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Identification of patterns of neuronal connectivity—partial spectra, partial coherence, and neuronal interactions

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Abstract

The cross-correlation histogram has provided the primary tool for inferring the structure of common inputs to pairs of neurones. While this technique has produced useful results it not clear how it may be extended to complex networks. In this report we introduce a linear model for point process systems. The finite Fourier transform of this model leads to a regression type analysis of the relations between spike trains. An advantage of this approach is that the full range of techniques for multivariate regression analyses becomes available for spike train analysis. The two main parameters used for the identification of neural networks are the coherence and partial coherences. The coherence defines a bounded measure of association between two spike trains and plays the role of a squared correlation coefficient defined at each frequency λ. The partial coherences, analogous to the partial correlations of multiple regression analysis, allow an assessment of how any number of putative input processes may influence the relation between any two output processes. In many cases analytic solutions may be found for coherences and partial coherences for simple neural networks, and in combination with simulations may be used to test hypotheses concerning proposed networks inferred from spike train analyses.

Keywords: Finite Fourier transform; Neural networks; Linear Models; Point Process Systems; Coherence; Partial Coherence

1. Introduction

The cross-correlation histogram computed from pairs of spike trains and various time domain measures derived from it have been used as the basis for inferring the parameters of underlying postsynaptic potentials as well as the patterns of neuronal connections. Moore et al. (1970) set out rules for making inferences about the structural relations between the observed neurones, and about neurones whose discharges are not directly observed. Moore et al. (1970) introduced the terms primary and secondary effects to describe the structure of the cross-correlation histogram. The primary effect is the peak or trough near the origin, shifted by a variable time u according to conduction delays, and thought to reflect the amplitude and form of the synaptic potentials involved. Kirkwood (1979) extended the analysis of the primary peak by proposing a model that related the parameters characterising the excitatory synaptic potential to the shape of the primary peak. This model has been widely applied. For example, Cope et al. (1987) studied the relation between single-fibre e.p.s.p.s from Ia-axons on to motoneurones determined by spike triggered averaging and the cross-correlation histogram between the same afferent and the motoneurone spikes; Bremner et al. (1991) applied the Kirkwood model to estimate e.p.s.p. parameters associated with common inputs to finger muscles in man. (see Cope et al. (1987)) for further discussion and additional references).

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Secondary effects, which occur further from the origin, often in the form of periodicities, are thought to be due to the temporal structure of both pre- and post-synaptic spike trains. Moore et al. (1970) suggested that the structure of the secondary effects in the cross-correlation histogram, together with the form of the auto-correlation histograms, could form the basis for inferring patterns of connectivity between neurones. For example, in the particular case that the secondary effect appears as a periodic component different from that of each neurone alone, then the most likely interpretation is that the observed cells share a common periodic input (Moore et al., 1970). In the general case, however, the contribution of the discharge patterns of the observed cells to the cross-correlation histogram may result in a complex, and not easily interpretable cross-correlation histogram (Moore et al., 1970; Perkel, 1970). Perkel (1970) suggested, however, that the several effects contributing to this histogram may be most readily separated through the techniques of spectral analysis.

In this report we illustrate how Fourier methods can extend the traditional time domain analyses of neuronal interactions. The cross-correlation histogram may be thought of as an estimate of the correlation between spikes in one spike train displaced in time with respect to those in a second spike train (Rosenberg et al., 1989). One could equally well consider measures of association between some function of the spike train, for example, its Fourier transform. This approach leads to frequency domain measures of association between spike trains (Rosenberg et al., 1989). One particular measure of association, analogous to the correlation squared, called the coherence has been used to infer the frequency content of common inputs first identified through the cross-correlation histogram (Farmer et al., 1993). Their study related the dominant periodicity of the secondary effect observed in the correlation to one of the components of the coherence. By examining the coherence in stroke patients compared with a subject with large afferent fibre neuropathy, Farmer et al. (1993) inferred that this periodic component was of a descending as opposed to a peripheral origin. In the present report we set out the theoretical framework showing explicitly how the coherence between pairs of neurones may reflect the structure of a single common input, and how this framework may be extended to detect the presence of several common inputs.

The analysis depends on the properties of the finite Fourier transform and linear models that incorporate this transform, and consequently may be seen as simple extensions of well established multiple regression and multivariate analyses techniques. The application of these techniques considerably extends the range of tools available for the description and analysis of neuronal interactions. To facilitate access to the original statistical literature an attempt has been made to follow the terminology and notation for point process parameters and time series analysis used in this literature (e.g., Brillinger, 1975a, 1981, 1983; Cox and Isham, 1980; Cox and Lewis, 1972). Since there are important and subtle mathematical differences between the representation of point processes and the usual signals that occur in the analyses of many dynamical systems we have tried to set down precise definitions and assumptions for these parameters. An understanding of these assumptions and the limits to the analyses of neuronal interactions imposed by them should be helpful in the applications of the techniques presented in this paper.

2. Stochastic point process parameters

2.1. Notation

The recorded spike trains are denoted by $N_1(t)$, $N_2(t)$,..., indicating the number of events (spikes) in an interval from zero to time t. To indicate the number of events in a small interval $\mathrm{d}t$ the notation $\mathrm{d}N(t)$ is used, and defined as $\mathrm{d}N(t) = N(t + \mathrm{d}t) - N(t)$. For $\mathrm{d}t$ sufficiently small $\mathrm{d}N(t)$ will take on the value zero or one depending on whether or not an event has occurred in the interval $\mathrm{d}t$. When a parameter is introduced its name will be displayed in italics. If $f(\lambda)$ is a parameter, then $\hat{f}(\lambda)$ denotes an estimate of this parameter. The semi-open interval of real numbers t satisfying the relation $a < t \leq b$ is denoted by $(a, b]$. If $\mathbf{Z}$ is a complex number, its magnitude squared is denoted by $|\mathbf{Z}|^2$. $E\{\cdot\}$ denotes the averaging operator or mathematical expectation of a random variable and $E\{X|Y\}$ conditional expectation of the random variable X with respect to Y. $\delta(u)$ denotes the Dirac delta function where

$$\int_{-\infty}^{+\infty} \delta(u - u_0) f(u)\, \mathrm{d}u = f(u_0).$$

$X(t)$ denotes a zero mean time series with sampled values denoted by x_t for $t = 0,..., T - 1$ for a record of duration T.

2.2. Assumptions

The recorded spikes are assumed to be realizations of stochastic point processes with the following properties: (a) that events of the process $N(t)$ do not occur simultaneously, i.e., the process is orderly allowing an interpretation of point process parameters either as expected values or probabilities. (b) the parameters characterizing the process do not change with time (the process is stationary), (c) the number of events occurring in intervals widely separated in time are independent (the process is mixing). These assumptions are discussed in

Brillinger (1972), Cox and Lewis (1972), Daley and Vere-Jones (1988) in general, and in Conway et al. (1993), Halliday et al. (1995) in the context of spike train analysis.

2.3. Stochastic point process parameters

Before discussing the problem of identification of patterns of neuronal connectivity we introduce certain parameters that characterise stochastic point processes. Each of the parameters defined may be estimated consistently as $T \to \infty$, and estimation procedures are considered in detail in Brillinger (1975b), Conway et al. (1993), Halliday et al. (1995), Rosenberg et al. (1989).

Let (M, N) represent a bivariate point process. The mean intensity of process N is defined as

$$P_N = \lim_{h \to 0} \mathrm{Prob}\{N \text{ event in } (t, t+h]\}/h \qquad (1)$$

and since the process is orderly may be interpreted as

$$E\{\mathrm{d}N(t)\} = P_N \,\mathrm{d}t \qquad (2)$$

The *second-order cross product density* at lag u, $P_{NM}(u)$, is defined as

$$P_{NM}(u) = \lim_{h,h' \to 0} \mathrm{Prob}\{N \text{ event in } (t+u, t+u+h] \text{ and } M \text{ event in } (t, t+h']\}/hh' \qquad (3)$$

and may be interpreted through the relation

$$E\{\mathrm{d}N(t+u)\,\mathrm{d}M(t)\} = P_{NM}(u)\,\mathrm{d}u\,\mathrm{d}t \qquad (4)$$

A *conditional mean intensity*, $m_{NM}(u)$, is defined as

$$m_{NM}(u) = \frac{P_{NM}(u)}{P_M} \qquad (5)$$

and interpreted as

$$m_{NM}(u) = \lim_{h \to 0} \mathrm{Prob}\{N \text{ event in } (t+u, t+u+h] \text{ given an } M \text{ event at } t\}/h \qquad (6)$$

or in terms of a conditional expectation as

$$E\{\mathrm{d}N(t+u) | M \text{ event at time } t\} = \frac{P_{NM}(u)}{P_M} \qquad (7)$$

In the case that $u \neq 0$ the product density Eq. (3) and the conditional intensity Eq. (6) may be obtained for each process alone by setting M equal to N. The value of $P_{NN}(u)$ at $u = 0$ is defined to make the function continuous at this point.

Under the assumption of mixing ((c)), as u becomes large, increments of the process become independent, so that

$$\lim_{|u| \to \infty} P_{NM}(u) = P_N P_M \qquad (8)$$

This phenomenon leads to the definition of a *cross-covariance*, *cross-intensity or cumulant density*, $q_{NM}(u)$, as

$$q_{NM}(u) = P_{NM}(u) - P_N P_M \quad u \neq 0 \qquad (9)$$

which tends to zero as $|u| \to \infty$. $q_{NM}(u)$ may also be interpreted through

$$\mathrm{cov}\{\mathrm{d}N(t+u), \mathrm{d}M(t)\} = q_{NM}(u)\,\mathrm{d}u\,\mathrm{d}t \qquad (10)$$

where 'cov' denotes covariance. In the case of the individual processes, however, one must write

$$\mathrm{cov}\{\mathrm{d}N(t+u), \mathrm{d}N(t)\} = (\delta(u)P_N + q_{NN}(u))\,\mathrm{d}u\,\mathrm{d}t \qquad (11)$$

Following Bartlett (1963) the *cross-spectrum*, $f_{NM}(\lambda)$, between process M and N may be defined as the Fourier transform of the cross-covariance density Eq. (10) as

$$f_{NM}(\lambda) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} \mathrm{e}^{-i\lambda u} \frac{\mathrm{cov}\{\mathrm{d}N(t+u), \mathrm{d}M(t)\}}{\mathrm{d}t} \qquad (12)$$

and the *auto-spectrum*, $f_{NN}(\lambda)$, as the Fourier transform of the auto-covariance density Eq. (11) as

$$f_{NN}(\lambda) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} \mathrm{e}^{-i\lambda u} \frac{\mathrm{cov}\{\mathrm{d}N(t+u), \mathrm{d}N(t)\}}{\mathrm{d}t} \qquad (13)$$

with a similar expression for $f_{MM}(\lambda)$. Expressions Eqs. (12) and (13) are referred to as cumulant spectra (Brillinger, 1972). Point process spectra differ from spectra associated with ordinary time series (Lewis, 1972). In the point process case as $\lambda \to \infty$ $f_{NN}(\lambda) = P_N/2\pi$, whereas in the time series case the value of the limiting value of the spectrum is zero. The spectrum of a Poisson process is also equal to $P_N/2\pi$. Thus, point process spectra will fluctuate about a value proportional to that for a Poisson process of the same mean rate as the spike train. Corresponding to Eqs. (12) and (13) are the inverse transforms giving the second-order cumulants

$$q_{NM}(u) = \int f_{NM}(\lambda)\,\mathrm{e}^{i\lambda u}\,\mathrm{d}\lambda$$

$$q_{NN}(u) = \int \left\{ f_{NN}(\lambda) - \frac{P_N}{2\pi} \right\} \mathrm{e}^{i\lambda u}\,\mathrm{d}\lambda \qquad (14)$$

The cumulants may be estimated either directly from the cross-correlation histogram or as the inverse Fourier transform of the cross-spectrum (Halliday et al., 1995).

3. The finite fourier transform and linear models for neuronal interactions

Our approach to the identification of patterns of neuronal connectivity will depend on the use of linear models for the interactions between spike trains. These models will be based on the finite Fourier transforms of the observed processes. The extension of this approach to hybrids of point processes and time series processes is set out in Halliday et al. (1995). The finite Fourier transform has proved to be of substantial use in the analysis of random processes assumed to satisfy these models. We will show that models based on it can play an important role in the analysis of neuronal interactions.

The finite Fourier transform of the point process, spike train, $N(T)$, denoted $d_N^T(\lambda)$, is defined as

$$d_N^T(\lambda) = \int_0^T e^{-i\lambda t}\, dN(t) = \sum_j e^{-i\lambda \tau_j} \tag{15}$$

where the τ_j are the times of occurrence of the spikes from process $N(T)$. The central limit theorems given in Brillinger (1983) suggest that the auto- and cross spectra of the point processes $N(T)$ and $M(T)$, may be estimated, respectively, as

$$\hat{f}_{NN}(\lambda) = \frac{1}{2\pi LT} \sum_{l=1}^{L} d_N^T(\lambda, l)\, \overline{d_N^T(\lambda, l)}$$

$$\hat{f}_{NM}(\lambda) = \frac{1}{2\pi LT} \sum_{l=1}^{L} d_N^T(\lambda, l)\, \overline{d_M^T(\lambda, l)} \tag{16}$$

where the spike train records are divided into L disjoint sections each of duration T, and $d_N^T(\lambda, l)$ represents the finite Fourier transform of the lth section. (see Halliday et al. (1995), Rosenberg et al. (1989); for applications of this procedure to spike trains and hybrids of spike trains and continuous processes). The definitions of spectra given by expressions Eqs. (12) and (13) and those in Eq. (16) are asymptotically equivalent.

The linear point process model and its frequency domain representation via the finite Fourier transform may be developed as follows. Suppose that $M(t)$ is a point process input to and $N(t)$ the point process response of a linear time invariant point process system. Following Brillinger (1975a) we set down a series of models for the relation

$$\begin{aligned}\mu_1(t) &= \lim_{h\to 0} \text{Prob}\{N \text{ event in } (t, t+h] | M\}/h \\ &= E\{dN(t)|M\}/dt\end{aligned} \tag{17}$$

corresponding to a sequence of input processes. In the absence of any input, $M \equiv 0$, μ_1 exists and is equal to a constant

$$\mu_1(t) = \alpha_0 \tag{18}$$

where α_0 is interpreted as the rate of the output process N in the absence of an input process M, i.e., α_0 represents the rate of the spontaneous activity of the point process system modelled by Eq. (17). Now, if the input to the system corresponds to a single event at time u, then $\mu_1(t)$ would become

$$\mu_1(t) = \alpha_0 + \alpha_1(t-u) \tag{19}$$

where $\alpha_1(t-u)$ represents the effect on the output process of the single event that occurred at time u. Similarly, if a number of events occurred at times $u_1, u_2, \ldots, u_k$, and there were no interactions between the effects of these inputs, then expression Eq. (19) would become

$$\mu_1(t) = \alpha_0 + \alpha_1(t-u_1) + \alpha_1(t-u_2) + \cdots + \alpha_1(t-u_k) \tag{20}$$

or, written in more compact notation as

$$\mu_1(t) = \alpha_0 + \int \alpha_1(t-u)\, dM(u) \tag{21}$$

to give the linear model

$$E\{dN(t)|M\} = \left[\alpha_0 + \int \alpha_1(t-u)\, dM(u)\right] dt \tag{22}$$

$\alpha_1(u)$, by analogy with the terminology used for linear systems operating on continuous process, may be called the *average impulse response* (see, Brillinger (1975a)), and its Fourier transform

$$A(\lambda) = \int \alpha_1(u)\, e^{-i\lambda u}\, du \tag{23}$$

the transfer function of the system.

If $N(t)$ and $M(t)$ are observed over the interval $0 < t < T$, and are assumed to satisfy the model

$$dN(t) = \left[\alpha_0 + \int \alpha_1(t-u)\, dM(u)\right] dt + \varepsilon(t) \tag{24}$$

where $\varepsilon(t)$ is a zero mean process satisfying the assumptions of stationarity and mixing, then, following Brillinger (1983), the Fourier transform of Eq. (24) becomes

$$d_N^T\left(\frac{2\pi s}{T}\right) \approx A(\lambda)\, d_M^T\left(\frac{2\pi s}{T}\right) + d_s^T\left(\frac{2\pi s}{T}\right) \tag{25}$$

for $2\pi s/T$ near λ, with $s = 0, \ldots, T-1$, and where

$$A(\lambda) = \int a(u)\, e^{-i\lambda u}\, du \quad \text{and} \quad d_s^T\left(\frac{2\pi s}{T}\right)$$

the Fourier transform of the error process $\varepsilon(t)$. Expression Eq. (24) represented as

$$y_k = a x_k + \varepsilon_k \tag{26}$$

where k indexes distinct frequencies near λ suggests a relation between the frequency domain representation of the single input single output linear point process model and the standard simple linear regression model. This relation further suggests that the full range of regression techniques is available for the analysis of interactions between spike trains in the frequency domain.

The analogy with regression techniques may be made explicit. The solution to Eq. (22) leads to the following relations

$$\alpha_0 = P_{\mathrm{N}} - \int \alpha_1(u)\,\mathrm{d}u$$

$$q_{\mathrm{NM}}(u) = P_{\mathrm{N}}\alpha_1(u) + \int \alpha_1(u-v)q_{\mathrm{MM}}(v)\,\mathrm{d}v \tag{27}$$

The Fourier transform of the second expression in Eq. (27) can be shown to be

$$f_{\mathrm{NM}}(\lambda) = A(\lambda)f_{\mathrm{MM}}(\lambda) \tag{28}$$

indicating that $A(\lambda)$ may be estimated from the auto- and cross-spectra of the observed processes N and M. From the central limit theorems for finite Fourier transforms set out in Brillinger (1983) the cross-spectrum and auto-spectrum can be thought of as covariance and variance parameters, respectively. Their ratio, the transfer function, consequently may be thought of as analogous to a regression coefficient evaluated at each frequency λ.

The analogy may be pursued further using the relation

$$d_\varepsilon(t) = \mathrm{d}N(t) - \left[\alpha_0 + \int \alpha_1(t-u)\,\mathrm{d}M(u)\,\mathrm{d}t\right] \tag{29}$$

where $d_\varepsilon(t)$ represents an error process with stationary increments. The spectrum of the error process, $f_{\varepsilon\varepsilon}(\lambda)$, can be shown to be

$$f_{\varepsilon\varepsilon}(\lambda) = f_{\mathrm{NN}}(\lambda)[1 - |R_{\mathrm{NM}}(\lambda)|^2] \tag{30}$$

where

$$|R_{\mathrm{NM}}(\lambda)|^2 = \frac{|f_{\mathrm{NM}}(\lambda)|^2}{f_{\mathrm{NN}}(\lambda)f_{\mathrm{MM}}(\lambda)} \tag{31}$$

The value of the error spectrum depends on the value of the ratio of the magnitude squared of the cross-spectrum between the input and output processes to the product of their spectra. The closer this ratio is to one the smaller the error. This ratio is called the coherence, is denoted by $|R_{\mathrm{NM}}(\lambda)|^2$, and provides a measure of the degree of linear predictability of process N from process M. The coherence has the same form as the square of the correlation coefficient, takes on values between zero and one, and plays the role of the squared correlation coefficient defined at each frequency λ.

4. Frequency domain measures of association for vector valued processes

The development of the linear point process model extends directly to the general case of vector valued processes. Let $\{\underline{N}(t), \underline{M}(t)\}$ represent an $(s+r)$ real valued stationary point process. The model Eq. (24) extends directly to a multivariate linear model relating $\underline{N}(t)$ to $\underline{M}(t)$ as

$$d\underline{N}(t) = \left\{\alpha_{\underline{\mathrm{N}}} + \int \alpha_{\underline{\mathrm{NM}}}(t-u)\,\mathrm{d}\underline{M}(u)\right\}\mathrm{d}t + d_\varepsilon(t) \tag{32}$$

where

$$d\underline{N}(t) = \begin{bmatrix} \mathrm{d}N_1(t) \\ \mathrm{d}N_2(t) \\ \vdots \\ \mathrm{d}N_s(t) \end{bmatrix}, \qquad \alpha_{\underline{\mathrm{N}}} = \begin{bmatrix} \alpha_{\mathrm{N}_1} \\ \alpha_{\mathrm{N}_2} \\ \vdots \\ \alpha_{\mathrm{N}_s} \end{bmatrix},$$

$$d\underline{M}(u) = \begin{bmatrix} \mathrm{d}M_1(u) \\ \mathrm{d}M_2(u) \\ \vdots \\ \mathrm{d}M_r(u) \end{bmatrix}, \qquad d_\varepsilon(t) = \begin{bmatrix} \mathrm{d}\varepsilon_1(t) \\ \mathrm{d}\varepsilon_2(t) \\ \vdots \\ \mathrm{d}\varepsilon_s(t) \end{bmatrix} \tag{33}$$

and

$$\alpha_{\underline{\mathrm{NM}}}(u) = \begin{bmatrix} \alpha_{\mathrm{N_1M_1}}u & \alpha_{\mathrm{N_1M_2}}(u) & \cdots & \alpha_{\mathrm{N_1M_r}}(u) \\ \alpha_{\mathrm{N_2M_1}}(u) & \alpha_{\mathrm{N_2M_2}}(u) & \cdots & \alpha_{\mathrm{N_2M_r}}(u) \\ \vdots & \vdots & \vdots\vdots\vdots & \vdots \\ \alpha_{\mathrm{N_sM_1}}(u) & \alpha_{\mathrm{N_sM_2}}(u) & \cdots & \alpha_{\mathrm{N_sM_r}}(u) \end{bmatrix} \tag{34}$$

In the multivariate case the finite Fourier transform of the linear model becomes

$$\mathrm{d}_{\underline{\mathrm{N}}}^{\mathrm{T}}\left(\frac{2\pi k}{T}\right) \approx A_{\underline{\mathrm{NM}}}(\lambda)\,\mathrm{d}_{\underline{\mathrm{M}}}^{\mathrm{T}}\left(\frac{2\pi k}{T}\right) + d_{\underline{\varepsilon}}^{\mathrm{T}}\left(\frac{2\pi k}{T}\right) \tag{35}$$

where

$$A_{\underline{\mathrm{NM}}}(\lambda) = \begin{bmatrix} A_{\mathrm{N_1M_1}}(\lambda) & A_{\mathrm{N_1M_2}}(\lambda) & \cdots & A_{\mathrm{N_1M_r}}(\lambda) \\ A_{\mathrm{N_2M_1}}(\lambda) & A_{\mathrm{N_2M_2}}(\lambda) & \cdots & A_{\mathrm{N_2M_r}}(\lambda) \\ \vdots & & & \vdots \\ A_{\mathrm{N_sM_1}}(\lambda) & A_{\mathrm{N_sM_2}}(\lambda) & \cdots & A_{\mathrm{N_sM_r}}(\lambda) \end{bmatrix} \tag{36}$$

is the $(s+r)$ matrix of transfer functions, $(2\pi k/T)$ is near λ for $k = 0,\ldots, T-1$, and where the remaining terms are the Fourier transforms of the vectors defined by expressions Eq. (33)

Expression Eq. (32) may be written in more compact notation as

$$\underline{Y}_{\mathrm{k}} \approx \mathbf{A}\underline{X}_{\mathrm{k}} + \underline{\varepsilon}_{\mathrm{k}} \tag{37}$$

where k indexes distinct frequencies near λ, and $\mathbf{A}$ the matrix of transfer functions, is analogous to a matrix of parameters to be estimated in regression analysis. Expression Eq. (35) shows the extension of Eq. (25) to the multivariate case (Brillinger, 1980). The approximate relation Eq. (35) applies to both the point process and continuous time series case, as well as hybrids of the two (Brillinger, 1983; Halliday et al., 1995).

4.1. Partial spectra and partial coherences

The matrix of error spectra for the general model for the pair of vector valued processes $\underline{M}$ and $\underline{N}$ may be shown to be

$$\mathbf{F}_{\underline{\varepsilon\varepsilon}}(\lambda) = \mathbf{F}_{\underline{NN}}(\lambda) - \boldsymbol{F}_{\underline{NM}}(\lambda)\mathbf{F}_{\underline{MM}}(\lambda)^{-1}\mathbf{F}_{\underline{MN}}(\lambda) \quad (38)$$

where the $\mathbf{F}$'s represent spectral density matrices of the vectors indicated by the subscripts. A typical entry, $f_{\varepsilon_a\varepsilon_b}(\lambda)$, of the matrix $\mathbf{F}_{\underline{\varepsilon\varepsilon}}(\lambda)$ is defined as the partial spectrum between processes N_a and N_b after removing the linear effects of processes $\underline{M}$, and written as

$$f_{\varepsilon_a\varepsilon_b}(\lambda) = f_{N_aN_b/\underline{M}}(\lambda) \quad (39)$$

where $a = b$ defines the partial auto-spectrum and $a \neq b$ the partial cross-spectrum.

The idea of partial spectra can be extended to partial coherences, where the partial coherence between N_a and N_b gives the coherence between these processes after removing the linear contribution from processes $\underline{M}$, and is defined as

$$|R_{N_aN_b/\underline{M}}(\lambda)|^2 = \frac{|f_{N_aN_b/\underline{M}}(\lambda)|^2}{f_{N_aN_a/\underline{M}}(\lambda) f_{N_bN_b/\underline{M}}(\lambda)} \quad (40)$$

Expressions Eqs. (39) and (40) may also be evaluated for partial parameters of order $k \leq r$ having removed the linear effects of k components of $\underline{M}$ (Rosenberg et al., 1989). For example, in the case of a two input two output system there are two output partial cross-spectra of order-1, given as

$$f_{43/1}(\lambda) = f_{43}(\lambda) - \frac{f_{41}(\lambda) f_{13}(\lambda)}{f_{11}(\lambda)}$$
$$f_{43/2}(\lambda) = f_{43}(\lambda) - \frac{f_{42}(\lambda) f_{23}(\lambda)}{f_{22}(\lambda)} \quad (41)$$

where the subscripts 1 and 2 represent input processes and 3 and 4 output processes, and one partial cross-spectrum of order-2, written as

$$f_{43/12}(\lambda) = f_{43}(\lambda) - [f_{41}(\lambda) \quad f_{42}(\lambda)] \times \begin{bmatrix} f_{11}(\lambda) & f_{12}(\lambda) \\ f_{21}(\lambda) & f_{22}(\lambda) \end{bmatrix}^{-1} \begin{bmatrix} f_{13}(\lambda) \\ f_{23}(\lambda) \end{bmatrix} \quad (42)$$

which in the special case that the processes 1 and 2 are independent becomes

$$f_{43/2}(\lambda) = f_{43}(\lambda) - \left[\frac{f_{41}(\lambda) f_{13}(\lambda)}{f_{11}(\lambda)} + \frac{f_{42}(\lambda) f_{23}(\lambda)}{f_{22}(\lambda)}\right] \quad (43)$$

where the two terms in the brackets represents the independent contributions of processes 1 and 2 to $f_{43}(\lambda)$. Expressions Eqs. (41) and (43) can be seen to be analogous to the partial covariances between N_3 and N_4 controlling for N_1 or N_2 in expressions Eq. (41) and for both N_1 and N_2 in expression Eq. (43).

The inverse relations corresponding to the partial spectra define partial cumulant densities. For example, the partial cumulant density of order-2 corresponding to expression Eq. (42) would be

$$q_{43/12}(u) = \int_{-\pi}^{\pi} f_{43/12}(\lambda)\, e^{i\lambda u}\, d\lambda \quad (44)$$

with similar expressions for the partial cumulant densities of order-1. The partial cumulant densities may not be evaluated easily directly in the time domain. However, the process of removing a particular linear contribution to the correlation between two processes can easily be carried out in the frequency domain (Halliday et al., 1995).

The first-order partial coherences may be written in terms of the first-order partial spectra as

$$|R_{43/1}(\lambda)|^2 = \frac{|f_{43/1}(\lambda)|^2}{f_{44/1}(\lambda) f_{33/1}(\lambda)}$$
$$|R_{43/2}(\lambda)|^2 = \frac{|f_{43/2}(\lambda)|^2}{f_{44/2}(\lambda) f_{33/2}(\lambda)} \quad (45)$$

From the definitions of the partial spectra it follows directly that the first-order partial coherences may also be written in terms of the ordinary coherence. For example, $|R_{43/1}(\lambda)|^2$ may be written as

$$|R_{43/1}(\lambda)|^2 = \frac{|R_{43}(\lambda) - R_{41}(\lambda) R_{13}(\lambda)|^2}{(1 - |R_{41}(\lambda)|^2)(1 - R_{13}(\lambda)|^2)} \quad (46)$$

where the separate terms in the numerator are referred to as the coherencies. The relevant second-order partial coherence for the two input two output system may be written in terms of the partial spectra as

$$|R_{43/12}(\lambda)|^2 = \frac{|f_{43/12}(\lambda)|^2}{f_{44/12}(\lambda) f_{33/12}(\lambda)} \quad (47)$$

or in terms of the first-order partial coherences as

$$|R_{43/12}(\lambda)|^2 = \frac{|R_{43/1}(\lambda) - R_{42/1}(\lambda) R_{23/1}(\lambda)|^2}{(1 - |R_{42/1}(\lambda)|^2)(1 - |R_{23/1}(\lambda)|^2)} \quad (48)$$

Although the expressions for the higher-order partial coherences appear complicated, their general form is clear. Each higher order partial coherence may be calculated in terms of all lower order partial coherences, which in turn may be calculated in terms of the partial-spectra (Rosenberg et al., 1989). The partial spectra themselves are calculated in terms of the ordinary spectra Eq. (38), therefore, given the ordinary auto- and cross-spectra all of the partial coherences may be estimated by simple algebraic manipulations of the ordinary spectra. This is precisely analogous to the procedure for calculating partial correlations in multiple regression analysis. Alternatively, one may estimate the partial spectra via expression Eq. (38), and in addition obtain by matrix inversion the partial cumulants.

Expression Eq. (38) for the matrix of error spectra of the general model for a pair of vector valued processes may also be written as

$$\mathbf{F}_{\varepsilon\varepsilon}(\lambda) = \mathbf{F}_{\underline{NN}}(\lambda)^{1/2} [\mathbf{I}_s - \mathbf{F}_{\underline{NN}}(\lambda)^{-1/2}\mathbf{F}_{\underline{NM}}(\lambda)\mathbf{F}_{\underline{MM}}(\lambda)^{-1}\mathbf{F}_{\underline{MN}}(\lambda) \mathbf{F}_{\underline{NN}}(\lambda)^{-1/2}]\mathbf{F}_{\underline{NN}}(\lambda)^{1/2} \quad (49)$$

which for $s = r = 1$ reduces to expression Eq. (30), so that it can be seen, by analogy with expression Eq. (30) that

$$\mathbf{F}_{\underline{NN}}(\lambda)^{-1/2}\mathbf{F}_{\underline{NM}}(\lambda)\mathbf{F}_{\underline{MM}}(\lambda)^{-1}\mathbf{F}_{\underline{MN}}(\lambda)\mathbf{F}_{\underline{NN}}(\lambda)^{-1/2} \quad (50)$$

may be viewed as a generalised coherence between two vector valued processes $\underline{M}$ and $\underline{N}$.

5. Applications of the frequency domain representation of the linear model for the relation between spike trains

In this section we illustrate how the coherence provides a useful tool for inferring the structure of common inputs and how partial coherences may be used to decide whether two processes are linked as input–output or if the correlation between them is a consequence of common inputs. These simple operations may form the basis for inferring the structure of more complex networks than those discussed. Three simple neuronal networks are analysed. (a) Two neurones receiving a common excitatory or a common inhibitory input (Fig. 1A). This example may be considered as analogous to a pair of motoneurones coupled by a branched stem common input giving rise to what has been called short term synchrony (Sears and Stagg, 1976; Kirkwood, 1979). (b) Two different sets of common inputs to a pair of neurones (Fig. 1B). The common inputs are excitatory to both neurones, and (c) Two different sets of common inputs, one inhibitory and the other excitatory, to a pair of neurones (Fig. 1C). The common inputs in (c) are themselves correlated. This example combines the effects of common branched stem inputs where the common inputs themselves are correlated. The correlation of the common inputs may be considered as analogous to synchronised presynaptic inputs on to motoneurones as discussed by Datta and Stephens (1990), Kirkwood (1991). In each of these examples neurones receive a large number of inputs independent of the common inputs as well as of each other (indicated by the dashed lines in Fig. 1A–C). Given the simultaneous measurement of a number of spike trains, the systematic application of coherence and partial coherence measures is a powerful tool for determining plausible patterns of neuronal connectivity.

5.1. Example 1: paired neurones with a single common excitatory input

N_1 represents the single common input to two neurones whose output spike trains are denoted by N_4 and N_5. N_2 and N_3 represent independent inputs to the paired neurones as indicated by the schematic diagram of the neural network shown in Fig. 1A. The common input, N_1, is assumed to be independent of processes N_2 and N_3, which in turn are independent of each other.

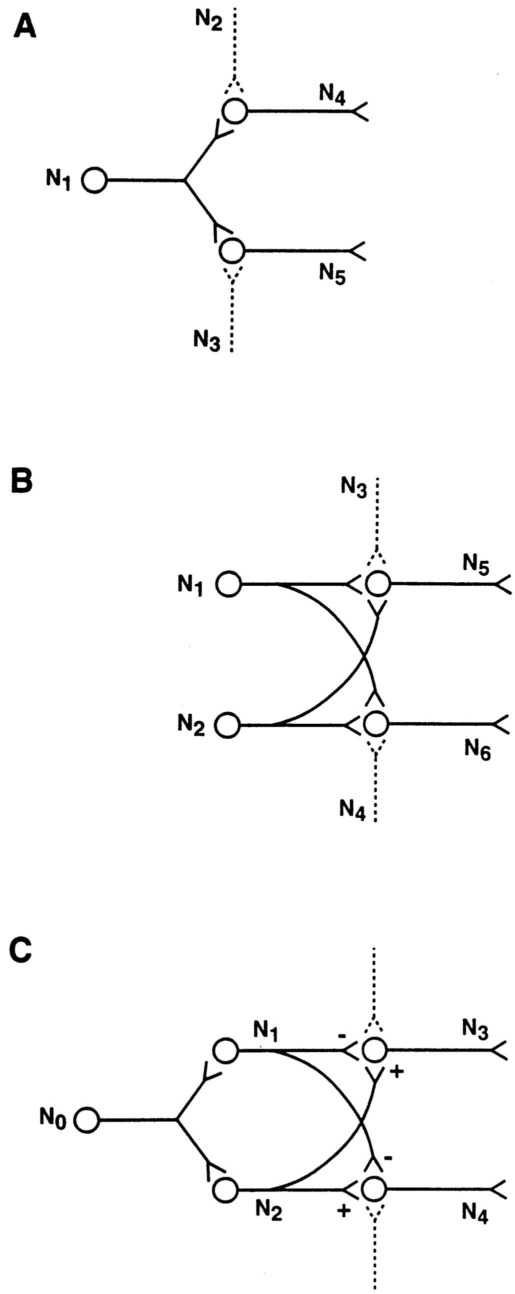

Fig. 1. Diagrammatic representation of the three neural networks investigated in this report. (A) A pair of neurones with spike trains N_4 and N_5, receiving the single common input, N_1, where N_1 may be either excitatory or inhibitory. The spike trains N_2 and N_3 are independent of each other as well as of N_1. (B) A pair of neurones with spike trains N_5 and N_6 with two independent common excitatory inputs, N_1 and N_2, where N_1 and N_2 are both excitatory. In addition to the common inputs each of the paired neurones receives inputs, N_3 and N_4, independent of each other and of the common excitatory inputs. (C) A pair of neurones, N_3 and N_4, with two common inputs, one of which is excitatory, N_2, and the other inhibitory, N_1. The common inputs themselves receive a common excitatory input, N_0.

Under these assumptions the coherence between N_4 and N_5 may be developed directly from the linear model Eq. (25) (see Perkel (1970), Tick (1963) for a similar approach to problems of this kind). It follows from Eq. (35) that the finite Fourier transforms of N_4 and N_5, d_4^T and d_5^T, suppressing the dependencies on λ, may be written as

$$d_4^T = h_{41}d_1^T + d_{\varepsilon_{41}}^T + h_{42}d_2^T + d_{\varepsilon_{42}}^T$$
$$d_5^T = h_{51}d_1^T + d_{\varepsilon_{51}}^T + h_{53}d_3^T + d_{\varepsilon_{53}}^T \quad (51)$$

where the subscripts in each term indicate particular processes, and the h's and ε's the transfer functions and error processes, respectively. Expressions Eq. (51) are in turn used, according to Eq. (16), to derive the cross-spectrum and auto-spectra from which, after some manipulation, gives the estimated coherence between N_4 and N_5 suppressing the dependencies on λ as

$$|\hat{R}_{45}|^2 = \hat{f}_{11}^2 \frac{|\hat{h}_{41}|^2|\overline{\hat{h}_{51}}|^2}{(\hat{f}_{11}|\hat{h}_{41}|^2+\hat{f}_{22}|\hat{h}_{42}|^2+\hat{f}_{\varepsilon_{42}}+\hat{f}_{\varepsilon_{41}})(\hat{f}_{11}|\hat{h}_{51}|^2+\hat{f}_{33}|\hat{h}_{53}|^2+\hat{f}_{\varepsilon_{53}}+\hat{f}_{\varepsilon_{51}})} \quad (52)$$

If contributions to the coherence from independent inputs and the noise series are large compared with that of the common input, and constant over the range of frequencies of interest, then the estimated coherence between N_4 and N_5 is approximately

$$|\hat{R}_{45}(\lambda)|^2 \approx K_1\hat{f}_{11}^2(\lambda) \quad (53)$$

where K_1 is a constant. Under the appropriate conditions one might expect that the coherence between the discharges from such a pair of neurones, provided the common input is not dominant, would represent a scaled version of the square of the auto-spectrum of this common input.

The example illustrated by Fig. 2 takes a sinusoidally modulated spike train as a common input to a pair of neurones. The spike train in the absence of the modulating signal had a Gaussian distribution of intervals. The auto-spectrum of the modulated spike train is shown in Fig. 2A. In this example the modulation frequency was set at 10 Hz, and appears as a sharp peak in the spectrum at 10 Hz, whereas the second peak centred about 25 Hz corresponds to the mean rate. Below and in register with the auto-spectrum is the

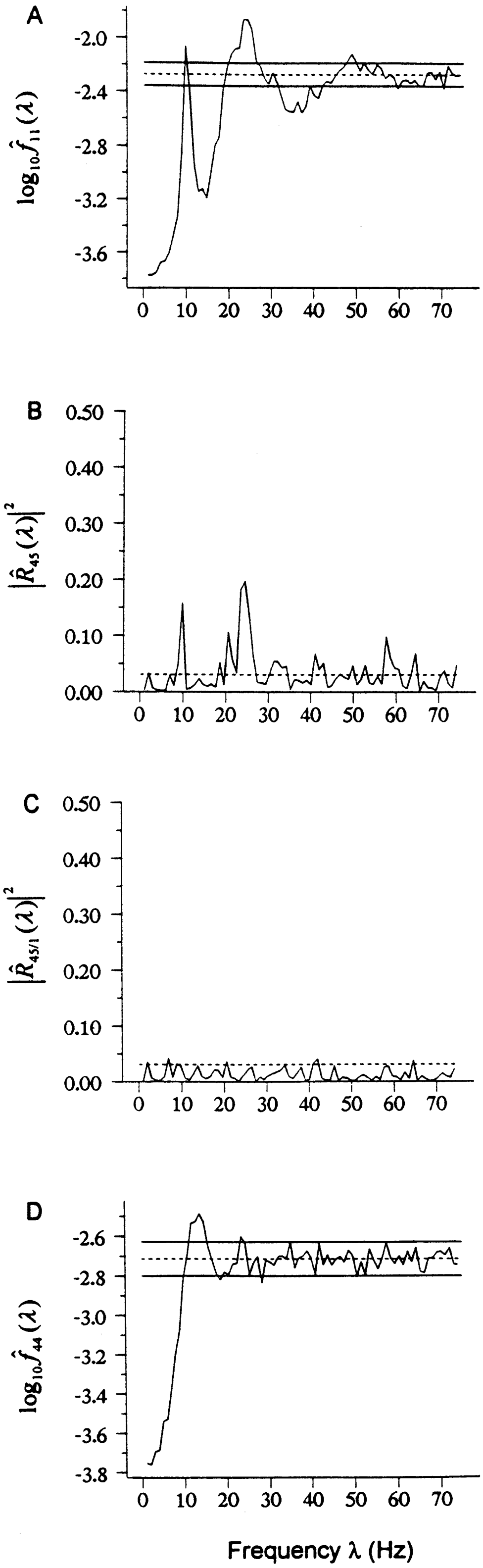

Fig. 2.

Fig. 2. Frequency domain analysis of the neural network in which a pair of neurones N_4 and N_5 receive a common excitatory input N_1. Estimated (A) auto-spectrum of the common input, N_1, to the pair of neurones N_4 and N_5, (B) coherence between the discharges from N_4 and N_5, (C) partial coherence between N_4 and N_5 taking into account the contribution from N_1, and (D) auto-spectrum of N_4 (which is similar to that of N_5). The solid horizontal lines in (A) and (D) represent an approximate 95% confidence interval for the estimated auto-spectra, and the dashed horizontal lines the asymptotic value of the estimate equal to $\text{Log}_{10} P/2\pi$, where P is the mean rate of the spike train. The horizontal dashed lines in (B) and (C) represent the upper level of the approximate 95% confidence interval for the estimated coherence under the assumption that the two processes are independent.

coherence estimated from a sample of the discharges from the pair of neurones driven by the common input (Fig. 2B). The peaks in the coherence are seen to reflect the two dominant frequency components that appear in the spectrum of the common input. The auto-spectra of the two output processes were similar to each other, showing a dominant peak near 13 Hz (Fig. 2D), and clearly different from either of the peaks in the coherence, and the input auto-spectrum (Fig. 2A).

When it is possible to record from a suspected common input process, the partial coherence may be used to provide an indication of whether the observed coupling between the two neurones is a consequence of the common input (Brillinger, 1975a; Rosenberg et al., 1989). One would expect that the sample partial coherence, $|\hat{R}_{45/1}(\lambda)|^2$, in this example would be close to zero, as is shown in Fig. 2C. In this example, the pairwise coherences between the three recorded process are all significant. The combined application of the coherence and partial coherence would then lead to the conclusion that the coupling between N_4 and N_5 is not direct, but a consequence of N_1.

The corresponding time domain estimates are shown in Fig. 3. Fig. 3A shows the auto-covariance of the modulated common input, Fig. 3C and D the auto-covariances of the two outputs. The estimated cross-covariance (cumulant) between the two outputs is shown in Fig. 3B. Although there is some suggestion of periodicities in this estimate for lag $u < 0$, it is not clear that the presence of two distinct components in the modulated input could be accurately inferred. This example illustrates some the difficulties highlighted by Moore et al. (1970), Perkel (1970) who emphasised that the cross-correlation histogram resulting from shared inputs may not have a simple interpretation. Indeed, from expression Eq. (51) it follows that the cross-covariance between the two output processes would be proportional to the convolution between the common input and the two output processes. The periodicities of the three processes would be confounded, and any inference regarding the periodicity of the common input need not be correct. However, the techniques introduced by Gerstein and his colleagues may be used to unravel the three neurone case (e.g., Aertsen et al., 1989; Gerstein and Perkel, 1972; Palm et al., 1988).

5.2. Example 2: paired neurones with a single common inhibitory input.

This example only differs from Example 1 in that the single input, N_1, common to processes N_4 and N_5 is inhibitory. In this example the three pairwise cross-covariances would allow the identification of a common inhibitory input from N_1 to N_4 and N_5. From the rules of Moore et al. (1970) common inhibition can be expected to give a peak in the cross-covariance centred

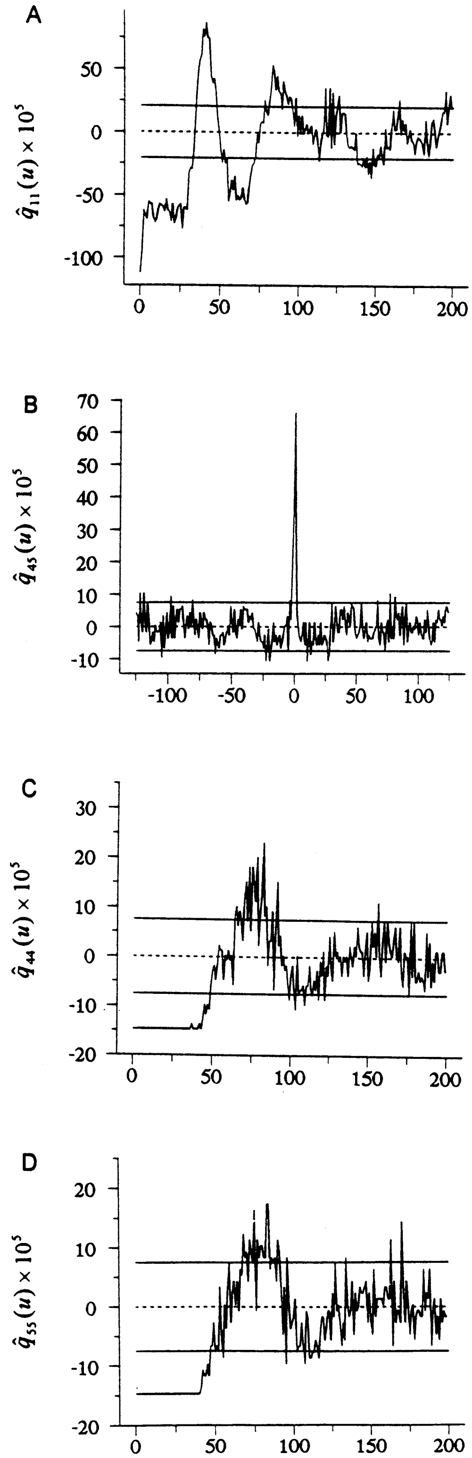

Fig. 3. Time domain analysis of the neural network in which a pair of neurones N_4 and N_5 receive a common excitatory input N_1. Estimated (A) second-order cumulant of the common input, N_1, to the pair of neurones N_4 and N_5, (B) second-order cumulant between N_4 and N_5, and (C) and (D) the second-order cumulants of the discharge of neurones N_4 and N_5. The solid horizontal lines in each panel represent approximate 95% confidence intervals, and the dashed horizontal lines the asymptotic value of the estimate, which in each case is zero.

near lag $u = 0$ (Fig. 4A). The magnitude of this peak would be expected to be smaller than if the common input was excitatory, as in *Example 1* (Fig. 3B). The

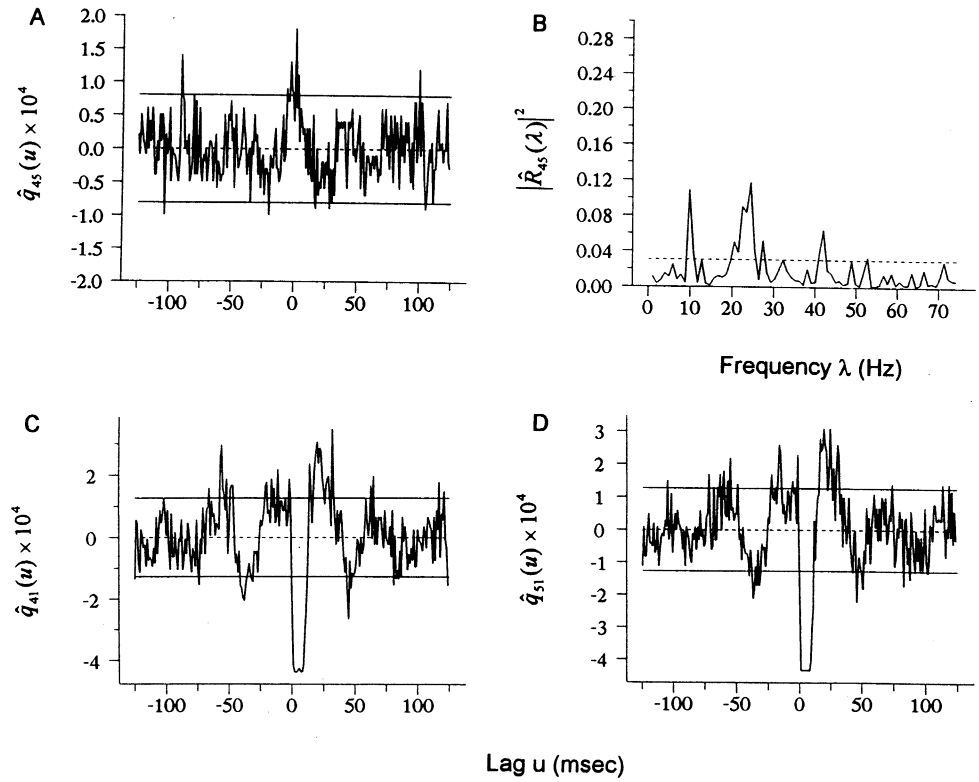

Fig. 4. Estimated (A) cumulant between N_4 and N_5 when the common input process, N_1, is inhibitory, (B) coherence between N_4 and N_5, (C) the second-order cumulant between N_1 and N_4 illustrating the inhibitory effect of N_1 on N_4, and (D) the second-order cumulant between N_1 and N_5 illustrating the inhibitory effect of N_1 on N_5. The solid horizontal lines in (A), (C) and (D) represent approximate 95% confidence intervals, and the dashed horizontal line the asymptotic value of the estimate equal to zero. The horizontal dashed line in (B) represents the upper level of the approximate 95% confidence interval at frequency λ under the assumption that the two processes are independent.

remaining cross-covariances, $q_{41}(u)$ and $q_{51}(u)$, (Fig. 4C and D) have troughs near lag $u = 0$ suggesting inhibitory connections from N_1 on to N_4 and N_5. The three cross-covariances taken together would be sufficient to identify common inhibition. The coherence, $|R_{45}(\lambda)|^2$ (Fig. 4B), would further the analysis by identifying the frequency structure of the common inhibitory input.

5.3. *Example 3: paired neurones with two common excitatory inputs.*

The following example is based on the schematic neural network shown in Fig. 1B. The common inputs to the paired neurones are denoted by N_1 and N_2. The output processes from the pair of neurones are denoted by N_5 and N_6. Processes N_3 and N_4 represent independent inputs to the paired neurones as indicated in Fig. 1B.

By direct extension of the procedure set out above, the coherence between processes N_5 and N_6 may be written, suppressing the dependencies on λ, as

$$|R_{56}|^2 = \frac{|\hat{f}_{11}\hat{h}_{51}\overline{\hat{h}_{61}} + \hat{f}_{22}\hat{h}_{52}\overline{\hat{h}_{62}}|^2}{(\hat{f}_{11}|\hat{h}_{51}| + \hat{f}_{22}|\hat{h}_{52}| + \hat{f}_{33}|\hat{h}_{53}| + \hat{f}_{\varepsilon_{51}} + \hat{f}_{\varepsilon_{52}} + \hat{f}_{\varepsilon_{53}})(\hat{f}_{11}|\hat{h}_{61}| + \hat{f}_{22}|\hat{h}_{62}| + \hat{f}_{44}|\hat{h}_{64}| + \hat{f}_{\varepsilon_{61}} + \hat{f}_{\varepsilon_{65}} + \hat{f}_{\varepsilon_{64}})} \quad (54)$$

Under the same considerations used in discussing *Example 2*, one would expect that the coherence, $|R_{56}|^2$, would have two components proportional to the magnitude squared of the sum of scaled versions of the auto-spectra of the two common input processes written as

$$|\hat{R}_{56}(\lambda)|^2 \approx K_2|\hat{f}_{11}\hat{h}_{51}\overline{\hat{h}_{61}} + \hat{f}_{22}\hat{h}_{52}\overline{\hat{h}_{62}}|^2 \quad (55)$$

where K_2 is a constant.

In this example the simulation was set up so that the common input N_1 was periodic with centre frequency of 10 Hz, and that of the second common input, N_2, periodic with a centre frequency of 30 Hz. The auto-spectra of the two common inputs are shown in Fig. 5A and B. The peaks in the auto-spectra of the common inputs centred about 10 and 30 Hz (Fig. 5A and B) are in turn reflected in the coherence between processes N_5 and N_6, $|R_{56}(\lambda)|^2$, by significant peaks centred about the same frequencies (Fig. 5C). The coherence, $|R_{56}(\lambda)|^2$, alone (Fig. 5C) may suggest either a single frequency

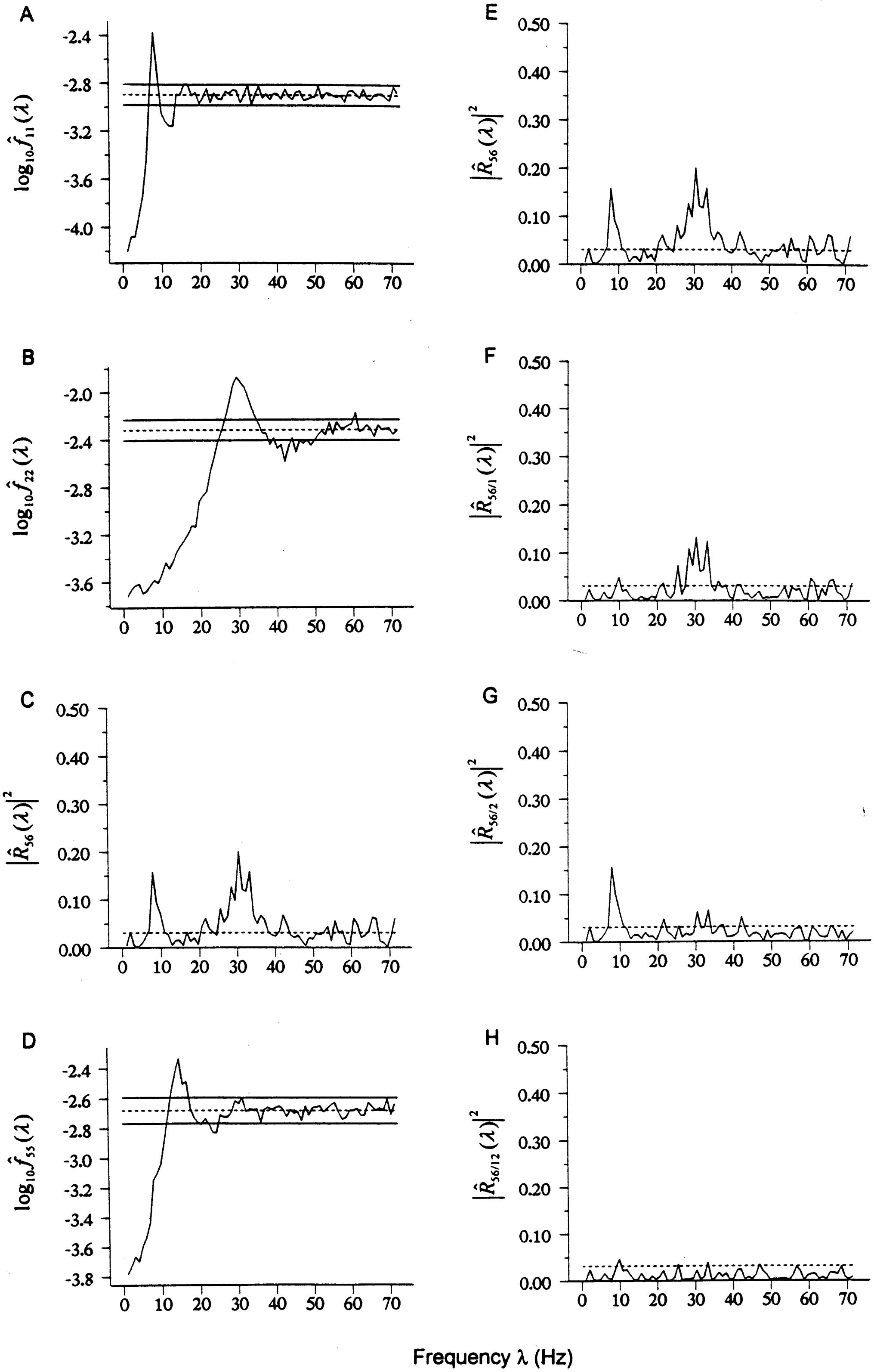

Fig. 5. Frequency domain analysis of the neural network in which a pair of neurones N_5 and N_6 receive two common excitatory inputs N_1 and N_2. Estimated (A, B) auto-spectra of the two common inputs N_1 and N_2 to neurones N_5 and N_6, (C, E) coherence between N_5 and N_6 in response to the shared inputs N_1 and N_2, (D) auto-spectrum of one of the paired neurones N_5 (which is similar to that of N_6), (F) first-order partial coherence between N_5 and N_6 taking into account the common input N_1, (G) first-order partial coherence between N_5 and N_6 taking into account the common input N_2, and (H) second-order partial coherence between N_5 and N_6 taking into account the common inputs N_1 and N_2. The solid horizontal lines in (A, B, D) provide approximate 95% confidence intervals for the estimated auto-spectra, and the dashed horizontal lines the asymptotic value of the estimate equal to $\text{Log}_{10} P/2\pi$, where P is the mean rate of the spike train. The horizontal dashed line in (C, E–H) represents the upper level of the approximate 95% confidence interval at frequency λ.

modulated periodic common input as in *Example 1* or two independent inputs at the different frequencies. If one has access to the suspected common inputs, the analysis may be furthered through the application of first- and second-order partial coherences. The only significant peak in the first-order partial coherence between processes N_5 and N_6 taking into account N_1, $|R_{56/1}(\lambda)|^2$, is centred about 30 Hz (Fig. 5F)—the 10 Hz component present in $|R_{56}(\lambda)|^2$ (Fig. 5E) has been removed. The partial coherence $|R_{56/2}(\lambda)|^2$ removes the peak in $|R_{56}(\lambda)|^2$ centred about 30 Hz leaving the component at 10 Hz (Fig. 5G). The second-order partial coherence between N_5 and N_6 taking into account processes N_1 and N_2, $|R_{56/12}(\lambda)|^2$, is not significant, further suggesting that N_1 and N_2 are the only common inputs to N_5 and N_6.

5.4. Example 4: paired neurones, N_3 and N_4, with two common inputs, one of which is excitatory, N_2, and the other inhibitory, N_1: these common inputs are themselves correlated by the common excitatory process N_0.

The common input, N_0, is strongly periodic (Fig. 6A). This periodicity, by expression Eq. (53), appears in the coherence $|R_{12}(\lambda)|^2$ as peaks centred about 10 Hz and its higher harmonics (Fig. 6B and F).

The auto-spectra of the two neurones, N_1 and N_2, driven by N_0 are shown in Fig. 6C and D, respectively. These spectra have components related to the 10 Hz component of the common input as well to the intrinsic periodicity at 25 Hz of each of these cells. Consequently the coherence between N_3 and N_4 (Fig. 6E) will reflect the combined influence of the rhythmic components of the common inputs (Fig. 6A, C and D).

The successive application of partial coherences will help to identify this more complex network. For ease of interpretation the two coherences $|R_{12}(\lambda)|^2$ and $|R_{43}(\lambda)|^2$ are replotted in Fig. 6F and H. The first-order partial coherence between N_1 and N_2 taking into account N_0 is not significant (Fig. 6G). The strong coherence between N_1 and N_2 at 10 Hz and its higher harmonics may be attributed to a common input process. The observation that none of the significant components of $|R_{12}(\lambda)|^2$ appear in $|R_{12/0}(\lambda)|^2$ suggest a single common input as opposed to several independent common inputs with frequencies at multiples of 10 Hz. The partial coherence $|R_{43/0}(\lambda)|^2$ (Fig. 6I) shows a reduction corresponding to the peak at 10 Hz in $|R_{43}(\lambda)|^2$ (Fig. 6H), which in turn corresponds to the periodicity of the input common to N_1 and N_2 (Fig. 6A). The strongly periodic 10 Hz signal arising from N_0 acts across two synaptic junctions to appear in the coherence between N_3 and N_4. The remaining peaks in $|R_{43/0}(\lambda)|^2$ (Fig. 6I) may be attributed to different and possibly independent sources of common inputs. The third-order partial coherence between N_3 and N_4 taking into account processes N_0, N_1 and N_2, $|R_{43/012}(\lambda)|^2$, is not very significant (Fig. 6J), identifying these processes as additional sources of common inputs to N_3 and N_4.

The separate effects of each of these processes on the coherence between N_3 and N_4 may be assessed by considering the effects of each process alone in combination with N_0 on the coherence between N_3 and N_4. The two second-order partial coherences $|R_{43/01}(\lambda)|^2$ and $|R_{43/02}(\lambda)|^2$ (Fig. 7B and C) show that each process, N_1 and N_2, reduces the coherence between N_3 and N_4 (Fig. 7A) over the same range of frequencies, although one of these processes, N_1, appears to have a stronger effect than N_2. The coherences do not provide any indication of whether this second set of common inputs are inhibitory or excitatory. The cross-covariances, however, do provide this information. The cross-covariance between N_3 and N_4, $q_{43}(u)$ (Fig. 7D), gives the expected peak centred about lag $u = 0$, combining the effects of the different levels of common input processes described by $|R_{43/0}(\lambda)|^2$ (Fig. 7A). Note the absence of significant secondary features in $q_{43}(u)$ suggesting a nonperiodic common input, contrary to the rules of Moore et al. (1970). The separate effects of each of the common inputs N_1 and N_2 on N_3 or N_4 can be assessed by the cross-intensities of each of these inputs on to N_3 and N_4. From Fig. 7F and H process N_1 may be said to be inhibitory to N_3 and N_4, whereas, N_2 is seen to be excitatory to N_3 and N_4 (Fig. 7E and G).

6. Summary of results

(a) The finite Fourier transform of the model of a linear point process system leads to a regression type analysis of the relation between spike trains that considerably develops the range of tools available for spike train analysis.

(b) The analysis and simulation of simple neural networks based on the frequency domain representation of these networks can be used to identify common inputs to pairs of neurones, and to estimate their frequency content.

(c) Measures of coherence in combination with those of partial coherence and cumulants provide a powerful approach for identifying plausible patterns for neural networks based on the analysis of spike trains alone.

(d) When inferring the structure of common inputs the coherence alone will not distinguish between multiple common inputs with different dominant frequency components, and a single input that is frequency modulated to give the same components of frequency as found in the several common inputs. In favourable cases, the selective application of partial coherences in combination with cumulants can, however, be used to distinguish frequency modulated from multiple common inputs.

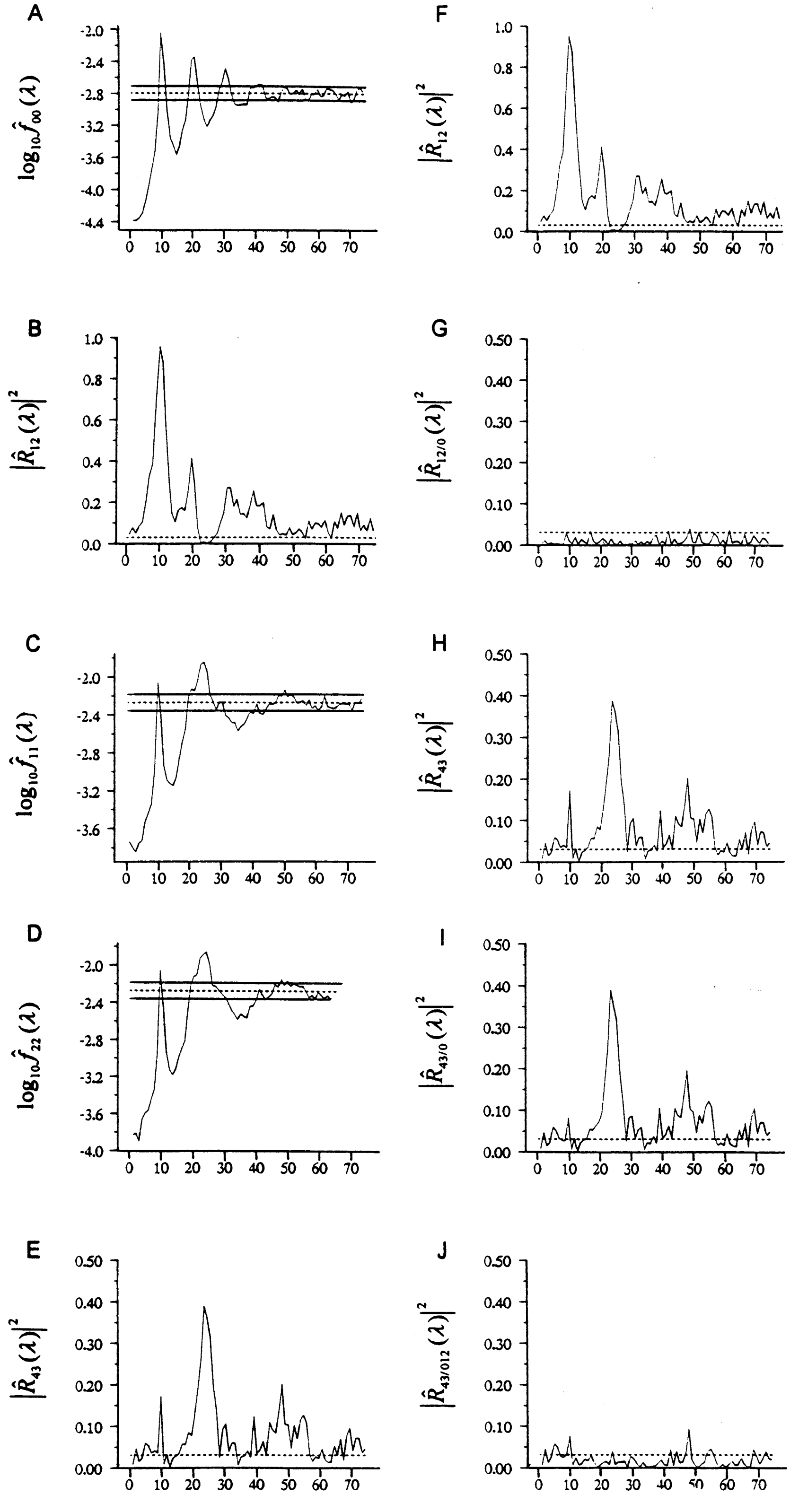

Fig. 6. Frequency domain analysis of the neural network in which a pair of neurones N_3 and N_4 receive two common inputs, one of which is excitatory, N_2, and the other inhibitory, N_1. N_1 and N_2 in turn receive the common excitatory input N_0 Estimated (A) auto-spectrum of common excitatory input N_0 to neurones N_1 and N_2, (B, F) coherence between N_1 and N_2 in response to shared input N_0, (C) auto-spectrum of the common inhibitory input, N_1, to neurones N_3 and N_4, (D) auto-spectrum of the common excitatory input, N_2, to neurones N_3 and N_4, (E, H) coherence between N_3 and N_4, (G) first-order partial coherence between N_1 and N_2 taking into account the common input N_0, (I) first-order partial coherence between N_3 and N_4 taking into account process N_0, (J) third-order partial coherence between N_3 and N_4 taking into account processes N_0, N_1 and N_2. The solid horizontal lines in (A, C, D) represent approximate 95% confidence intervals for the estimated auto-spectra, and the dashed horizontal lines the asymptotic value of the estimate equal to $\text{Log}_{10} P/2\pi$, where P is the mean rate of the spike train. The horizontal dashed line in (B, E–J) represents the upper level of the approximate 95% confidence interval at frequency λ.

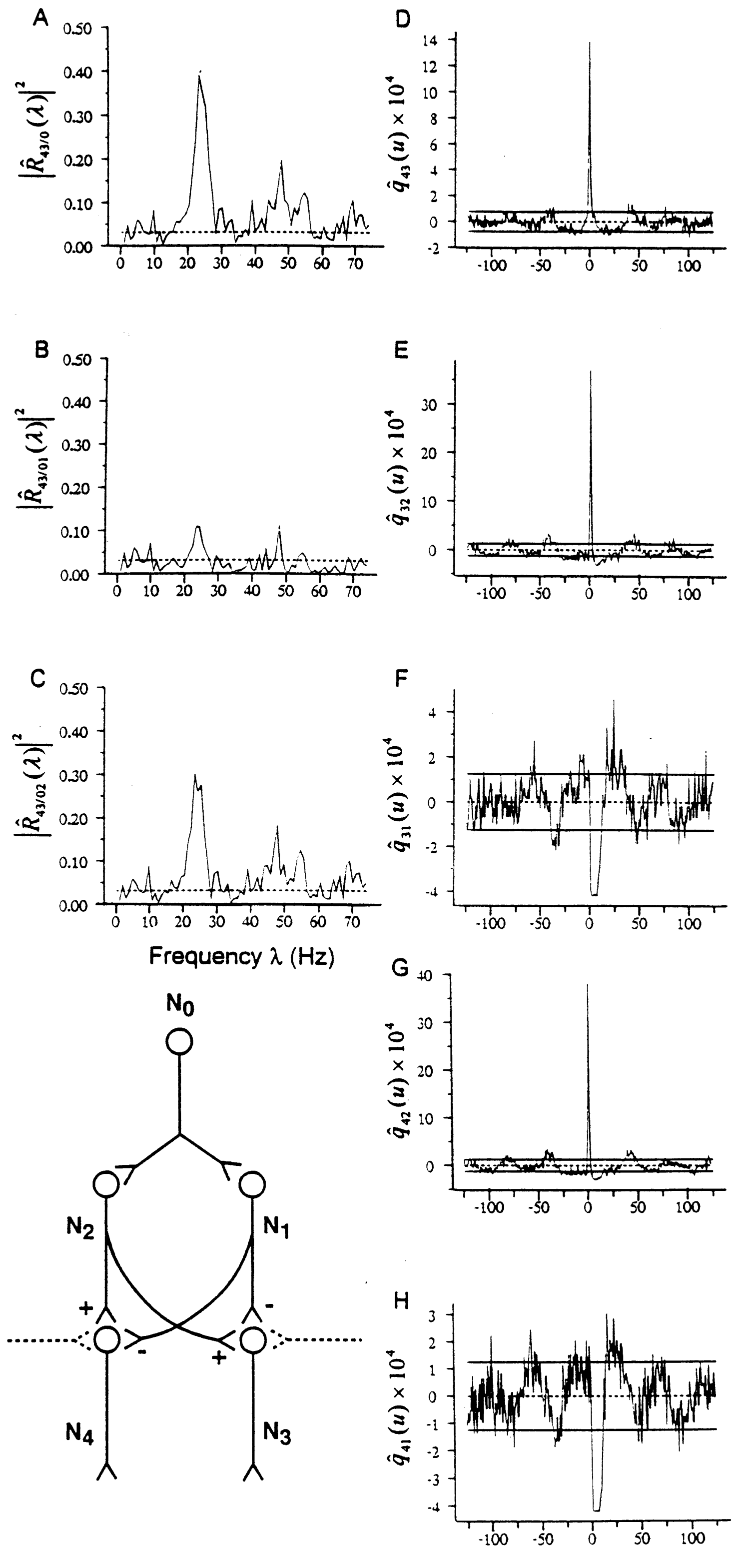

Fig. 7. For the same network as Fig. 6 (shown in the lower left hand corner of Fig. 7), estimated (A) first-order partial coherence between processes N_3 and N_4 taking into account process the common input process N_0, (B) second-order partial coherence between N_3 and N_4 taking into account processes N_0 and N_1, (C) second-order partial coherence between N_3 and N_4 taking into account processes N_0 and N_2, (D) second-order cumulant between N_3 and N_4, (E) second-order cumulant between excitatory process N_2 and N_3, (F) second-order cumulant between inhibitory process N_1 and N_3, (G) second-order cumulant between excitatory process N_2 and N_4, (H) second-order cumulant between inhibitory process N_1 and N_4. The horizontal dashed line in (A–C) represents the upper level of the approximate 95% confidence interval at frequency λ. The solid horizontal lines in (D–H) represent approximate 95% confidence intervals, and the dashed horizontal lines the asymptotic value of the estimate, which in each case is zero.

7. Concluding remarks

The starting point for our study was an investigation of the suggestion that the frequency content of a common presynaptic input to synchronously discharging motor-units may be inferred from the coherence estimated from the discharge of the two motor-units (Farmer et al., 1993). We have shown that, under certain conditions, this coherence reflects the auto-spectrum of the common input. The analysis techniques based on a linear model for point process systems may be extended to estimate how any number of input processes influence the correlation between any two output processes. If we assume that the processes arise on an equal footing, in the sense that no structural information is available on the underlying neural network, then the systematic application of coherences, partial coherences and cumulant density functions leads to plausible models for the pattern of connectivity between these processes, and whether a given interaction between two processes is excitatory or inhibitory. As pointed out by Moore et al. (1970) much of the value of the statistical measures for analysing neuronal interactions lies in their usefulness in developing or testing hypotheses about neuronal network structures. The Fourier based methods described in this report extend the time domain procedures considered by Moore et al. (1970) to a wider class of problems, and at the same time allow analytic solutions to questions about the structure of common inputs to pairs of neurones.

The coherences, and particularly the partial coherences, however, must be interpreted with caution, since their application assumes a simple linear model for the neuronal interactions. In cases where the association between two neurones is entirely a consequence of a single common process that acts in a more complex manner on each of these neurones, the partial coherence taking into account the effect of this process will not necessarily be zero (see Appendix A). A non-significant partial coherence cannot therefore always be taken as an indication that a particular process does not influence the coherence, it may do so, but in a non-linear way. The partial coherence, however, will be correctly interpreted when it is significant.

The partial coherences in the case of multiple common inputs to a pair of neurones reveal an interesting feature of neuronal discharges. The partial coherences have identified particular frequency bands within a neuronal discharge that may be associated with particular inputs to the neurone. The preservation of the frequency content of the common inputs in the discharge of a neurone implies that these neurones carry information in a single spike train related to different inputs to the neurone. Rosenberg and Rigas (1985) demonstrated that single Ia-afferents from cat muscle spindles carry information in different frequency bands related to length and fusimotor inputs. The partial coherences applied to neural networks made up from realistic models of motoneurones may be indicating a general property of neuronal spike trains.

Appendix A

A.1. Simulation—paired neurones with common inputs

We have set up a conductance based neurone model in which a pair of model neurones can receive a specified number of common inputs as well as a specified number of independent inputs. The basic simulation generates spike trains from the pair of model neurones. The spike trains of the common inputs are also available. Details of the model may be found in Farmer et al. (1993).

A.2. The effect of non-linearities on the partial coherence

When assessing the effect that a third process may have on the coupling between two other processes the interpretation of the partial coherence in cases where there is little difference between the estimated ordinary and partial coherences requires considerable care. The absence of a significant difference may occur for several reasons. The third process may not influence the coupling between the other two processes or the effect of the common input is non-linear. In the non-linear case even if the common input is the only source of coupling between the two processes there may be no significant difference between the estimates of the ordinary coherence and the partial coherence taking into account the contribution from the common input.

We may approach one type of non-linear behaviour as follows. Let $X(t)$ represent the common input giving rise to two processes $Y_1(t)$ and $Y_2(t)$. The partial coherence between the output processes taking into account $X(t)$ will be close to zero when the partial cross-spectrum between these processes is close to zero, i.e., when

$$f_{Y_1Y_2/X}(\lambda) = f_{Y_1Y_2}(\lambda) - \frac{f_{Y_1X}(\lambda)f_{XY_2}(\lambda)}{f_{XX}(\lambda)} \quad \text{(A1)}$$

is close to zero, then $|R_{N_1N_2/M}(\lambda)|^2$ will be close to zero. The development of an expression for the cross-spectrum when the common input exerts this non-linear effect on each of the output neurones may be developed as follows.

Given the common input $X(t)$, then a possible model containing a quadratic term for the input effects on each output may be written as

$$Y_j(t) = \sum a_j(u)X(t-u) + \sum\sum b_j(u, v)X(t-u)X(t-v) + \text{noise}_j \quad j = 1, 2 \tag{A2}$$

Assume that $X(t)$ is Gaussian, and neglecting the noise term, then

$$f_{Y_jX}(\lambda) = A_j(\lambda)f_{XX}(\lambda) \quad \text{and}$$
$$f_{Y_1Y_2}(\lambda) = A_1(\lambda)\overline{A_2(\lambda)}f_{XX}(\lambda) + 2\int B_1(\lambda - v, v)\overline{B_2(\lambda - v, v)}f_{XX}(v) f_{XX}(\lambda - v)\,\mathrm{d}v \tag{A3}$$

where $A_j(\cdot)$ and $B_j(\cdot)$ are the Fourier transforms of $a_j(\cdot)$ and $b_j(\cdot)$, and so generally

$$f_{Y_1Y_2/X}(\lambda) = f_{Y_1Y_2}(\lambda) - \frac{f_{Y_1X}(\lambda)f_{XY_2}(\lambda)}{f_{XX}(\lambda)} \neq 0 \tag{A4}$$

Non-linearities cause difficulties, and their possible presence must be taken into account in the interpretation of partial coherences, particularly in situations when there is no significant difference between the ordinary and partial coherences. One cannot conclude that an absence of an effect means that process $X(t)$ has no influence on the coupling between processes $Y_1(t)$ and $Y_2(t)$. In this non-linear case X(t) may be the only source of coupling between $Y_1(t)$ and $Y_2(t)$ and the partial coherence taking $X(t)$ into account will not necessarily be zero.

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