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Delay estimation for cortico-peripheral relations

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Abstract

In neurophysiology, time delays between concurrently measured time series are usually estimated from the slope of a straight line fitted to the phase spectrum. We point out that this estimate is valid only in the case in which, one signal is a mere time-delayed copy of the other one. We present a procedure for delay estimation that applies to a much wider class of systems with nontrivial phase spectrum like for example lowpass filters. The procedure is based on the Hilbert transform relation between the phase of a linear system and its log gain. The Hilbert transform relation is nonlocal in frequency space, a fact that limits its applicability to experimental data. We explore these limits, and demonstrate that the method is applicable to neurophysiological time series. We present the successful application of the Hilbert transform behavior method to concurrently recorded epicortical brain activity and peripheral tremor. We point out and explain physiologically unreasonable delay estimates given by the traditional method. Finally, we discuss the assumptions underlying the applicability of the Hilbert transform method in the neuroscience context.

Keywords: Time delay estimation; Linear system theory; Hilbert transform relation; Minimum phase; Cross-spectral analysis; Phase spectra

1. Introduction

In recent years, there has been a growing interest in the study of functional coupling between different parts of the nervous system. Stimulated by new techniques for measuring signals of high quality both by MEG and EEG there have been numerous studies into the coupling within the brain itself and with peripheral muscle activity; for a recent review see Mima and Hallett (1999a).

Cross-spectral analysis provides very powerful tools for the analysis of neurophysiological systems in the frequency domain (Timmer et al., 2000). In particular, the existence of a linear association can be reliably tested for by the coherency function. Once a correlation has been found, the nature of the relation can be examined, and specifically one might ask whether there is a time delay between the processes. This question is of great neurophysiological importance as it might shed light on the pathways by which the processes interact.

Methods for the identification of time delays in biological systems have received a lot of attention. Delay estimation between cortical signals and peripheral muscle activity allows to differentiate a transmission via oligosynaptic corticospinal pathways, the conduction times of which are well known from cortical stimulation studies in humans (Rothwell et al., 1991), from a mediation via polysynaptic extrapyramidal systems conducting much slower than the corticospinal tract. This delay estimation is to date usually accomplished by estimating the slope of the phase spectrum by a straight line fit which has led to heterogeneous results (Mima and Hallett, 1999b; Mima et al., 1999; Brown et al., 1998Brown et al., 1999Halliday et al., 1998). We point out that this method can only be applied in the rather special case of one signal being a mere time-shifted copy of the other one. On the contrary, we demonstrate that using a procedure called Hilbert transform method

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delay estimation is possible for the very wide class of linear, causal, minimum-phase systems. These systems are characterized by nontrivial transfer functions, in contrast to the simple time shift systems to which the straight line fit method applies.

The paper is organized as follows. In Section 2, we outline the methods and present the experimental neurophysiological data. This section also gives the necessary background on cross-spectral analysis. In particular, we point out the differences between the Hilbert transform procedure and the method of fitting a straight line to the phase curve. In Section 3, we test the Hilbert transform method on simulated data and evaluate its performance in the presence of observational noise, an inevitably strong component of most measurements in human physiology. We explore the limitations of the method in this case. Subsequently, we present the application of the Hilbert transform method to simultaneous measurements of electrocorticogram (ECoG), electromyogram (EMG) and accelerogram (Acc) in Section 4. We demonstrate the advantages of the Hilbert transform method on this data by comparing it to the traditional delay estimation procedure. In Section 5, we discuss the results in the neuroscience context. In particular, we discuss the justification and implications of the assumption of minimum-phase behavior of the system.

2. Materials and methods

2.1. Data recording

We analyzed three female and three male patients with intractable focal epilepsy prior to undergoing surgery to remove an epileptic focus. The patients had subdural epicortical grid electrodes implanted covering parts of the primary sensorimotor area of the cortex.

All data were sampled at a rate of 520 Hz. The ECoG was recorded with a time constant of 0.3 s and a lowpass filter at 160 Hz. In parallel to the ECoG bipolar surface EMG and Acc were recorded from those regions of the body which showed a motor response on cortical electrostimulation. Hand muscles were recorded with the hands extended against gravity with uniaxial accelerometer fixed on the dorsum of the hand. The EMG was bandpass-filtered between 50 and 260 Hz on-line. The duration of each recording was between 40 and 60 s. As we focus on the methodological side here, recordings from two patients have been selected as examples for this paper. The recording procedure and the neurophysiological results for the full data set have been reported elsewhere (Raethjen et al., 2000a,b).

2.2. Cross-spectral analysis

In this section, we briefly discuss the necessary background on cross-spectral analysis. For a more detailed treatment and further references, see the recent review by Timmer et al. (2000).

The power spectrum $S_x(\omega)$ of a zero mean process $X(t)$ is defined as the Fourier transform of the auto-covariance function $\mathrm{ACF}(\tau)=\langle X(t)X(t-\tau)\rangle$,

$$S_x(\omega)=\frac{1}{2\pi}\sum_{\tau}\mathrm{ACF}(\tau)\mathrm{e}^{-i\omega\tau},\quad \omega\in(-\pi,\pi] \tag{1}$$

The estimation of the power spectrum is performed by direct spectral estimation (Brockwell and Davis, 1991), based on the Fourier transform $\mathrm{FT}_x(\omega_k)$ of the tapered measured data $x(t)$,

$$\mathrm{FT}_x(\omega_k)=\frac{1}{\sqrt{N}}\sum_{t=1}^{N}x(t)\mathrm{e}^{-i\omega_k t} \tag{2}$$

with

$$\omega_k=\frac{2\pi k}{N},\quad k=-\frac{N}{2},\ldots,\frac{N}{2}-1 \tag{3}$$

The periodogram $\mathrm{Per}_x(\omega_k)$ is defined as the squared modulus of $\mathrm{FT}_x(\omega_k)$. Whenever the auto-covariance function $\mathrm{ACF}(t)$ is decaying fast enough for larger lags, the real and imaginary part of the Fourier transform $\mathrm{FT}_x(\omega_k)$ are asymptotically Gaussian distributed with variance determined by $S_x(\omega)$. Therefore, the periodogram $\mathrm{Per}_x(\omega_k)$ is distributed as χ^2_2, a random variable, which does not represent a consistent estimator for the spectrum because its variance is equal to its mean. To obtain a consistent estimator of the spectrum, the periodogram is smoothed by a window function W_j,

$$\hat{S}_x(\omega_k)=\frac{1}{2\pi}\sum_{j=-h}^{h}W_j\,\mathrm{Per}_x(\omega_{k+j}) \tag{4}$$

The hat symbol is used to indicate estimators of theoretical quantities throughout the paper.

Similar to the univariate case, the cross-spectrum $\mathrm{CS}(\omega)$ is defined as the Fourier transform of the cross-covariance function $\mathrm{CCF}(\tau)=\langle X(t)Y(t-\tau)\rangle$. Again, the estimation is based on smoothing the cross-periodogram.

The cross-spectrum between input and output of a linear process is related to the spectrum of its input by the complex-valued transfer function $A(\omega)$,

$$\mathrm{CS}(\omega)=A(\omega)S_x(\omega) \tag{5}$$

The gain is defined as the modulus of the transfer function,

$$|A(\omega)|=\frac{|\mathrm{CS}(\omega)|}{S_x(\omega)} \tag{6}$$

and characterizes the systems amplitude transmission.

Normalizing the modulus of the cross-spectrum by the spectra of both processes gives the coherency $\mathrm{Coh}(\omega)$,

$$\mathrm{Coh}(\omega)=\frac{|\mathrm{CS}(\omega)|}{\sqrt{S_x(\omega)S_y(\omega)}} \tag{7}$$

The coherency is a bounded measure of linear association with a value of 1 in case of a perfect linear relationship between the time series and a coherency of 0 in case of linear independence within a given frequency band.

The argument of the cross-spectrum is called phase,

$$\phi(\omega)=\arg \mathrm{CS}(\omega) \tag{8}$$

Gain, coherency and phase spectra are estimated by replacing the spectra in Eqs. (6) and (7) and Eq. (8) by the above spectral and cross-spectral estimates.

The estimates for the spectrum, the gain and the phase are asymptotically Gaussian distributed with variances given by:

$$\mathrm{var}(|\hat{A}(\omega_k)|)=\frac{1}{v}\left(3+\frac{1}{\mathrm{Coh}(\omega)^2}\right)|A(\omega_k)|^2 \tag{9}$$

$$\mathrm{var}(\hat{\phi}(\omega))=\frac{1}{v}\left(\frac{1}{\mathrm{Coh}(\omega)^2}-1\right) \tag{10}$$

where v is the so called equivalent number of degrees of freedom, determined by the window function $W(j)$ used (Brockwell and Davis, 1991). Eq. (10) holds if the coherency is significantly larger than zero. For a coherency towards zero, the distribution of the estimated phase approaches the uniform distribution in $[-\pi,\pi]$. Therefore, the phase spectrum cannot be estimated reliably in the case of small coherency. The same holds for the gain spectrum as can be seen from Eq. (9).

Based on the coherency, the time series can be tested for linear independence. The critical value s for the null hypothesis of zero coherency for a significance level α is given by:

$$s=\sqrt{1-\alpha^{\frac{2}{v-2}}} \tag{11}$$

While the interpretation of the coherency is straightforward, the interpretation of phase-spectra is more complex.

2.3. Phase spectra of linear delay processes

In this section, we point out that while phase spectra contain information about a delay in the system, the estimation of this delay from the phase spectrum is a non-trivial task.

Any linear process containing a delay, for ease of notation referred to as a delay process, can be separated into the concatenation of one process without delay and one process representing nothing but the delay. The latter simply represents a time shift of the output with respect to the input. The phase spectrum of such a time shift δ is well known to be,

$$\phi(\omega)=\delta\omega \tag{12}$$

Eq. (12) is the basis for the previously mentioned straight line fit approach to delay estimation from the phase spectrum. Indeed, it can be shown that for processes consisting of nothing but a delay a consistent estimator of the delay can be obtained by a weighted least squares line fitted to the phase spectrum (Hamon and Hannan, 1974; Rosenberg et al., 1989). As mentioned before, corticomuscular delay estimation is to date usually done by this procedure.

Nevertheless, the phase spectrum of a delay process in general is given by:

$$\phi(\omega)=\delta\omega+\arg A(\omega) \tag{13}$$

where $A(\omega)$ denotes the transfer function of the process without delay. Eq. (13) shows that the estimation of the delay time from the slope of the phase curves is valid only if the argument of the transfer function arg $A(\omega)$ is identically zero. This is the case if and only if the one process is a time-delayed version of the other one, i.e. $y(t)=x(t-\delta)$. In all other cases, we need to estimate the arg $A(\omega)$ and the delay time δ. This can be done by the method described in the next section.

2.4. Delay estimation by the Hilbert transform method

It is known that for linear systems satisfying what is called the minimum-phase condition, the argument of the transfer function is related to the log of its modulus by the following Hilbert transform relation (Oppenheim and Schafer, 1975)[1],

$$\arg A(\omega)=\frac{1}{2\pi}\int_0^{\pi}\log|A(\theta)|\left(\cot\frac{\omega-\theta}{2}+\cot\frac{\omega+\theta}{2}\right)\mathrm{d}\theta \tag{14}$$

The minimum-phase condition can be expressed in various forms, the most intuitive being that a linear system satisfies the minimum-phase condition if it has a causal, stable inverse. Another characterization builds on the properties of the system function, given by the z-transform of the unit sample response (Oppenheim and Schafer, 1975). The system function evaluated on the unit circle is the transfer function. A process has the minimum-phase property if the system function has no poles or zeros outside the unit circle. While the assumptions of linearity, causality and stationarity ensure that

[1] The application of the Hilbert transform and the notion of phase in the present context should not be confused with the application of the Hilbert transform for the construction of an analytic signal $x_a(t)$ from a measured time series $x(t)$ such that $x(t)$ is the real part of the complex analytic signal $x_a(t)$. This analytic signal is given by $x_a(t)=x(t)+i\tilde{x}(t)$, where $\tilde{x}(t)$ is calculated from the time series $x(t)$ by the Hilbert transform. The analytic signal can be decomposed into a slowly varying amplitude time series $A(t)=|x_a(t)|$ and a phase time series $\phi(t)=\arg\ x_a(t)$. For examples of this alternative use of the Hilbert transform in studies concerning cortico-muscular interactions see Tass et al. (1998) and Gross et al. (2000).

the system function has no poles outside the unit circle, the zeros are not determined by these conditions. We will discuss further justifications of the minimum-phase assumption and consequences of its violation in detail in Section 5. For now, we only note that all members of the very general class of autoregressive models possess the minimum-phase property, regardless of their specific parameters and order.

Eq. (14) is the center piece of the delay estimation procedure to be described in the following. As the modulus of the system function is defined to be the gain we can get an estimate for arg $A(\omega)$ by simply replacing the spectra in Eq. (6) by their estimates given in Section 2.2,

$$\arg \hat{A}(\omega_l) = \frac{1}{2M} \sum_{k=1, k\neq l}^{M} \log|\hat{A}(\omega_k)| C(\omega_l, \omega_k) \tag{15}$$

with

$$C(\omega_l, \omega_k) = \cot\frac{\omega_l - \omega_k}{2} + \cot\frac{\omega_l + \omega_k}{2} \tag{16}$$

and M being the number of independent spectral estimates determined by the length of the time series T, the sampling frequency f_s and the effective number of degrees of freedom v via,

$$M = \frac{f_s T}{2v} \tag{17}$$

As the estimate of the gain is asymptotically Gaussian distributed, the same holds true for the estimate of arg $A(\omega)$ with variance given by:

$$\mathrm{var}(\arg \hat{A}(\omega_l)) = \left(\frac{1}{2M}\right)^2 \sum_{k=1, k\neq l}^{M} \left(\frac{C(\omega_l, \omega_k)}{|A(\omega_k)|}\right)^2 \mathrm{var}|A(\omega_k)| \tag{18}$$

We will refer to the right hand side of Eq. (14) as the minimum phase of the system, a term whose physiological impact will be discussed in more detail in Section 5. For now, we only note that for minimum-phase systems the minimum phase is a consistent estimator of arg $A(\omega)$ (Nakano and Tagami, 1988).

One might argue that an ambiguity arises from the fact that the gain spectrum is only defined up to a constant factor, corresponding to a normalizing factor in the output time series. However, this factor does not influence the minimum-phase estimate, as can be seen from Eq. (14) by virtue of the symmetry properties of the cotangent function.

For minimum phase systems, the Hilbert transform thus provides an alternative way of obtaining the phase spectrum. More importantly for systems consisting of the superposition of a minimum phase system and a delay system, the contribution of the minimum phase system to the phase spectrum can be estimated by the Hilbert transform. The precise amount of the delay can be estimated from the difference between the phase spectrum of the minimum phase system (estimated from the Hilbert transform) and the phase spectrum of the compound system (estimated from the argument of the cross-spectrum). To this end, it is important to note that the gain spectrum is independent of the delay. We can thus apply the Hilbert transform to the gain spectrum of the compound system in order to obtain the phase spectrum of the minimum phase system and compare it with the phase spectrum of the compound system calculated from the cross-spectrum. If the system is indeed the superposition of a minimum phase system and a delay system, this difference should follow a straight line, with the slope of the line given by the amount of the delay. Consequently, an estimate of the delay δ can be obtained by maximizing the following expression:

$$\mathrm{obj}(\delta) = \sum_{B} \frac{\hat{\mathrm{Coh}}^2(\omega)}{1 - \hat{\mathrm{Coh}}^2(\omega)} \cos(\hat{\phi}(\omega) - \arg \hat{A}(\omega) - \delta\omega) \tag{19}$$

where Σ_B denotes the sum over all ω in a proper band B of frequencies contained in $[0,\pi]$. This procedure for estimating parameters in $\phi(\omega)$ from discrete stationary time series was proposed by Hamon and Hannan (1974) and was shown to be an approximation of the maximum likelihood method by Hannan (1975) and Knapp and Carter (1976). The definition of the objective function obj(δ) in Eq. (19) is motivated by the need to find a time delay δ such that the deviation of the model given in Eq. (13) from the phase estimates is minimal. Taking the cosine of the deviation resolves the 2π ambiguity of the phase estimate. The assignment of weights proportional to the inverse of the coherency follows from the fact, that the variance of the phase estimates is inversely proportional to the coherency.

3. Simulations

In this section, we will test the Hilbert transform method on minimum-phase model systems with known transfer function and delays. While Nakano and Tagami (1988) showed that the method yields consistent delay estimates in the limit of infinitely long noise-free time series and Boeijinga and da Silva (1989) applied it to low-noise EEG recorded invasively in cat, we here study the performance of the Hilbert transform method in the presence of observational noise. We thereby check the applicability of the Hilbert transform method to experimental neurophysiological time series containing substantial amounts of observational noise.

3.1. The influence of observational noise

We apply the method to a well known model-system, namely an autoregressive process of order 2, short AR(2) process. This system is defined by:

$$y(t) = a_1 y(t-1) + a_2 y(t-2) + x(t-\delta) \quad (20)$$

where $x(t)$ is the input and $y(t)$ is the output of the system and δ is the delay between the input and output. The input $x(t)$ is taken to be Gaussian white noise. It is important to note that while due to stationarity shifting the Gaussian white noise $x(t)$ by a time delay δ does not change its auto-spectrum it still affects the cross-spectrum between $x(t)$ and $y(t)$.

From a physical point of view an AR(2) process can be interpreted as a stochastically driven, damped, resonant, harmonic oscillator with period and relaxation time determined by the parameters a_1 and a_2 (Honerkamp, 1994). Its phase spectrum can be calculated analytically. For ease of comparison with the experimental results, we use a fictitious sampling rate of 500 Hz in the simulations, a realization length of 2^{15} and $a_1 = -1.9691$, $a_2 = 0.9753$, corresponding to both a mean oscillation period T and relaxation time τ of 80 samples. Observational noise was added for a signal-to-noise ratio of 1. We define the signal-to-noise ratio to give the ratio of the variances of the signal and the observational noise. δ was chosen to be ten sampling units, corresponding to a delay time of 20 ms. Fig. 1 shows the result of a simulation of an AR(2) process with the above parameters. In Fig. 1(a), the spectra of the driving white noise (dashed line) and the resulting AR(2) process (solid line) are plotted. In Fig. 1(b), the estimated coherency between the two signals is shown. The coherency is smaller than 1 due to the added observational noise. It is larger in the region with large spectral power of the AR(2) process, as in the case of linearly correlated processes the coherency is a function of the frequency dependent signal-to-noise ratio (Timmer et al., 1998a). Fig. 1(c) displays the gain, exhibiting a maximum at the peak frequency of the oscillator. Here and throughout all the plots in this paper confidence intervals are given for the 95% level. Fig. 1(d) shows the minimum phase, estimated from the gain by the Hilbert transform together with its confidence intervals (solid line with error bars) and the analytically calculated phase curve of an AR(2) process with the given parameters (dashed line). The characteristic shape of the phase curve is well captured by the estimate. Nevertheless for frequencies larger than the resonance frequency, the estimate is significantly smaller than the theoretical value; a point that will be elaborated later. In Fig. 1(e), the phase estimates and their confidence intervals (error bars) are plotted together with the curve

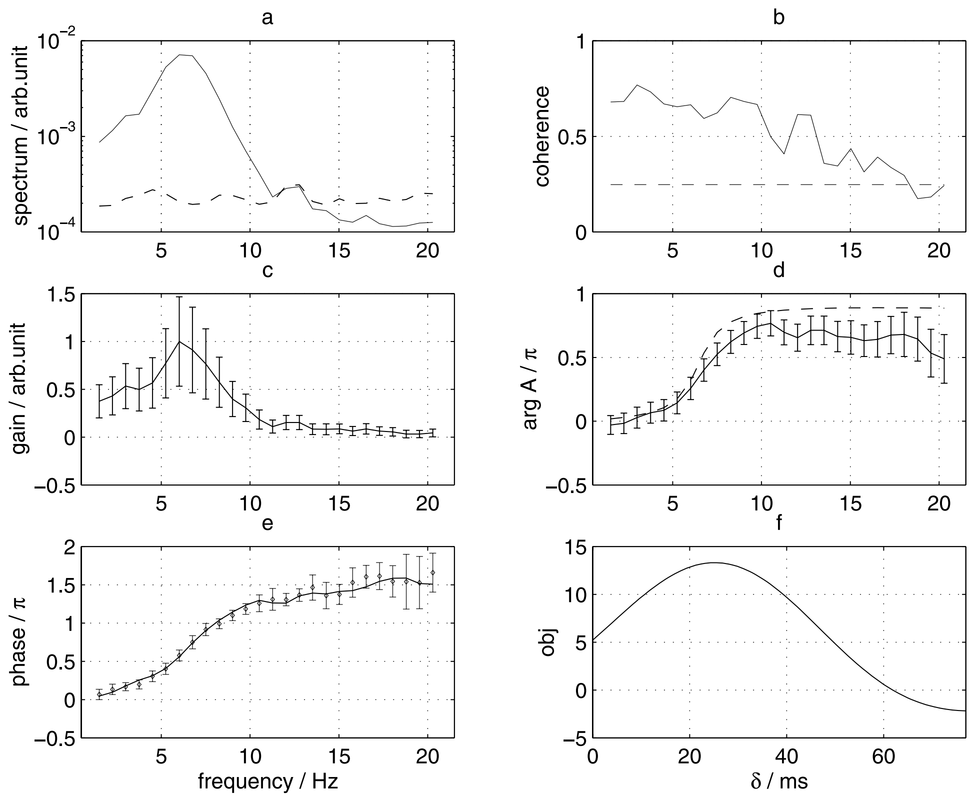

Fig. 1. Results for an AR(2) process with parameters $a_1 = -1.9691$ and $a_2 = 0.9753$ with signal-to-noise-ratio of 1. From top left to bottom right the subplots display: (a) the spectra of the AR(2) process (solid line) and its driving noise (dashed line); (b) the coherency between the two signals (solid line) and the critical value s (dashed line) for the null hypothesis of zero coherency defined in Eq. (11); (c) the gain normalised to a maximum value of 1; (d) the minimum phase estimate with its 95% confidence interval; (e) the estimated phase spectrum between the two signals together with the best fit of the sum of the minimum phase and the delay term identified from the objective function; (f) the objective function obj(δ) defined in Eq. (19).

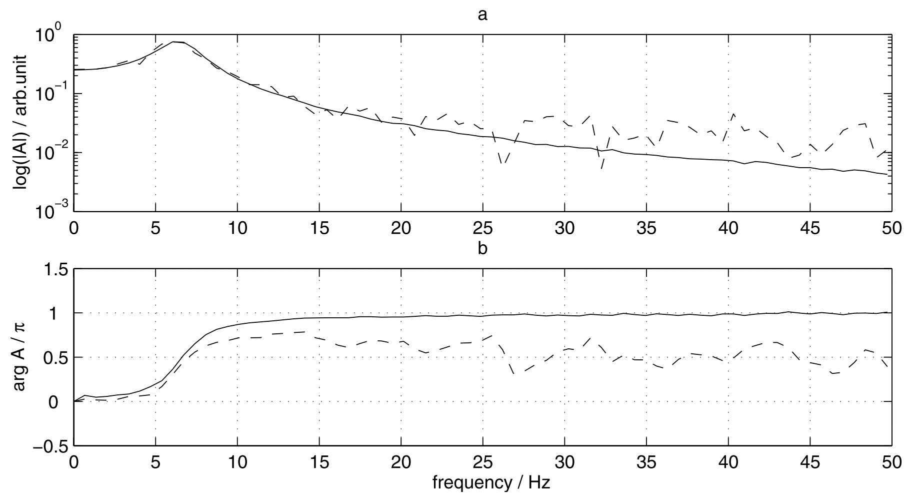

Fig. 2. Comparison of an AR(2) process with $snr = \infty$ (solid curves) with the same process with $snr = 1$ (dashed curves). Displayed are: (a) the estimate for the gain $|A(\omega)|$ (a); (b) the minimum phase arg $A(\omega)$.

calculated from the estimated minimum phase and delay time according to Eq. (13). The model well explains the observed phase curve. In Fig. 1(f), the objective function obj(δ) is displayed, which exhibits a maximum at about 25 ms. Thus, the delay time is overestimated by about 5 ms.

This bias can be understood from Fig. 2 which compares the results of a simulation of the above AR(2) process for the noise-free case (solid lines) with those for a signal-to-noise ratio of 1 (dashed lines). It can be seen from Fig. 2(a) that compared to the noise-free case in the presence of observational noise, the gain $|A(\omega)|$ is overestimated for frequencies greater than 20 Hz. This is due to the fact that for high frequencies the spectrum of the AR(2) process is small compared to the spectrum of the observational noise. The gain thus approaches a constant, given by the frequency-independent gain between the white noise input to the AR(2) process and the white observational noise covering its output (Jenkins and Watts, 1968). This introduces a negative bias into the minimum-phase estimate, as follows from Eq. (15) by taking into account that $C(\omega_l,\omega_k)$ is negative for $\omega_l > \omega_k$. The greater variability of the gain estimate in the presence of observational noise is due to the reduced coherency (Eq. (9)).

In order to quantitatively study this bias, we analyzed realizations of the AR(2) process defined before with varying amounts of observational noise added to the time series. Table 1 summarizes the results from 100 realizations for every noise-level. The variance of the delay estimate is very small, even with low signal quality. The bias increases with decreasing signal-to-noise ratio and it depends more on the SNR of the output than on that of the input. All of this is consistent with the explanation given for the bias above.

We stated that the strong bias in the delay estimates for time series with large observational noise is due to the fact, that for higher frequencies the spectrum of the AR(2) process is small compared to the noise spectrum. This in turn means that the method is more robust against observational noise when applied to processes with a broad band spectrum. We demonstrate this for an AR(2) process with a mean period of oscillation of $T = 80$ samples as before but with a smaller relaxation time of $\tau = 10$ samples resulting in a broader spectrum. The result is given in Table 2 showing that indeed the bias is much smaller than for the previously studied AR(2) process with $\tau = 80$ samples (Table 1).

We note that the bias only depends on the spectral properties of the process. Thus, the results of the simulations apply to a wide range of processes with spectra comparable to the ones of the processes studied here.

We pointed out that in order to decide whether the method can be applied to specific experimental data the signal-to-noise ratio has to be estimated. In practice, it is often impossible to determine the noise level without additional information such as bandlimits for the signal. In these cases, one can use the coherency function to obtain an estimate for the signal-to-noise ratio.

If one time series $Y(t)$ is a linear function of another time series $X(t)$ but the measurements of $Y(t)$ and $X(t)$ are covered by white observational noise of variance σ_x^2 and σ_y^2, the observed resulting coherency is given by Timmer et al., (1998a):

$$\mathrm{Coh}(\omega) = \sqrt{1 - \frac{\sigma_x^2 S_y + S_x \sigma_x^2 + \sigma_x^2 \sigma_y^2}{(S_x + \sigma_x^2)(S_y + \sigma_y^2)}} \qquad (21)$$

where the argument ω was suppressed on the right hand side for ease of notation and σ_x^2 and σ_y^2 denote the constant power spectra of observational noise. Given the coherency, Eq. (21) can in turn be used to identify pairs of SNRs consistent with the observed level of coherency.

3.2. Causality

From the above description of the Hilbert transform method, it follows that in principle the direction of the relationship has to be known in advance. This would severely restrict its domain of applicability. Fortunately, in practice this problem can be resolved by studying both alternative directions and comparing the results. We exemplify this in Fig. 3 on the same AR(2) process data that has been previously analyzed in Fig. 1 but for now we assume the driver to be the response and vice versa. Spectra and coherency displayed in Fig. 3a and b, respectively, are unchanged compared to Fig. 1(a) and (b). The gain spectrum (Fig. 3(c)) is changed as it is now calculated by dividing the unchanged cross-spectrum by the output of the AR(2) process which is incorrectly assumed to be the input. Consequently, the minimum phase shown in Fig. 3(d) is also changed. The objective function Fig. 3(f) displays a maximum at about 55 ms, while the true delay is 20 ms. This estimate can be identified as misleading from Fig. 3(e) displaying the phase estimates and their confidence intervals (error bars) together with the curve calculated from the estimated minimum phase and delay time according to Eq. (13). This fit provides an important check for the validity of the results and allows for the identification of driver and response by comparing the results based on assuming the one and the other direction. This example should also be taken as a word of caution against interpreting any local maximum of the objective function obj(δ) as evidence for an according delay. It is in contrast always necessary to evaluate the goodness of fit of the data to the model using plots like Fig. 3(e).

4. Applications

In this section, we present the application of the Hilbert transform method to concurrently recorded ECoG, EMG and Acc.

As stated in the previous section, we first have to estimate the signal-to-noise ratio of the data. For the accelerometric signal this can be done from the high frequency part of the power spectrum where the signal amplitude is negligible due to the mechanical properties of the hand. This yields an estimate for the SNR in the order of 4 for the Acc time series. From the observed coherency spectrum, we can then infer from Eq. (21) a SNR in the order of 1 for the ECoG time series. As the spectrum of the Acc of the hand in physiologic tremor is similar to that of the AR(2) process with $\tau = 80$ samples, we can obtain an estimate for the bias from Table 1. We find that the bias is in the order of 5 ms rendering the method applicable in this case.

For the EMG and ECoG data, there is no direct way to estimate the SNR for the individual time series. However, we can use the observed coherency spectrum for inference about the SNRs as described above. Given the coherency of about 0.45 over a broad band of frequencies that can be seen from Fig. 4(b) SNRs in the order of 1 can be established from Eq. (21). The spectra of EMG and ECoG are rather flat, such that we can refer to Table 2 for an estimate of the bias, which is in the order of 2 to 3 ms in this case.

4.1. EcoG–Acc relation

We first study the relation between the ECoG and Acc, recorded simultaneously from the dorsum of the hand. The result is shown in Fig. 5. We see from Fig. 5(a) that the hand oscillates at its resonance frequency while the ECoG has a rather flat spectrum over the region of significant coherency (Fig. 5(b)). The gain (Fig. 5(c)) consequently exhibits a maximum at the resonance frequency. The minimum phase displayed in Fig. 5(d) calculated from the gain by the Hilbert trans-

Table 1
Summary of the results obtained for the simulation of an AR(2) process with $T = 80$ and $\tau = 80$ with additive observational noise and a delay time of 20 ms

SNR_{input}	SNR_{output}											
	∞		4		2		1		0.5		0.25	
	$\hat{\delta}$	SD	$\hat{\delta}$	SD	$\hat{\delta}$	SD	$\hat{\delta}$	SD	$\hat{\delta}$	SD	$\hat{\delta}$	SD
∞	20.1	0.0	23.4	0.5	24.4	0.5	25.6	0.7	26.9	0.9	28.9	1.3
4	20.2	0.2	23.9	0.6	25.0	0.8	26.0	0.8	27.6	1.2	29.8	1.5
2	20.2	0.4	24.1	0.6	25.3	0.8	26.7	1.0	28.3	1.1	30.1	1.4
1	20.2	0.4	24.8	0.8	25.9	0.9	27.0	1.2	29.0	1.3	31.2	1.5
0.5	20.2	0.6	25.4	1.2	26.7	1.4	28.2	1.6	30.6	1.5	32.7	2.1
0.25	20.2	1.0	26.3	1.5	27.9	1.4	30.2	2.2	32.3	2.2	35.0	2.6

The realization length was 2^{15}. The following abbreviations are used: $\hat{\delta}$ and SD are the mean and standard deviation of the delay time estimated from 100 realizations, SNR_{input} and SNR_{output} denote the signal-to-noise ratios of the input and output of the AR(2) process, respectively.

Table 2
Summary of the results obtained for the simulation of an AR(2) process with $T = 80$ and $\tau = 10$, additive observational noise and a delay time of 20 ms

SNR_{input}	SNR_{output}											
	∞		4		2		1		0.5		0.25	
	$\hat{\delta}$	SD	$\hat{\delta}$	SD	$\hat{\delta}$	SD	$\hat{\delta}$	SD	$\hat{\delta}$	SD	$\hat{\delta}$	SD
∞	20.0	0.0	20.7	0.2	21.1	0.2	21.6	0.3	22.3	0.4	23.0	0.5
4	20.0	0.2	20.9	0.3	21.3	0.4	21.9	0.4	22.6	0.5	23.4	0.7
2	20.0	0.4	21.0	0.4	21.5	0.4	22.1	0.5	22.8	0.7	23.7	0.8
1	20.0	0.5	21.2	0.6	21.8	0.7	22.3	0.7	23.1	0.9	24.2	1.0
0.5	20.1	0.7	21.5	0.8	22.0	0.8	22.8	1.0	23.4	1.0	24.9	1.2
0.25	20.1	0.9	21.8	1.1	22.6	1.1	23.4	1.2	24.5	1.4	25.7	1.5

The realization length was 2^{15}. The following abbreviations are used: $\hat{\delta}$ and SD are the mean and standard deviation of the delay time estimated from 100 realizations, SNR_{input} and SNR_{output} denote the signal-to-noise ratios of the input and output of the AR(2) process, respectively.

form fits the observed phase spectrum very well (Fig. 5(e)). In Fig. 5(f), a delay of 19 ms can be identified from the objective function.

In a total of eight recordings from one patient and four recordings from the second patient, the delay could be estimated by the Hilbert transform method. The delay estimates are very well reproducible. The delay was (19.3 ± 2.0) and (18.0 ± 3.5) ms, respectively. This is in keeping with a transmission via fast pyramidal pathways. It should be emphasized that a delay estimate cannot be obtained by a straight line fit in this case, as the phase curve obviously exhibits a nonlinear behavior.

One might argue that the phase estimate in Fig. 5(e) has an approximately constant slope from 8 to 14 Hz and does extrapolate back to the origin, just as it would be expected for a system consisting of nothing but a delay between the input and the output. This, however, does not mean that the phase spectrum can be well described by a pure delay model, as this model does not fit the data for frequencies smaller than 8 Hz. If, however, a simple delay model would apply, the phase would follow a straight line over the whole range of significant coherency. On the contrary, Fig. 5(d) clearly show that a pure delay model does not apply to the data, as in this case arg $A(\omega)$ should be identically zero. Furthermore, for a pure delay model to be valid, the spectra of the input and the output signal of the system must be identical. This claim can hardly be made based on Fig. 5(a), although it should be kept in mind that differences in the observed spectra might also be due to colored observational noise.

We recommend not to use the straight line fit method if the phase spectrum does not follow a straight line over the whole frequency range of significant coherency (FRSC). Nevertheless, there are cases in which the phase spectrum follows a straight line only over part of the FRSC and a fit of a straight line over only this part of the FRSC gives a correct delay estimate. Whether this estimate is correct or not can not be judged based on the straight line fit method. However, the Hilbert transform method provides a way of checking this estimate. Only if we find that the minimum phase is constant over the region for which we see a linear increase of the phase spectrum, the slope of the phase spectrum provides a valid estimate of the delay. This is why a straight line fit to the portion from 8 to 14 Hz of the phase spectrum in Fig. 5(e) does not give a correct delay estimate, as clearly the minimum phase shown in Fig. 5(d) is not constant from 8 to 14 Hz.

The transfer function shown in Fig. 5(d) closely resembles the one of an AR(2) process. This is in line with previous studies, showing AR(2) characteristics for the resonant relationship between muscle activity and the corresponding limb acceleration in the physiological situation (Timmer et al., 1998a).

4.2. EcoG–EMG relation

As a second example, we present the results for the relation between concurrently measured ECoG and EMG recorded from the hand muscle extensor carpi ulnaris. In Fig. 4(a), we display the spectra of ECoG and EMG in the region of significant coherency, which can be seen from Fig. 4(b). Both spectra do not exhibit significant peaks rendering the gain function (Fig. 4(c)) rather uninformative. The minimum phase, displayed in Fig. 4(d) shows a monotonous increase with frequency. In Fig. 4(e), the resulting fit to the phase estimates, for a delay time of 21 ms identified from the objective function obj(δ) (Fig. 4(f)), is displayed.

In a total of 12 recordings from one patient and 15 recordings from the second patient, the delay could be estimated by the Hilbert transform method. The delay was (18.0 ± 1.6) and (15.0 ± 3.1) ms, respectively. As for the EcoG–Acc relation the delay estimates are very well reproducible. They are again in accordance with a transmission via fast pyramidal pathways.

It is interesting to compare this finding to the result of the straight line fit method as the approximately linear increase of the phase estimates with frequency suggests that it might be applicable here. Following the argument of Mima and Hallett (1999b), we do not impose the restriction of zero phase at zero frequency a priori but rather fit a straight line taking into account only the observed values for the phase spectrum over the FRSC. The slope of this straight line yields a delay estimate of about 40 ms. This is not only in contradiction to the neurophysiologically reasonable assumption of a conduction via fast pyramidal pathways but also in contradiction to the results derived for the EcoG–Acc relation before. This error can be understood from the minimum phase displayed in Fig. 4(d), which is monotonically increasing with frequency. Consequently, the straight line fit overestimates the delay, as it does not account for this contribution to the phase spectrum.

The phase spectra between the ECoG and the EMG are more variable than for the EcoG–Acc interaction and are therefore more difficult to interpret. While the delay estimates are very well reproducible the shape of the minimum phase component differs considerably from patient to patient and also from recording to recording within the same subject.

5. Discussion

The Hilbert transform method provides a valuable approach to disentangle the effects of a delay and the transfer function on the phase spectrum. As pointed out before there are however a number of assumptions involved in the derivation of the Hilbert transform relations which we want to discuss in more detail here.

The first obvious assumption is the one of linearity. On the one hand, it is well known that the fundamental processes underlying the generation and transmission of cortical signals are nonlinear (Porter and Lemon, 1993). On the other hand, it is important to note that the Hilbert transform method does not rely on the linearity of the processes but rather on the linearity of the relation between them. The large coherency observed between the signals shows that under the given recording conditions the relation between the processes is to a good approximation described by a linear filter. Thus, the Hilbert transform seems to be applicable with respect to the assumption of linearity.

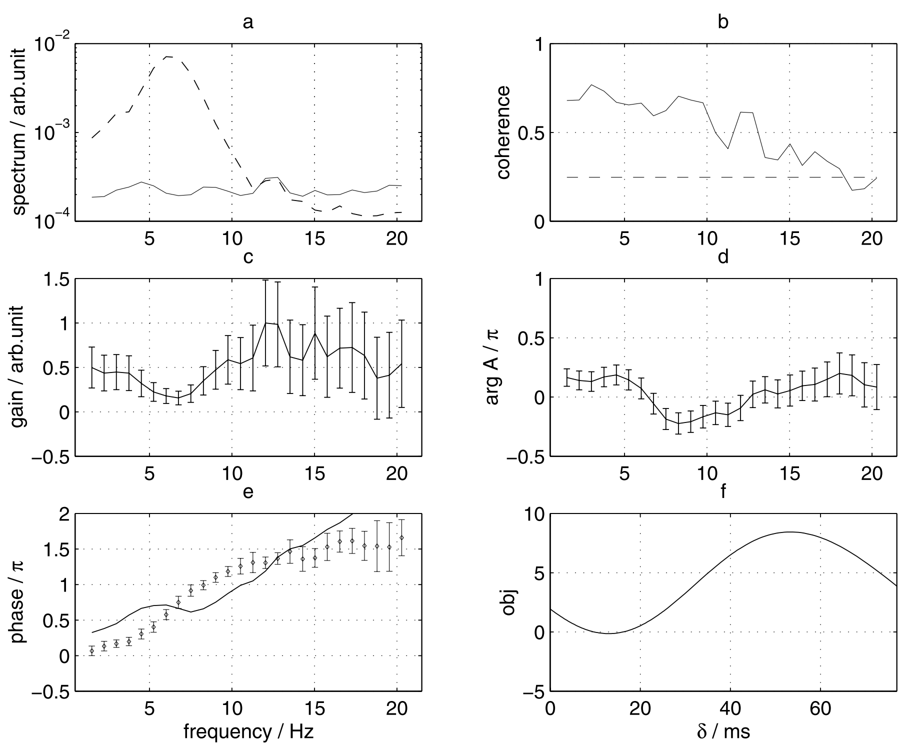

Fig. 3. Results for an AR(2) process with parameters $a_1 = -1.9691$ and $a_2 = 0.9753$ with signal-to-noise-ratio of 1 assuming the wrong driver-response relationship. From top left to bottom right, the subplots display: (a) the spectra of the AR(2) process (dashed line) and its driving noise (solid line); (b) the coherency between the two signals (solid line) and the critical value s (dashed line) for the null hypothesis of zero coherency defined in Eq. (11); (c) the gain normalised to a maximum value of 1; (d) the minimum phase estimate with its 95% confidence interval; (e) the estimated phase spectrum between the two signals together with the best fit of the sum of the minimum phase and the delay term identified from the objective function; (f) the objective function obj(δ) defined in Eq. (19).

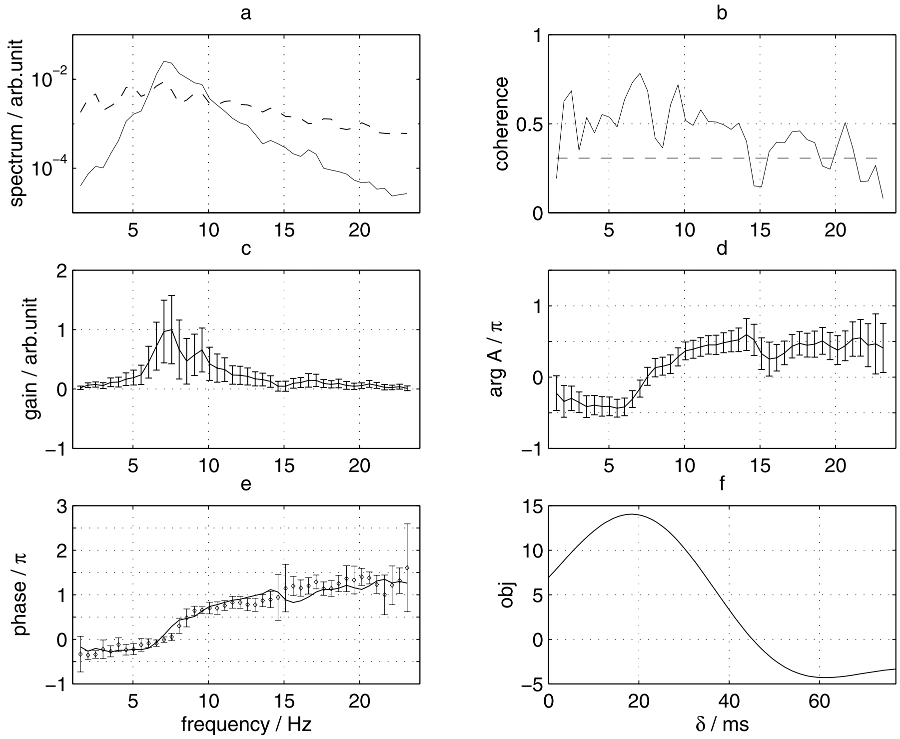

Fig. 4. Results for the EcoG–Acc relation. Displayed are from top left to bottom right: (a) the spectra of the ECoG (dashed line) and accelerometric signal (solid line); (b) the coherency between the two signals (solid line) and the critical value s (dashed line) for the null hypothesis of zero coherency defined in Eq. (11); (c) the gain normalised to a maximum value of 1; (d) the minimum phase estimate with its 95% confidence interval; (e) the estimated phase spectrum between the two signals together with the best fit of the sum of the minimum phase and the delay term identified from the objective function; (f) the objective function obj(δ) defined in Eq. (19).

Furthermore, the method theoretically rests on the assumption of causality or, in other words, prior knowledge about the direction of interaction. We have pointed out how this information can be obtained a posteriori by comparing the results for both alternative directions.

The assumption of minimum-phase behavior has to be motivated carefully, as has been pointed out by Victor (1989). It is well known that any linear system can be decomposed into a sequence of up to three filters: a time shift filter, a minimum-phase filter and an allpass filter. The Hilbert transform relation given in Eq. (14) applies only to minimum-phase filters. The Hilbert transform method employs the difference in the phase spectrum of a minimum-phase system and the composition of a minimum-phase system and a time shift filter, in order to estimate the delay introduced by the time shift filter. A violation of the minimum-phase assumption is therefore tantamount to including an allpass filter into the system. The properties of allpass systems thus allow us to study the error made in the application of the Hilbert transform method to a non-minimum-phase system. An allpass system has unit amplitude response. While its phase response is not uniquely determined by this condition two important characteristics are guaranteed. Firstly, the group delay, defined as the first derivative of the phase with respect to frequency, is positive for all frequencies. And secondly, it is not constant, thus the phase does not increase linearly with frequency.

The second characteristic implies that in principle non-minimum-phase systems can be identified by the fact that the model underlying Eq. (19) does not fit the data. Consider a system consisting of the composition of a minimum-phase system and an allpass. As an allpass has unit gain, it does not influence the minimum phase arg $A(\omega)$ of the system. However, it adds a component to the phase spectrum of the system that is not increasing linearly with frequency. So while for the system consisting only of a time shift and a minimum-phase filter a δ can be found in Eq. (19) such that the sum of $\delta\omega$ and arg $A(\omega)$ fits the observed phase spectrum, this is not possible if the systems contains an allpass component. It is thus important to note that although the application of the Hilbert transform is based on the assumption that no allpass component is contained in the system, this assumption can be confirmed a posteriori by the fact that the sum of the minimum phase system and the delay component describes the observed phase spectrum well. In practice, however, this model fit might be hard to infer based on bandlimited data, because only the region of significant coherency can be used to test the model. Nevertheless, the very good fit of the model to the experimental data

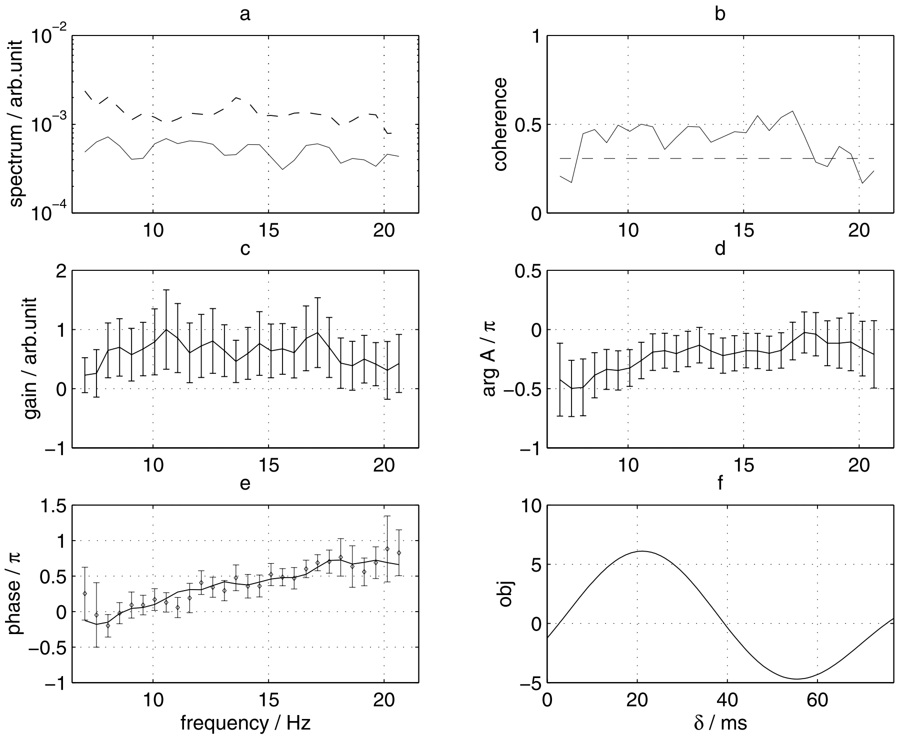

Fig. 5. Results for the EcoG–EMG relation. Displayed are from top left to bottom right: (a) the spectra of the ECoG (dashed line) and EMG (solid fine) signal; (b) the coherency between the two signals (solid line) and the critical value s (dashed line) for the null hypothesis of zero coherency defined in Eq. (11); (c) the gain normalised to a maximum value of 1; (d) the minimum phase estimate with its 95% confidence interval; (e) the estimated phase spectrum between the two signals together with the best fit of the sum of the minimum phase and the delay term identified from the objective function; (f) the objective function obj(δ) defined in Eq. (19).

in Fig. 5(d) and Fig. 4(d) provides an indication that the minimum-phase assumption is valid for our data.

The fact that allpass systems have a positive group delay is very important for the interpretation of the delay estimates obtained by the Hilbert transform method. We first note that this property of allpass systems is the motivation for the term minimum phase. As stated before, given a particular gain spectrum, the conditions of linearity and causality do not determine the phase spectrum uniquely, but there are rather infinitely many phase spectra consistent with every given gain spectrum. Out of these phase spectra, it is the one with the smallest group delay that is linked to the gain spectrum by the Hilbert transform. This implies that for non-minimum-phase systems, the delay calculated by the Hilbert transform method provides an upper bound for the true delay time. Combining the results on the delay time for the EcoG–EMG and the EcoG–Acc relation compiled in Table 3 we can thus establish an upper bound of about 20 ms for the delay time between cortex and periphery. This upper bound is sufficient to infer that the transmission has to be via fast oligosynaptic pyramidal pathways, pathways that are well understood in terms of neurobiology. Their constituents, namely the transmission via nerve fibres, the integration on the spinal motoneuronal level and the electromechanical coupling in the periphery do not only transmit the cortical signal hardwired but also change it in a dynamical manner (Kandel et al., 1991). They mostly have lowpass characteristics in terms of signal processing. Lowpass filters are minimum phase, as well as any serial combination of minimum-phase systems. We thus have strong neurophysiological evidence that the system under study exhibits minimum-phase behavior to a good degree of approximation and the delays can indeed be estimated correctly except for the positive bias introduced by observational noise.

We have pointed out and explained a positive bias introduced into the delay estimates by observational noise. We demonstrated that the bias depends both on the amount of noise and on the spectrum of the process. The bias is worst for narrow-band signals, which consequently have to be measured with little noise in

Table 3
Summary of mean and standard deviations of the delay estimates between concurrently recorded ECoG and peripheral EMG and Acc given in milliseconds

Patient #	EcoG–EMG		ECoG–Acc	
	Mean	SD	Mean	SD
1	18.0	1.6	19.3	2.0
2	15.0	3.1	18.0	3.5

order to render the Hilbert transform method applicable. We exemplified how the applicability of the method can be checked on model systems and presented a successful application to relations between ECoG and EMG and between ECoG and Acc.

So far, we have discussed separately the problems originating from a violation of the minimum-phase assumption on the one hand and from observational noise on the other hand. We note however that from a theoretical point of view observational noise just corresponds to a special case of non-minimum-phase systems. The observational noise contributes an additive component to the gain spectrum, while changing only the confidence intervals of the phase spectrum but not the phase spectrum itself. Although the minimum-phase estimate is invariant under a multiplication of the gain by a constant factor it is changed by adding a constant to the gain and it is thus not a consistent estimator of the phase spectrum of a minimum-phase system with additive observational noise.

We pointed out that a prerequisite for the commonly used straight line fit method of delay estimation is the assumption of a hardwired transmission that is the peripheral signal being a mere time delayed version of the cortical activity. This is an obvious oversimplification of the biological situation and explains the superiority of the Hilbert transform method as shown in the examples of the present paper.

The delay between ECoG and Acc should consist of two contributions, the delay between ECoG and EMG plus the one between EMG and Acc. So as a check for consistency of the results, we also estimated the delay between EMG and Acc and found it to be (2.6 ± 2.9) ms. This is in keeping with the results for the EcoG–EMG and EcoG–Acc delay reported in Table 3. It is also in line with our previous studies (Timmer et al., 1998a,b) in which we found no delay between EMG and Acc. We however note that there are other studies in which the delay between EMG and Acc was estimated to be in excess of 10 ms (Halliday et al., 1995; Wessberg and Vallbo, 1996; McAuley et al., 1997). All of these studies are based on the straight line fit method, which might be the reason for the discrepancy with our results. Further studies are needed in order to resolve this issue.

The phase spectra of the EcoG–Acc relation indicate that the dynamics of this system are well described by a second order linear stochastic oscillator like an AR(2) system. However, the phase spectra of the EcoG–muscle interaction are more variable and therefore more difficult to interpret. The shape of the minimum phase component differs considerably from patient to patient and also from recording to recording within the same subject. It is well recognized that the corticospinal system is extremely dynamic and flexible with regard to the relationship between corticospinal cellular discharge and muscular contraction (Porter and Lemon, 1993). The diversity of the results in previous studies on the timing relations of corticomuscular interaction ranging from zero-delay corticomuscular synchronization to delays compatible with corticospinal transmission (Conway et al., 1995; Halliday et al., 1998; Brown et al., 1998, 1999; Salenius et al., 1997) has already been attributed to these dynamics by Farmer (1998). It seems very likely that this is the basis for at least part of the varying shapes of the phase spectra in the present study. Therefore, these spectra cannot be interpreted in terms of a single biological mechanism. Nevertheless, it is the great advantage of the Hilbert transform method that it allows to understand a part of it, that is the pure delay, without assuming a full parametric model for the system, like for example AR(2).

A problem that should be mentioned is that of an unmeasured confounder, namely a common input to both the central and the peripheral signal. As in this case, there is no direct connection between the measured variables, any technique of delay estimation must fail. In general, the estimated delay time between cortex and periphery will typically be the difference between the delay times from the unmeasured confounder to the cortex and the periphery. This is not a problem specific to delay estimation but it is inherent to any bivariate time series analysis and can only be resolved by measuring the confounder and using multivariate techniques of time series analysis such as graphical models (Dahlhaus et al., 1997; Dahlhaus, 2000).

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