signal morphologically simulates real epileptiform graphoelements (spike-and-wave complexes). Then the artificial signal was filtered to obtain a similar spectrum as the real signal. Known time delays were set between pairs of signals. Finally white noise was added to the signals. Pairs of signals were subsequently analyzed.

Type II signal was taken from a real epileptiform EEG signal. Chosen segments that contained epileptiform graphoelements, were cut from the real signal. Known time delays were set and white noise was added.

The third type of signal was also created from the real signal (Fig. 1). First, the transfer functions between pairs of real signals from left and right frontal electrodes were computed. All transfer functions were averaged, giving the final averaged transfer function. The signal was delayed by a chosen delay and subsequently distorted by averaged transfer function. Finally, noise was added to both signals. With this approach we obtained a pair of signals with a known time delay but of different shapes.

Methods of analysis

All the methods and algorithms described below were created and evaluated using the Matlab program (MathWorks Inc.).

To describe the properties and accuracy all of the methods were tested on signal segments with a duration of 32, 64, 128, 256 and 512 samples. To describe the dependence of accuracy on the level of additive white noise, methods were tested on signals with signal to noise ratio 50 and 20 dB. The accuracy index (A) was evaluated according the equation

$$A = 100 \cdot (1 - \frac{|T - T_P|}{T_P})[\%]$$

where Tp is artificially set time delay and T is the estimated time delay.

Linear cross-correlation

For each analyzed epoch a linear cross-correlation function was applied. The obtained time resolution was 2 ms. Position of the maximal value of the cross-correlation function determined the time delay between signals (Medvedev *et al.* 1996).

Phase/coherence using FFT

This method was set according to Gotman's approach (1981, 1983). Coherence and the cross-spectral phase were estimated *via* the FFT method. Coherence and lower 99 % confidence intervals were computed in the frequency range 1-50 Hz. The range of frequencies that correspond to a significant coherence (p<0.01) was identified. The correlation coefficient between phase and frequency was computed. If it significantly differed from zero (p<0.01) the least-square line was fitted through the linear part of the cross-spectral phase comprising at least a 10 Hz wide frequency band. The time delay was derived from the slope of this line.

Phase/coherence using autoregressive modeling

In principle this method is similar to previous methods, but in this case cross-spectral phase is estimated by autoregressive modeling (Kobayashi *et al.* 1992, 1994). Using auto- and cross-correlation coefficients the Yule-Walker equations were compiled from which the cross phase spectrum was derived. Time shift was also computed from the slope of the regression line fitted to the selected part of the phase.

An important feature in this approach is the selection of an adequate model. The method of an underestimated model order does not describe all signal details and an overestimated order causes false peaks in the spectrum with no relation to the signal. The model order was estimated by Minimal Description Length (MDL) criterion (Čmejla 2000). Other criteria (AIC, Hann-Quinn criterion, Pukill's modified criterion) gave similar results (Akaike 1974, Čmejla 2000), but the MDL criterion yielded the smallest variance.

To test the dependence of results on a model order value we used two approaches. The first one used an adaptive model order selection, according to the MDL criterion for each segment. A fixed model order with value M=16 was used as the second approach. This value was obtained as the best result in previous studies focused on search for an adequate model order for our signal types. This may be understood as some form of anticipatory information.

Results

Accuracy index for each method did not depend on the preset time delay. The accuracy was computed from signals with different time delays. With each method 3010 segments of each simulating signal of all lengths was analyzed. Results obtained by all tested methods are shown in Figure 2.

With decreasing duration of the analyzed segment the accuracy of all methods decreased. The estimates of time delay with FFT phase/coherence showed the worst results. This was the most sensitive method of all for shortening the analyzed epochs. FFT version was also very sensitive to additive noise. Increased signal-to-noise ratio is associated with a marked increase in accuracy. The accuracy of phase/coherence also decreased when applied on signal type III in comparison with an application to signal type II, i.e. this method was sensitive to convolution distortion caused by an averaged transfer function applied to one signal. Measurement with FFT phase/coherence was also complicated by difficulties with fitting of the regression line through the cross-spectral phase. However FFT phase/coherence is applicable to signals with low levels of additive noise and for epochs longer than 500 samples.

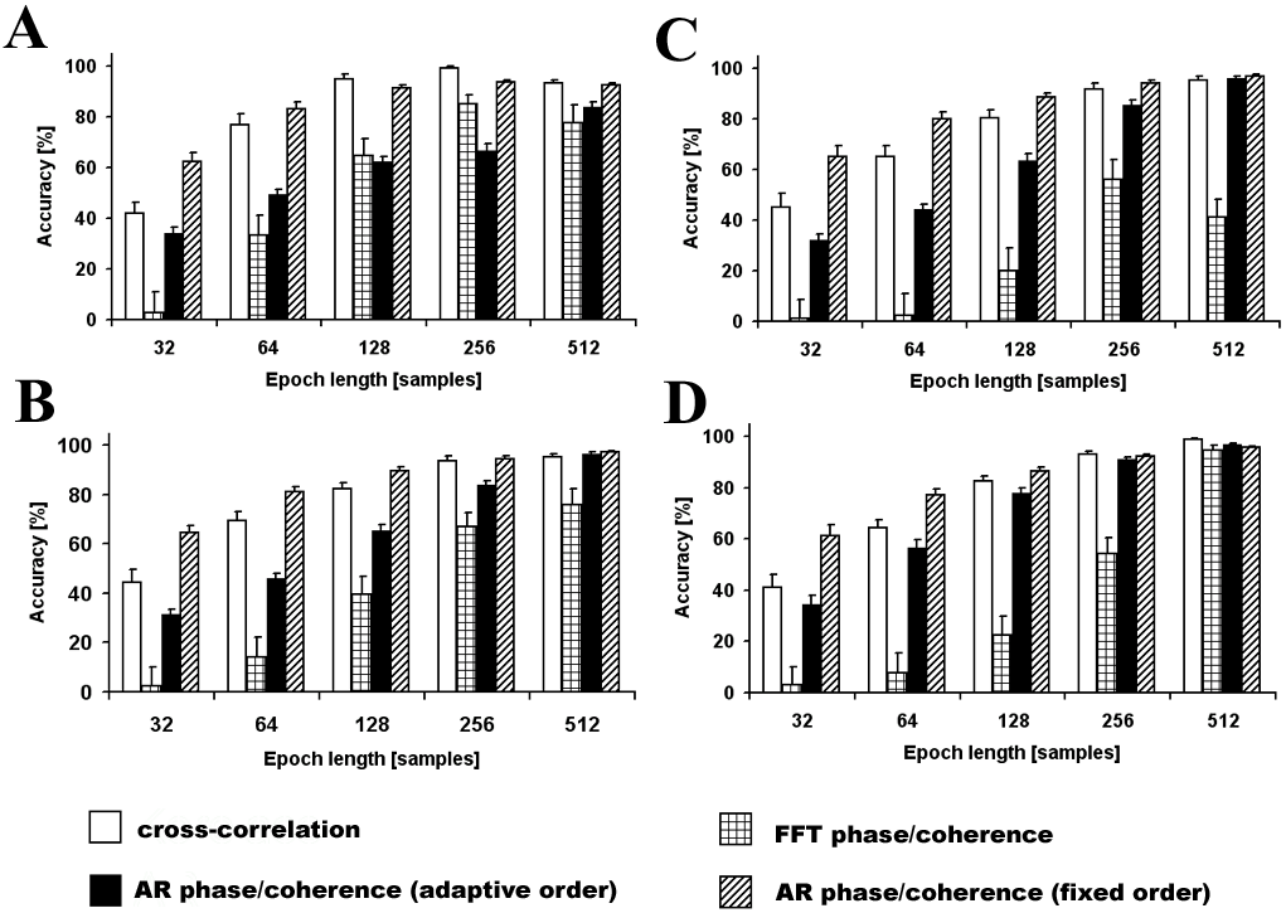

Fig. 2. Accuracy calculated for each method of time shift measurement applied to different length of analyzed signal segment. Graphs show mean values of accuracy index for each method and associated standard deviations. Abscissa – length of analyzed segments in samples. Ordinate – accuracy in percents. A: Accuracy tested on signal type I, signal to noise ratio was 20 dB. B: Accuracy results on signal type II, signal to noise ratio 20 dB. C: Accuracy with signal type III, signal to noise ratio 20 dB. D: Accuracy on signal type III, signal to noise ratio 50 db. Sampling frequency of all signals is 500 Hz.

The best results were obtained by autoregressive version of phase/coherence with a fixed model order. Estimates of the time shift obtained with this approach are sufficiently accurate even when applied to short segments. This method was resistant to additive white noise; an increased level of additive noise did not change the accuracy of the results. Distortion of the signal by the transfer function also did not influence the accuracy. Regression line could be well fitted through the cross-spectral phase even in analysis of the short epochs. The phase was also easily unwrapped, so the regression line could be fitted over a wider frequency range. From our results this method seems to be applicable even for segments formed by 64 samples, because an 80 % accuracy was observed. However, the variance for this epoch duration was relatively long. We suggest that this method can be applied with a high reliability to signal segments longer than 128 samples. For these durations of accuracy approaches 90 % with a variance of 3 %. For longer segments the accuracy index was close to 100 %.

Cross-correlation showed relatively good results even for short segments. This approach was also quite resistant to additive noise and to distortion of the signal by a transfer function. The results obtained by cross-correlations were even superior to results obtain by autoregressive phase/coherence with an adaptive model order.

Discussion

Methods of time shift measurement exhibited different properties under our experimental conditions. The accuracy was not related to the value of time delay. However it strongly depended on the length of the analyzed segment and on the level of additive noise.

The accuracy of linear cross-correlation on short signal segments and the resistance to additive noise were relatively good in comparison with phase/coherence *via*

FFT. However, the largest disadvantage of this method is its dependence on signal morphology. In situations when the spike-and-wave complex has a small spike and large wave component, cross-correlation can show a time delay that corresponds to time shift of wave component. The time delay of the spike component can significantly differ from the delay of the wave component, so they could even be opposite (Gotman 1983). It is generally accepted that more important information about the origin and spread of epileptic activity is provided by the time shift between spike components. Results obtained by cross-correlation might give false information. Similar problems can occur in situations, when fast rhythmic epileptiform activity is mixed with a slow wave artifact (Gotman 1983). A dependence on signal morphology could also be the reason for the resistance of cross-correlation to additive white noise.

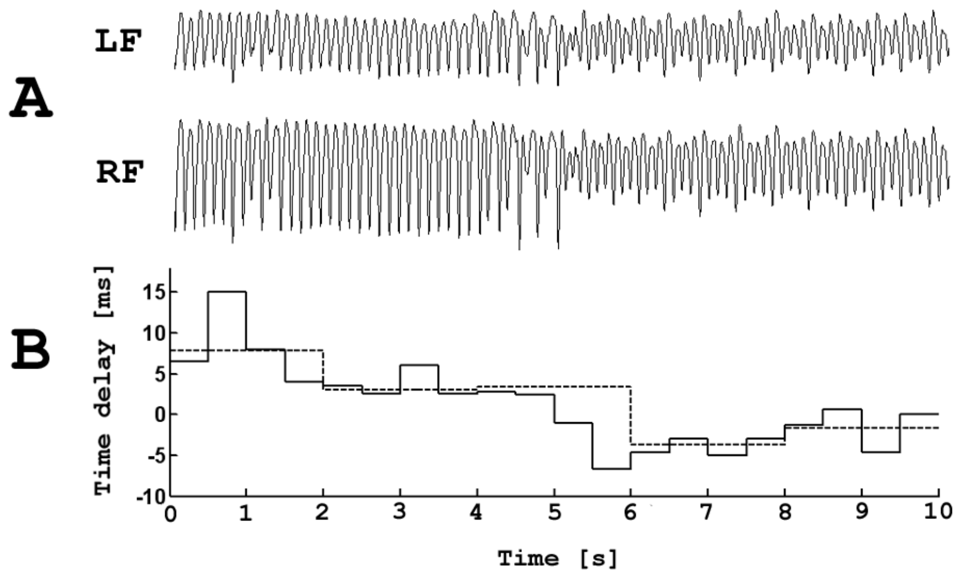

Fig. 3. Dynamic changes in time shift during the real ictal activity obtained by autoregressive version of phase/coherence. **A**: Examples of pair of real signals recorded from left (LF) and right (RF) frontal electrode during seizure. **B**: Time shift values obtained by analysis of 2-second long segments and by analysis of 0.5-second segments. Analysis of whole signal (10 seconds) showed time delay 3.358 ms. Abscissa – time in seconds. Ordinate – values of time delay in ms.

On the other hand, the estimate of time delay with the method of phase/coherence mostly depends on time delays of spike components (Kobayashi *et al.* 1992). This is due to the fact that spikes contain higher frequencies in the wider frequency band. If the time delays between spike and wave component differ, wave component influences the phase spectrum only in the lower frequencies. Possible troubles with the wave component could be bypassed, because this method allows selection of the appropriate frequency band for analysis of the time shift.

Our experiments showed that the FFT version failed for short signal segments and is very sensitive to additive noise. Estimation of cross-spectral phase with FFT requires analysis of very long segments lasting several seconds or averaging of spectra from a number of epochs. In our case, the FFT version showed accurate result even for nearly 1-second segments, but with shorter segments its accuracy rapidly decreased.

The autoregressive version is more robust and can be used with a high accuracy even on short signal epochs and is quite resistant to noise. It can thus be used for analysis of very short epochs of signals and even of single spikes. This is very important because epileptic activity recorded by surface electrodes is a dynamic process and the time delays between signals can rapidly change (Fig. 3), especially during prolonged bursts of epileptiform activity (Kobayashi *et al.* 1992). Another advantage of this method is the good fit of the regression line through the phase (Uhlíř and Sovka 2002). Fitting of regression line can be complicated in the FFT version. Better results with a version with fixed model order than with the version with adaptive order are probably due to the anticipatory information about the adequate model order for our signals obtained from previous studies.

Despite these methods which are useful tools in the analysis of small time shifts between EEG signals, a physiological interpretation of results obtained with these methods has to be very careful. It must be kept in mind, that we are working with signals recorded from the scalp or brain surface. Summation of activity from different cortical layers is thus recorded, with a predominance of activities from the superficial layers. Using the linear correlation method to analyze the spread of activity from penicillin foci Tharp (1971) reported that signals from distant sites can lead signals from the focus. We obtained similar data with all the above mentioned techniques when we analyzed the spread of activity from a single epileptic focus induced by bicuculline methiodide. The discharges from the projection area in a homotopic region of contralateral hemisphere were shown to precede discharges recorded in the primary focus (Jiruška *et al.*, unpublished results). Discharges of an epileptic focus are initiated in deep cortical layers and thus surface registration might not exactly correlate with the actual beginning of this discharge (Pockberger *et al.* 1984). Methods of time shift measurements provide exact results from a mathematical point of view, but many biological factors have to be taken into account to obtain correct neurophysiological result.

In conclusions, properties of different methods for short time shift measurements were tested. All methods were applicable to signal segments longer than one second. The best results were obtained with the autoregressive version of phase/coherence method, which was proved to be most suitable for analysis of short epochs of signals and relatively resistant to additive noise. However, the results of all these methods should be interpreted very cautiously.

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