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Mechanisms of evoked and induced responses in MEG/EEG

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Abstract

Cortical responses, recorded by electro-encephalography and magneto-encephalography, can be characterised in the time domain, to study event-related potentials/fields, or in the time-frequency domain, to study oscillatory activity. In the literature there is a common conception that *evoked*, *induced* and *on-going* oscillations reflect different neuronal processes and mechanisms. In this work we consider the relationship between the mechanisms generating neuronal transients and how they are expressed in terms of evoked and induced power. This relationship is addressed using a neuronally realistic model of interacting neuronal sub-populations. Neuronal transients were generated by changing neuronal input (a *dynamic* mechanism) or by perturbing the systems coupling parameters (a *structural* mechanism) to produce induced responses. By applying conventional time-frequency analyses we show that, in contradistinction to common conceptions, induced and evoked oscillations are perhaps more related than previously reported. Specifically, structural mechanisms normally associated with induced responses can be expressed in evoked power. Conversely, dynamic mechanisms posited for evoked responses can induce responses, if there is variation in neuronal input. We conclude, it may be better to consider evoked responses as the results of mixed dynamic and structural effects. We introduce *adjusted* power to complement induced power. Adjusted power is unaffected by trial-to-trial variations in input and can be attributed to structural perturbations without ambiguity.

1 Introduction

Cortical oscillatory activity, as disclosed by local field potentials (LFPs), electroencephalographic (EEG) and magneto-encephalographic (MEG) recordings, can be categorised as ongoing, evoked or induced oscillations (Galambos 1992; Tallon-Baudry and Bertrand, 1999). Evoked and induced oscillations differ in their phase-relationships to the stimulus. Evoked oscillations are phase-locked to the stimulus, whereas induced oscillations are not. Operationally, these two phenomena are revealed by the order of trial-averaging and spectral analysis. To estimate evoked power, the MEG/EEG signal is first averaged over trials and then subject to time-frequency analysis to give an event-related response (ERR). To estimate induced oscillations, the time-frequency decomposition is applied to each trial and the ensuing power is averaged across trials. The power of evoked and background components are subtracted from this total power to reveal induced power. In short, evoked responses can be characterised as the power of the average; while induced responses are the average power that cannot be explained by the power of the average.

A common conception is that evoked oscillations reflect a stimulus-locked ERR, in time-frequency space and that induced oscillations are generated by some distinct high-order process. Following Singer and Gray (1995) this process is often described in terms of 'binding' and/or neuronal synchronisation. The tenet of the binding hypothesis is that coherent firing patterns can induce large fluctuations in the membrane potential of neighbouring neurons which, in turn, facilitate synchronous firing and information transfer (as defined operationally in Varela, 1995). **Oscillatory activity that is classified as induced** are the measured correlate of these massively synchronous neuronal assemblies. Oscillations are induced because their self-organised emergence is not evoked directly by the stimulus, but induced vicariously through nonlinear and possibly autonomous mechanisms.

Here we propose an alternative view that evoked and induced responses are, perhaps, more related than previously thought and that a mixture of mechanisms can generate both. Critically, we make a distinction between the mechanisms causing neuronal transients and how the response is measured operationally, in terms of evoked and induced oscillations. Having established this distinction, we then examine the relationship between the mechanisms and the time-frequency characterisations.

To pursue this we used a model neuronal system in which the mechanisms generating responses were under experimental control. This model was a neural mass model that we have used in previous studies to look at measures of linear and nonlinear coupling in EEG/MEG (David *et al* 2004), The mechanisms of phase-locking in the genesis of ERPs and other phenomena (David *et al* in press). Furthermore, this model is the basis of the forward model in the dynamic causal modelling of ERP data in SPM (<http://www.fil.ion.ucl.ac.uk/spm>; David *et al* submitted). Neuronal models play a necessary role in this context because they afford direct access to the processes and mechanisms producing evoked and induced oscillations. Once the mechanisms responsible for induced responses are established, one can assess the specificity of their expression in evoked and induced response components.

1.1 Overview

This paper is divided into three sections. In the first we establish a key distinction between *dynamic* mechanisms, normally associated with classical evoked responses like the ERP and *structural* mechanisms implicit in the genesis of induced responses. Dynamic effects are simply the effect of inputs on a systems response. Conversely, structural mechanisms entail a transient change in the systems causal structure i.e. its parameters (e.g. synaptic coupling). These changes could be mediated by nonlinear effects of input. We relate the distinction between dynamic and structural mechanisms to series of dichotomies in dynamical system theory and neurophysiology. These include the distinction between driving and modulatory effects in the brain. This section concludes with a review of how neuronal responses are characterised operationally, in terms of evoked and induced power, and how these characterisations relate to dynamic and structural perturbations.

In the second section we show that structural mechanisms can indeed produce induced oscillations. In the example provided, responses are induced by a stimulus-locked modulation of the backward connections from one source to another. However, we show that this structural effect is also

expressed in evoked oscillations when dynamic and structural effects interact. In the final section we show the converse, namely that dynamic mechanisms can produce induced oscillations, even in the absence of structural effects. This can occur when trial-to-trial variations in input suppress high-frequency responses after averaging. Our discussion focuses on the rather complicated relationship between the two types of mechanisms that can cause responses in EEG/MEG and the ways in which evoked and induced responses are measured. We introduce *adjusted* power as a complement to induced power that resolves some of these ambiguities.

2. Theory

2.1 Dynamic and structural mechanisms

In this section we introduce two distinct mechanisms that underlie neuronal transients. The distinction arises from a simple view of neuronal responses, as the response of an input-state-output system to perturbations. Any analytic system can be described by an equation governing the dynamics of its states and a function that converts the current state x of the system into some output or measure y , in our case an EEG/MEG signal.

$$\begin{aligned}\dot{x} &= f(x, u, \theta) \\ y &= \lambda(x, \theta) + \varepsilon\end{aligned}\tag{1}$$

These states $x(t)$ cover all the variables that describe the state of a neuronal system (e.g. a collection of neuronal sub-populations that constitutes an EEG source). For example, the states could include the depolarisation of all the systems neuronal compartments, and any other variable that shapes its dynamics. $u(t)$ or inputs enter the state equations to changes states, directly or indirectly. This input can have both stochastic and deterministic (*i.e.* stimulus-locked) components. $\theta(t)$ are system parameters that encode its functional or causal architecture; for example, the connection strengths among neuronal units. $\varepsilon(t)$ represents observation noise. See Figure 1 for a schematic representation of these quantities.

Figure 1 about here

From Eq.(1), it is immediately clear that the states, and implicitly the systems response, can only be changed by perturbing $u(t)$ or $\theta(t)$. We will refer to these as dynamic and structural effects respectively. This distinction arises in a number of different contexts. From a purely dynamical point of view, transients elicited by dynamic effects are the systems response to input changes; for example, the presentation of a stimulus in an ERP study. If the system is dissipative and has a stable fixed point, then the response is a generalised convolution of the input.

$$y(t) = h(u, \theta) + \varepsilon$$

$$h(u, \theta) = \sum_i \int_0^t \dots \int_0^t \kappa_i(\sigma_1, \dots, \sigma_i) u(t - \sigma_1), \dots, u(t - \sigma_i) d\sigma_1, \dots, d\sigma_i \quad (2)$$

$$\kappa_i(\sigma_1, \dots, \sigma_i, \theta) = \frac{\partial^i y(t)}{\partial u(t - \sigma_1), \dots, \partial u(t - \sigma_i)}$$

where $\kappa(\sigma_1, \dots, \sigma_n, \theta)$ is called the n -th order Volterra kernel. This equation may look complicated but it is just a generalization of a conventional convolution equation to second and high-orders and obtains from a simple Taylor expansion of Eq.(1). See Friston (2001) for a fuller discussion. This generalized convolution has an equivalent representation in the frequency or spectral domain. Introducing the spectral density representation $s(\omega)$

$$u(t) = \int s_u(\omega) e^{-j\omega t} d\omega \quad (3)$$

we can rewrite the Volterra expansion, Eq (2) as

$$h(u, \theta) = \sum_i \int_{-\pi}^{\pi} \dots \int_{-\pi}^{\pi} e^{j(\omega_1 + \dots + \omega_i)t} \Gamma_i(\omega_1, \dots, \omega_i) s_u(\omega_1), \dots, s_u(\omega_i) d\omega_1, \dots, d\omega_i \quad (4)$$

where the functions

$$\Gamma_1(\omega_1, \theta) = \int_0^{\infty} e^{-j\omega_1 \sigma_1} \kappa_1(\sigma_1) d\sigma_1$$

$$\Gamma_2(\omega_1, \omega_2, \theta) = \int_0^{\infty} \int_0^{\infty} e^{-j(\omega_1 \sigma_1 + \omega_2 \sigma_2)} \kappa_2(\sigma_1, \sigma_2) d\sigma_1 d\sigma_2$$

...

are the Fourier transforms of the kernels. These functions are called *generalized transfer functions* and mediate the expression of frequencies in the output given those in the input. Critically, the influence of high-order kernels, or equivalently generalized transfer functions means that a given frequency in the input can induce a *different* frequency in the output. A simple example of this would be squaring a sine wave input to produce an output of twice the frequency.

The duration and form of the resulting dynamics effect depends on the *dynamical stability* of the system to perturbations of its states (*i.e.* how the systems trajectories change with the state). Structural effects depend on structural stability (*i.e.* how the systems trajectories change with the parameters). Systematic changes in the parameters can produce systematic changes in the response, even in the absence of input. For systems that show autonomous (*i.e.* periodic or chaotic)

dynamics, changing the parameters is equivalent to changing the attractor manifold, which induces a change in the systems states. We before have discussed this in the context of nonlinear coupling and classical neuromodulation (Friston 1997, Breakspear *et al* 2003). For systems with fixed points and Volterra kernels, changing the parameters is equivalent to changing the kernels and transfer functions. This changes the spectral density relationships between the inputs and outputs. As such, structural effects are clearly important in the genesis of induced oscillations because they can produce frequency modulation of ongoing activity that does not entail phase locking to any event.

This difference between dynamic and structural effects is closely related to the distinction between linear and nonlinear mechanisms but they are not synonymous. The second-order approximation of Eq.(1) makes their relationship clear¹

$$\begin{aligned} \dot{x} &= u_D \partial f / \partial u_D + u_D^2 \partial^2 f / \partial u_D^2 + \dots \\ &\quad + (J + u_M \partial J / \partial u_M + \dots + x_1 \partial J / \partial x_1 + \dots)x \\ J &= \partial f / \partial x \end{aligned} \tag{5}$$

Here, J is the system's Jacobian. The top line encodes dynamic effects that are mediated by a dynamic input $u(t)_D$. This can have both linear and nonlinear components. The second line represents structural effects that are mediated by structural inputs $u(t)_M$. Here the input does not change the states directly but changes them indirectly by modulating the systems Jacobian (*i.e.* its dynamic structure). The matrices $\partial J(\theta) / \partial u_M$ could be regarded as parameters of the system or, more intuitively, as changes in the architecture induced by inputs. Critically, structural effects are always nonlinear and involve an interaction with the states. For readers familiar with dynamic causal modeling with the bilinear model, bilinear effects are structural effects. These effects are often construed as the modulation of a coupling, in a neuronal network, by an experimental input. In terms of the spectral formulation, structural inputs have only second or high-order kernels and associated transfer functions.

In summary, dynamic effects are expressed directly on the states and conform to a convolution of inputs to form responses. Structural effects are expressed indirectly, through the Jacobian, and are inherently nonlinear, inducing high-order kernels and associated transfer functions.

2.2 Drivers and modulators

The distinction between dynamic and structural inputs speaks immediately to the difference between 'drivers' from 'modulators' (Sherman and Guillery, 1998). In sensory systems, a driver ensemble can be identified as the transmitter of receptive field properties. For instance, neurons in the lateral geniculate nuclei drive primary visual area responses, in the cortex, so that retinotopic mapping is conserved. Modulatory effects are expressed as changes in certain aspects of information transfer,

¹ For simplicity we consider a single dynamic input u_D and a single modulatory input u_M , which could be the same *i.e.* $u_D = u_M$

by the changing responsiveness of neuronal ensembles in a context-sensitive fashion. A common example is attentional gain. Other examples involve extra-classical receptive field effects that are expressed beyond the classical receptive field. Generally, these are thought to be mediated by backward and lateral connections. In terms of synaptic processes, it has been proposed that the post-synaptic effects of drivers are fast (ionotropic receptors), whereas those of modulators are slower and more enduring (*e.g.* metabotropic receptors). The mechanisms of action of drivers refer to classical neuronal transmission, either biochemical or electrical, and are well understood. Conversely, modulatory effects can engage a complex cascade of highly nonlinear cellular mechanisms (Turrigiano and Nelson, 2004). Modulatory effects can be understood as transient departures from homeostatic states, lasting hundreds of milliseconds, due to synaptic changes in the expression and function of receptors and intracellular messaging systems.

Classical examples of modularity mechanisms involve voltage-dependent receptors, such as NMDA receptors. These receptors do not cause depolarisation directly (*c.f.* a dynamic effect) but change the units sensitivity to depolarisation (*i.e.* a structural effect). It is interesting to note that backward connections, usually associated with modulatory influences, target supragranular layers in the cortex where NMDA receptors are expressed in greater proportion.

Having established the difference between dynamics and structural effects and their relationship to driving and modulatory afferents in the brain, we now turn to the characterisation of evoked and induced responses in terms of time-frequency analyses.

2.3 Evoked and induced responses

The criterion that differentiates induced and evoked responses is the degree to which oscillatory activity is phase-locked to the stimulus over trials. An ERR is the waveform that is expressed in the EEG signal after every repetition of the same stimulus. Due to physiological and measurement noise, the ERR is often only evident after averaging over trials. More formally, the *evoked* response $y(t)_e$ to a stimulus is defined as the average of measured responses in each trial $y(t)$

$$y(t)_e = \langle y(t) \rangle \quad (6)$$

where t is peristimulus time.

A time-frequency representation $s(\omega, t)$ of a response $y(t)$ obtains by successively filtering $y(t)$ using a kernel or filter-bank parameterised by frequencies $\omega_j = 2\pi\nu_j$, over the frequency range of interest:

$$s(\omega, t) = \begin{bmatrix} k(\omega_1, t) \otimes y(t) \\ \vdots \\ k(\omega_j, t) \otimes y(t) \end{bmatrix} \quad (7)$$

where \otimes denotes linear convolution. $k(\omega_j, t)$ can take several forms (Kiebel *et al.*, submitted). We used the Morlet wavelet:

$$k(\omega_j, t) = \sqrt{v_j} \exp\left(-\frac{1}{2}\left(t v_j / \sigma\right)^2\right) \exp(i \omega_j t). \quad (8)$$

σ is a user-specified constant, which sets the number of cycles of the wavelet, and therefore the temporal and frequency resolution of the wavelet transform. The total power, averaged over trials and the power of the average are respectively

$$\begin{aligned} g(\omega, t)_T &= \langle s(\omega, t) s(\omega, t)^* \rangle \\ g(\omega, t)_e &= \langle s(\omega, t) \rangle \langle s(\omega, t)^* \rangle \end{aligned} \quad (9)$$

where $*$ denotes the complex conjugate. $g(\omega, t)_e$ is evoked power and is simply the power of $y(t)_e$. Induced power $g(\omega, t)_i$ is defined as the component of total power that cannot be explained by baseline and evoked power². This implicitly partitions total power into three orthogonal components (induced, baseline and evoked).

$$\begin{aligned} g(\omega, t)_i &= g(\omega, t)_T - g(\omega)_b - g(\omega, t)_e \\ g(\omega, t)_T &= g(\omega, t)_i + g(\omega, t)_e + g(\omega)_b \end{aligned} \quad (10)$$

Baseline power $g(\omega)_b$ is a frequency-specific constant due to ongoing activity and experimental noise, both of which are assumed to be stationary, that is usually calculated over a period of time preceding stimulus presentation.

2.4 Evoked and induced power and their mechanisms of generation

In this subsection we establish how dynamic and structural mechanisms are expressed in terms of evoked and induced power. As illustrated in Figure 1, the inputs for the i -th trial $u^{(i)}$ can be decomposed into a deterministic stimulus-related component α and trial-specific background activity $\beta^{(i)}$, which is stochastic and unrelated to the stimulus

$$u^{(i)} = \alpha + \beta^{(i)}. \quad (11)$$

² A different definition is sometimes used, where induced responses are based on the difference in amplitude between single-trials and the ERR: $y(t) - y(t)_e$ (Truccolo *et al.*, 2002). The arguments in this work apply to both formulations. However, it is simpler for us to use Eq.(10) because it discounts ongoing activity. This allows us to develop the arguments by considering just one trial-type (a opposed to differences between trial types)

For simplicity, we will assume that the state-space defined by Eq.(1) operates largely in its linear regime, as suggested by studies which have found only weak nonlinearities in EEG oscillations (Breakspear and Terry, 2002; Stam et al., 1999). This allows us to focus on the first-order kernels and transfer functions. We will also assume the background activity is stationary. In this instance, the total power is, by Eq.(4)

$$\begin{aligned} g(\omega, t)_T &= |\Gamma(\omega, t)|^2 g(\omega, t)_u + g(\omega)_\varepsilon \\ g(\omega, t)_u &= g(\omega, t)_\alpha + g(\omega)_\beta \end{aligned} \quad (12)$$

In words, the total power is the power of the input, modulated by the transfer function $|\Gamma(\omega, t)|^2$, plus the power of the noise term. The power of the input is simply the power of the deterministic component, at time t , plus the power of ongoing activity. The evoked power is simply the power of the input, because the noise and background terms are suppressed by averaging

$$\begin{aligned} g(\omega, t)_e &= |\Gamma(\omega, t)|^2 \langle s(\omega, t)_\alpha \rangle \langle s(\omega, t)_\alpha^* \rangle \\ &= |\Gamma(\omega, t)|^2 g(\omega, t)_\alpha \end{aligned} \quad (13)$$

The baseline power at $t = t_0$ is

$$g(\omega)_b = |\Gamma(\omega, t_0)|^2 g(\omega)_\beta + g(\omega)_\varepsilon \quad (14)$$

This means that induced power is

$$g(\omega, t)_i = (|\Gamma(\omega, t)|^2 - |\Gamma(\omega, t_0)|^2) g(\omega)_\beta \quad (15)$$

This is an important result. It means that the only way induced power can be expressed is if the transfer function $\Gamma(\omega, t, \theta)$ changes at time t . This can only happen if the parameters of the neuronal system change. In other words, only structural effects can mediate induced power. However, this does not mean to say that structural effects are expressed only in induced power. They can also be expressed in the evoked power: Eq.(13) shows clearly that evoked power at a particular point in peri-stimulus time depends on both $g(\omega, t)_\alpha$ and $\Gamma(\omega, t, \theta)$. This means that structural effects mediated by changes in the transfer function can be expressed in evoked power, provided $g(\omega, t)_\alpha > 0$. In other words, structural effects can modulate the expression of stationary components due to ongoing activity and also deterministic components elicited dynamically. To summarize so far:

- Dynamic effects (of driving inputs) conform to a generalized convolution of inputs to form the systems response
- Structural effects can be formulated as a time-dependent change in the parameters (that may be mediated by modulatory inputs). This translates into time-dependent change in the convolution kernels and ensuing response.
- If the ongoing activity is non-zero and stationary, only structural effects can mediate induced power
- If stimulus-related input is non-zero, structural effects can also mediate evoked power, *i.e.* dynamic and structural effects can conspire to produce evoked power.

In the next section we demonstrate these theoretical considerations in a practical setting, using a neural mass model of event-related responses. In this section and in the simulations below, we have only considered effect of a single trial-type. In practice, one would normally compare the responses evoked and induced by two trial types. However, the conclusions are exactly the same in both contexts. One can regard the simulations below as a comparison of one trial-type to a baseline that caused no response (and had no baseline power).

3. Modelling induced oscillations

3.1 Neural-mass models

The classical approach to modeling MEG/EEG signals is to use neural mass models (Freeman, 1978; Lopes da Silva et al., 1974; Robinson et al., 2001). The idea is to model the state of a neuronal assembly, *i.e.* thousands of identical neurons, using operations that describe the mean input-output relationships. For example, one can summarize the state of a neuronal assembly with its mean membrane potential and firing rate. The expected potential can be obtained using a linear convolution of the mean firing rate with a gamma function. This function can be understood as the postsynaptic potential impulse response function. The output of the neuronal assembly is a mean firing rate, which is a nonlinear (sigmoid) function of the mean membrane potential. There are several models of MEG activity that are based upon this approach. In particular, the Jansen model (Jansen and Rit, 1995) mimics the canonical architecture of a mini-column, which can be treated as a cortical source. The Jansen model comprises three neuronal populations: excitatory and inhibitory interneurons and pyramidal cells. The MEG/EEG signal is assumed to be proportional to the depolarisation of pyramidal cells. The parameters of the model are the synaptic time constants, efficacies and coupling parameters that control the intrinsic connections within a source and extrinsic connections among sources. This model and various extensions have been used to simulate oscillatory activity (David and

Friston, 2003; David et al., 2004; Jansen and Rit, 1995), evoked responses (Jansen and Rit, 1995; David et al., in press) and epileptic activity (Wendling et al., 2000).

Here we model MEG/EEG signals using the Jansen model (Jansen and Rit, 1995), extended to cover neuronal ensembles with different kinetics (David and Friston, 2003) and extrinsic cortico-cortical connections (David *et al.*, in press; Crick and Koch, 1998). This model defines the state equation and observer in Eq.(1). The details of these equations are not important in the present context. A detailed description of the model can be found in David et al. (2005) and the Matlab scripts are also available to download from www.fil.ion.ucl.ac.uk/spm (as part of the DCM for ERPs toolbox; e.g., `spm_erp_fx.m`)

The model used here does not model explicitly the diversity of neuronal subpopulations and their processes, such as glial-neuron interactions. However, because the Jansen model is a lumped representation of diverse processes, one explicit parameter, such as coupling between regions, can be understood as representing diverse phenomena. For instance, when we manipulate coupling parameters, we explicitly modify the efficacy of cortico-cortical connections. The neural mechanisms responsible for this increase of connection strength are diverse: modulation of transmitter release, modulation of local synchronisation due to glial cells, *etc.* These relatively fine-scale processes are not included in the Jansen model, but the mean field approximation of neural mass models can, in many instances, capture the dynamics that emerge. We chose Jansen's neural mass model of EEG because there has been a considerable amount of work showing that it can reproduce most of the phenomena and dynamics seen in real EEG data.

The key thing is that the model has a relatively high degree of face validity, when it comes to modelling neuronal dynamics and, critically, allows selective dynamic or structural perturbation.

We consider a simple model composed of two sources, inter-connected with forward and backward connections (Figure **1B**). The sources receive two types of inputs. The first models afferent activity that delivers dynamic perturbations to the systems states (by changing post-synaptic currents). This dynamic perturbation had stochastic and deterministic components: background inputs $\beta^{(i)}$ comprised Gaussian noise that was delivered to both sources. The deterministic part modelled a stimulus with an impulse $\alpha(t) = \delta(t)$, delivered to the first source at the beginning of each trial. The second sort of input $u(t)_M$ induced a structural change by modulating extrinsic connections. As one might expect, the effects of these two input classes differ considerably. On the one hand, synaptic inputs perturb the system nearly instantaneously and the deterministic part evokes responses that are phase-locked to the stimulus. On the other hand, modulatory inputs modify the manifold that attracts ongoing activity, without necessarily resetting its phase. For simplicity, we restrict our modulatory effects to a modulation of the extrinsic backward connection, thus encompassing various synaptic mechanisms which modify the gain of excitatory synapses (Salinas and Theier, 2000). We chose this form of modulation because it was the simplest. Structural perturbations change the systems

parameters (*i.e.*, coupling parameters modelling synaptic efficacy). We elected to change one extrinsic connection; the backward connection. We chose the backward connection because backward connections are associated with modulatory effects, both in terms of physiology (e.g., the mediation of extra-classical receptive field effects, see also Allman et al 1985 and Murphy et al 1999) and anatomy (e.g., they terminate in supragranular layers that expressed large number of voltage-dependent NMDA receptors). See also Maunsell & van Essen, (1983) and Angelucci, *et al* (2002).

There may be many other modulatory mechanisms that will produce the same pattern of oscillatory activity and it will be an interesting endeavour to disambiguate the locus of structural changes using these sorts of models and empirical data (see David *et al* in press).

3.2 Structural perturbation and induced oscillations

We assume that the stimulus engages a cascade of neural events, involving recurrent hierarchical dynamics that modulates the systems structure. This is modelled by the deterministic modulatory input $u(t)_M$. In our model (Figure 1B), this increases the strength of backward connections between the sources. This could be regarded as modelling voltage-dependence in a massive pool of NMDA receptors located in the supragranular targets of backward connections; although many other mechanisms could be approximated by such changes in connectivity. In this example, we use the following structural perturbation

$$\begin{aligned} \theta(t)_B &= \theta_B(1 + u(t)_M) \\ u(t)_M &= \begin{cases} \frac{(t-t_0)}{\tau} \exp(-\frac{(t-t_0)}{\tau}) & t \geq t_0 \\ 0 & t < t_0 \end{cases} \end{aligned} \quad (16)$$

where t_0 and τ are the onset and time-constant of the modulating input, respectively. This input acts on the parameter θ_B of the state equation to smoothly modify the convolution of ongoing and driving inputs.

To illustrate the points of the previous section, we will consider two scenarios in which the modulatory effect arrives at the same time as the driving input and one in which it arrives after the dynamic perturbation has dissipated. Let us assume that the modulatory input has a slow time-constant $\tau = 150ms$ compared to the main frequency of ongoing oscillations (10Hz). The modulatory effects can be expressed with stimulus onset, or after some delay. In the first case, evoked oscillations will be modulated and these effects will be visible in the ERR. In the second case, phase-locking with the stimulus will have been lost and no effect will be seen in the ERR. However, in both cases, structural changes will appear as induced oscillations. This is illustrated in Figure 2 (using 500 trial-averages). In the upper panel we consider a modulatory input immediately after stimulus onset. As expected, evoked responses are much more pronounced relative to delayed modulation (lower panel). The induced power (C) shows that increases in the backward connection induce oscillations

in the alpha and gamma band. The induced power in Figure 2 has been frequency normalised (by removing the mean and dividing by the standard deviation at $t = 0$) to show increased power in the gamma band more clearly.

These simulations provide a nice model for induced responses using a structural perturbation, in this instance a slow modulation of the efficacy of backward connections in a simple hierarchy of neuronal populations. Critically, these simulations also show that responses can be evoked structurally by a modulation of dynamic perturbations. This dual mechanism depends on driving and modulatory effects occurring at the same time, causing evoked and induced responses in the same time-frequency window.

3.3 Structurally evoked responses and phase-resetting

Phase-resetting is a popular perspective on mechanisms responsible for evoked responses (David et al in press; Makeig et al., 2002;; Klimesh et al 2004). Phase-resetting is inferred when there is a phase-locking of responses, with no change in their amplitude. It is tempting to formulate phase-resetting in terms of dynamic and structural mechanisms and, in particular, the appearance of evoked responses that are mediated by structural mechanisms, as in Figure 2. We have argued previously (David *et al* in press) that phase-resetting entails an interaction between the input and the neuronal state of an ensemble (e.g. the phase of ongoing oscillations). The response component $u(t)_M \partial J / \partial u(t)_M x$ in Eq.(5) embodies this interaction. This means phase-resetting is a structural effect that is mediated by a deterministic, modulatory, component of the input.

However, the joint expression of evoked and induced responses does not imply phase-resetting. This is because phase-resetting is a very specific structural mechanism that entails a *reduction* of induced power. The reason is simple; if the stimulus does not change the amplitude of oscillations, the total power will be constant over peristimulus time. Phase-resetting will increase evoked power. Because induced power is the total power that cannot be explained by evoked and baseline power, it must fall. This provides the basis for a test for phase-resetting, which we will pursue in a later communication. Note that analyses framed in terms of phase-distributions over trials (*i.e.*, phase re-setting analyses) discount amplitude variations and assume that differences in phase-distributions are not mediated by amplitude differences.

Having established that evoked responses can be mediated by structural mechanisms we now show that induced responses can be mediated by dynamic mechanisms.

Figure 2 about here

4. Induced oscillations and trial-to-trial variability

Above we have considered the stimulus as a deterministic input. In this section we consider what would happen if the stimulus-related input was stochastic. This randomness is most easily understood in terms of trial-to-trial variability in the inputs. Following (Truccolo et al., 2002), we examine two random aspects of inputs, namely stochastic variations in gain and latency. We derive equations that predict the effects of this variability on evoked and induced responses and we test the predictions using the model of the previous section.

4.1 Trial-to-trial variability

As suggested in (Truccolo et al., 2002), we consider two types of variability in the input. The first relates to a trial-to-trial gain, or amplitude variations. For an identical stimulus, early processing may introduce variations in the amplitude of driving inputs to a source. Gain modulation is a ubiquitous phenomenon in the central nervous system (Salinas and Thier, 2000) but its causes are not completely understood. Two neurophysiological mechanisms that may mediate gain modulation include fluctuations of extra-cellular calcium concentration (Smith et al., 2002) and/or of the overall level of synaptic input to a neuron (Chance et al., 2002). These may act as a gain control signal that modulates responsiveness to excitatory drive. A common example of gain effects, in a psychophysiological context, is the effect of attention (McAdams and Maunsell, 1999; Treue and Martinez-Trujillo, 1999).

The second commonly observed source of variability is in the latency of input onset, *i.e.* the time between the presentation of the stimulus and the peak response of early processing. Azouz and Gray (1999) have investigated the sources of such latency variations at the neuronal level. Basically, they describe two major phenomena: (i) coherent fluctuations in cortical activity preceding the onset of a stimulus have an impact on the latency of neuronal responses (spikes). This indicates that the time needed to integrate activity to reach action potential threshold varies between trials. (ii) The other source of latency variability is fluctuations in the action potential threshold itself.

Both types of trial-to-trial variability, gain modulation and latency, can be modelled by introducing the random variables γ and τ with density functions $p(\gamma)$ and $p(\tau)$. In the context of random latencies, the expected Fourier transform of the stimulus-related component is modulated by the Fourier transform $s(\omega)_\tau$ of the probability density $p(\tau)$ ³

$$\begin{aligned}
s(\omega, t, \tau)_\alpha &= \int k(\omega, \sigma) \alpha(t - \sigma - \tau) d\sigma \\
\langle s(\omega, t, \tau)_\alpha \rangle &= \iint p(\tau) k(\omega, \sigma) \alpha(t - \sigma - \tau) d\sigma d\tau \\
&= \iint p(\tau) \exp(j\omega\tau) k(\omega, \sigma - \tau) \alpha(t - \sigma - \tau) d\sigma d\tau \\
&= \int p(\tau) \exp(j\omega\tau) d\tau \int k(\omega, \sigma - \tau) \alpha(t - \sigma - \tau) d\sigma \\
&= s(\omega)_\tau s(\omega, t)_\alpha
\end{aligned} \tag{17}$$

This is known as the characteristic function

$$s(\omega)_\tau = \int p(\tau) \exp(j\omega\tau) d\tau \quad (18)$$

A very tight latency distribution makes $g(\omega)_\tau = s(\omega)_\tau s(\omega)_\tau^*$ very broad over frequency and its effect is negligible. However, if the latencies are more dispersed the modulation by the characteristic function become tighter with a suppression of high frequencies. In terms of evoked responses

$$\begin{aligned} g(\omega, t)_e &= |\Gamma(\omega, t)|^2 \langle s(\omega, t, \tau)_\alpha \rangle \langle s(\omega, t, \tau)_\alpha^* \rangle \\ &= |\Gamma(\omega, t)|^2 g(\omega)_\tau g(\omega, t)_\alpha \end{aligned} \quad (19)$$

This equality shows that high frequency components are lost when latency varies randomly over trials. This means that ERR will be estimated badly at high frequencies. This variation effectively blurs or smoothes the average, and suppresses fast oscillations in the evoked response. However, the total power remains unchanged, because the power expressed in each trial does not depend on latency. Therefore the high frequencies lost from the evoked responses now appear in the induced response

$$\begin{aligned} g(\omega, t)_i &= (|\Gamma(\omega, t)|^2 - |\Gamma(\omega, t_0)|^2) g(\omega)_\beta + \eta g(\omega, t)_e \\ \eta &= \frac{1 - g(\omega)_\tau}{g(\omega)_\tau} \end{aligned} \quad (20)$$

In summary, the induced power has now acquired a stimulus-locked component. This component gets bigger as the dispersion of latencies increases and $g(\omega)_\tau$ get smaller. Note that this dynamically induced power can only be expressed in frequencies that show evoked responses, because both depend on $g(\omega, t)_\alpha$, the power in the stimulus-locked input.

A similar analysis can be pursued for variations in gain. Here we will assume, by definition $\langle \gamma \rangle = 1$

$$\begin{aligned} s(\omega, t, \gamma)_\alpha &= \gamma s(\omega, t)_\alpha \\ \langle s(\omega, t, \gamma)_\alpha \rangle \langle s(\omega, t, \gamma)_\alpha^* \rangle &= \langle \gamma \rangle^2 g(\omega, t)_\alpha = g(\omega, t)_\alpha \\ \langle s(\omega, t, \gamma)_\alpha s(\omega, t, \gamma)_\alpha^* \rangle &= \langle \gamma^2 \rangle g(\omega, t)_\alpha \end{aligned} \quad (21)$$

Giving

³ We have assumed here and below that the variation in latency is small in relation to the length of the wavelet used in the time-frequency decomposition.

$$g(\omega, t)_i = (|\Gamma(\omega, t)|^2 - |\Gamma(\omega, t_0)|^2)g(\omega)_\beta + \eta g(\omega, t)_e$$

$$\eta = \text{Var}(\gamma)$$
(22)

Gain variations also allow non-structural mechanisms to induce power. Here the time-dependent changes in stimulus-dependent power $g(\omega, t)_\alpha$ again contribute to induced responses. In this instance the contribution is not frequency specific, as with latency variations, but proportional to the variance in gain $\text{Var}(\gamma) = \langle \gamma^2 \rangle - 1$. To summarize:

- Induced power can be mediated by non-structural mechanisms if dynamic responses are caused by inputs that vary over trials
- Latency variations in stimulus-locked inputs effectively suppress high frequencies in the average that are effectively transferred from the evoked power to the induced power.
- Amplitude variations in stimulus-locked inputs do not affect evoked responses but cause evoked power to be recapitulated in the induced power as the variance of the amplitude increases.

We now illustrate these phenomena using simulations.

4.2 Simulations of dynamically induced responses

To ensure that any induced power in the simulations could not be mediated structurally we removed both the modulatory and stochastic input. Therefore, there were no structurally mediated changes in the systems manifold or kernels and, even if there were, they would not be seen because there was no ongoing activity. This means that any induced power must be caused dynamically. 2000 trials were simulated with variations in latency and gain respectively.

Figure 3 about here

First we simulated a pure latency jittering, without gain modulation (Figure 3). The stimulus onset latency $p(\tau) = N(0, \sigma_\tau^2)$ was sampled from a Gaussian distribution with zero mean and standard deviation $\sigma_\tau = 10$ ms. The upper left panel shows the event-related and evoked responses for a single trial. The black curve is the response of area 1; the grey curve is the response of area 2. These responses would constitute the ERR, after averaging, without trial-to-trial variability. The time-frequency decomposition of the response of area 1 shows two blobs; one located in the alpha band (around 10 Hz), the other in the gamma band (around 30 Hz). These correspond to the responses of

specific neuronal subpopulations. Figure **3B** shows the event-related and evoked responses after averaging over all trials. Latency variation causes evoked power to be lost at high frequencies, as it is smoothed away in the average (compare the evoked responses in panel **B** with the single-trial or total power in panels **A** and **C**). The lost power now appears in the induced responses, more markedly at higher frequencies (gamma band in Figure **3D**). This dynamically induced response has to occur at the same time as the evoked response but is expressed in higher frequencies.

Figure 4 about here

Finally, variation in gain was simulated. The gain γ for each trial was drawn from a lognormal distribution $p(\ln \lambda) = N(0, 0.36)$. Figure 4 summarises the results of these simulations using the same format as the previous figure. Figure **4B** shows the event-related and evoked responses after averaging over all trials. As expected, there is no significant difference between these evoked responses and the canonical, single-trial response in Figure **4A**. However the induced power (**D**) is not zero and, as predicted, formally very similar to the evoked-power. Critically, the induced and evoked responses generated by this mechanism have the same time-frequency deployment.

4. Discussion

4.1 Summary

In summary, we made a distinction between dynamic and structural mechanisms that underlie transient responses to perturbations. We then considered how responses are measured in time-frequency in terms of evoked and induced responses. Theoretical predictions, confirmed by simulations, show that there is no simple relationship between the two mechanisms causing responses and the two ways in which they are characterised. Specifically, evoked responses can be mediated both structurally and dynamically. Similarly, if there is trial-to-trial variability, induced responses can be mediated by both mechanisms. See figure 5 for a schematic summary.

Figure 5 about here

For evoked responses this is not really an issue. The fact that evoked responses reflect both dynamic and structural perturbations is sensible, if one allows for the fact that any input can have dynamic and structural effects. In other words, the input perturbs the states of the neuronal system and, at the same time, modulates interactions among the states. The structural component here can be viewed as a nonlinear (e.g. bilinear) effect that simply involves interactions between the input and parameters (e.g. synaptic status). Generally, the structurally mediated component of evoked responses will occur at the same time and frequency as the dynamically mediated components. This precludes ambiguity when interpreting evoked responses, if one allows for both dynamic and structural causes.

The situation is more problematic for induced responses. In the absence of trial-to-trial variability induced responses must be caused by structural perturbations. Furthermore, there is no necessary co-localisation of evoked and induced responses in time-frequency, because induced responses are disclosed by ongoing activity. However, if trial-to-trial variability is sufficient, induced responses with no structural component will be expressed. This means that induced responses that occur at the same time as evoked responses have an ambiguity in relation to their cause. Happily, this can be addressed at two levels. First, induced responses that do not overlap in peristimulus time cannot be attributed to dynamic mechanisms and are therefore structural in nature. Second, one can re-visit the operational definition of induced responses to derive a measure that is immune to the effects of trial-to-trial variability. Note that here we do not consider that the baseline activity is affected directly by the stimulus, but interacts with stimulus-dependent structural mechanisms to produce an induced response component. Clearly, this component will then form the input to other regions.

4.2 Adjusted power

In this subsection we introduce the notion of adjusted power as a complementary characterisation of structurally mediated responses. Adjusted power derives from a slightly more explicit formulation of induced responses as that component of total power that cannot be explained by evoked or ongoing activity. The adjusted response is simply the total power orthogonalised, at each frequency, with respect to baseline and evoked power.

$$\begin{aligned}
 g(\omega, t)_a &= g(\omega, t)_T - g(\omega, t)\hat{\eta} \\
 \hat{\eta} &= g(\omega, t)^+ g(\omega, t)_T
 \end{aligned}
 \tag{23}$$

$$g(\omega, t) = \begin{bmatrix} 1 & g(\omega, t_1)_e \\ \vdots & \vdots \\ 1 & g(\omega, t_T)_e \end{bmatrix}$$

+ denotes the pseudoinverse. Note that the evoked power has been augmented with a constant that models baseline power. This means baseline power does not have to be estimated explicitly. The motivation for this linear adjustment is inherent in Equations 20 and 22, which show that the confounding effects of trial-to-trial variability are expressed in proportion to evoked power. Eq. (23) is implicitly estimating baseline power and the contribution from evoked power and removing them from the total power. In other words, $\hat{\eta}$ is a 2-vector estimate of $g(\omega)_b$ and $(1 + \eta)$. After these components have been removed the only components left must be structural in nature

$$g(\omega, t)_a \approx (|\Gamma(\omega, t)|^2 - |\Gamma(\omega, t_0)|^2)g(\omega)_\beta
 \tag{24}$$

Figure 6 shows that the effect of trial-to-trial variability on induced responses disappears when using adjusted power. This means one can unambiguously attribute adjusted responses to structural mechanisms. As noted by one of our reviewers the ERP-adjusted response removes evoked response components, including those mediated by structural changes. However, structurally mediated induced components will not be affected unless they have the same temporal expression. The usefulness of adjusted power, in an empirical setting will be addressed in future work. The treatment in this paper can be regarded as establishing its motivation.

Figure 6 about here

4.3 Conclusion

We have divided neuronal mechanisms into dynamic and structural, which may correspond to driving and modularity neurotransmitter systems respectively. These two sorts of effects are not equivalent to evoked and induced responses in MEG/EEG. By definition, evoked responses exhibit phase-locking to a stimulus whereas induced responses do not. Consequently, averaging over trials discounts both ongoing and induced components and evoked responses are defined by the response averaged over trials. Evoked responses may be mediated primarily by driving inputs. In MEG/EEG, driving inputs affect the state of measured neuronal assemblies, i.e. the dendritic currents in thousands of pyramidal cells. In contradistinction, structural effects, mediated by modulatory inputs engage neural mechanisms which affect neuronal states, irrespective of whether they are phase-locked to the stimulus or not. These inputs are expressed formally as time-varying parameters of the state equations modelling the systems. Although the ensuing changes in the parameters may be slow and enduring their effects on ongoing or evoked dynamics may be expressed as fast or high frequency dynamics.

We have considered a further cause of induced oscillations; namely trial-to-trial variability of driving inputs. As suggested in (Truccolo et al., 2002), these can be modelled by varying latency and gain. We have shown that (i) gain variations have no effect on the ERR but increase induced responses in proportion to evoked responses, (ii) jitter in latency effectively smoothes the evoked responses and transfers energy from evoked to induced power, preferentially at higher frequencies.

The conclusions of this work, summarised in Figure 5, provide constraints on the interpretation of evoked and induced responses in relation to their mediation by dynamic and structural mechanisms. This is illustrated by the work of Tallon-Baudry and colleagues, who have looked at non-phase-locked episodes of synchronisation in the gamma-band (30-60 Hz). They have emphasised the role of these induced responses in feature-binding and top-down mechanisms of perceptual synthesis. The top-down aspect is addressed by their early studies of illusory perception (Tallon-Baudry *et al* 1996), where the authors "tested the stimulus specificity of high-frequency oscillations in humans using three types of visual stimuli: two coherent stimuli (a Kanizsa and a real triangle) and a non-coherent stimulus." They found an early phase-locked 40 Hz component, which did not vary with stimulation

type and a second 40 Hz component, appearing around 280 msec, that was not phase-locked to stimulus onset. This shows a nice dissociation between early evoked and late induced responses. The induced component was stronger in response to a coherent triangle, whether real or illusory and: "could reflect, therefore, a mechanism of feature binding based on high-frequency synchronisation". Because it was late, the induced response can only be caused by structural mechanisms (see Figure 5). This is consistent with the role of top-down influences and the modulatory mechanisms employed by backward connections in visual synthesis (Maunsell & van Essen, 1983, Bullier et al 2001, Albright & Stoner 2002).

Classical ERP/ERF research has focused on dynamic perturbations (Coles and Rugg, 1995). On the other hand, studies of event-related synchronisation (ERS) or desynchronization (ERD) are more concerned with structural effects that may be mediated by modulatory systems (Pfurtscheller and Lopes da Silva, 1999). Practically speaking, we have shown that it is not always possible to distinguish between dynamic and structural effects when inferring the causes of evoked and induced oscillations. However, certain features of induced oscillations might provide some hints: (i) induced oscillations in high frequencies concomitant with evoked responses in low frequencies may indicate a jittering of inputs. (ii) Induced oscillations that are temporally dissociated from evoked responses are likely to be due to modulatory or structural effects. Finally, we have introduced the notion of adjusted power that can be unambiguously associated with structural effects.

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References

- Albright, T. D. & Stoner, G. R. 2002. Contextual influences on visual processing. *Annu Rev Neurosci* 25, 339-79
- Allman, J., Miezin, F. & McGuinness, E. 1985. Stimulus specific responses from beyond the classical receptive field: neurophysiological mechanisms for local-global comparisons in visual neurons. *Annu Rev Neurosci* 8, 407-30
- Angelucci, A., Levitt, J. B. & Lund, J. S. 2002 Anatomical origins of the classical receptive field and modulatory surround field of single neurons in macaque visual cortical area V1. *Prog Brain Res* 136, 373-88
- Azouz, R., and Gray, C.M. 1999. Cellular mechanisms contributing to response variability of cortical neurons in vivo. *J. Neurosci.* 19(6):2209-2223.
- Breakspear, M., and Terry, J.R. 2002. Detection and description of non-linear interdependence in normal multichannel human EEG data. *Clin. Neurophysiol.* 113:735-753.
- Bullier, J., Hupe, J. M., James, A. C. & Girard, P. 2001. The role of feedback connections in shaping the responses of visual cortical neurons. *Prog Brain Res* 134, 193-204
- Chance, F.S., Abbott, L.F., and Reyes, A.D. 2002. Gain modulation from background synaptic input. *Neuron.* 35(4):773-782.
- Coles, M.G.H., and Rugg, M.D. 1995. Event-related brain potentials: An introduction. In: *Electrophysiology of mind* (Rugg MD, Coles MGH, eds), pp 1-26. Oxford: Oxford University Press.
- Crick, F., and Koch, C. 1998. Constraints on cortical and thalamic projections: the no-strong-loops hypothesis. *Nature.* 391:245-250.
- David, O., and Friston, K.J. 2003. A neural mass model for MEG/EEG: coupling and neuronal dynamics. *Neuroimage.* 20:1743-1755.
- David, O., Cosmelli, D., and Friston, K.J. 2004. Evaluation of different measures of functional connectivity using a neural mass model. *Neuroimage.* 21:659-673.
- David, O., Harrison, L., and Friston, K.J. In press. Modelling event-related responses in the brain. *NeuroImage.*
- David, O., Kiebel, S.J., Harrison, L.M., Mattout, J., Kilner, J.M., and Friston, K.J. Submitted. Dynamic causal modelling of evoked responses in EEG and MEG. *Neuroimage in Press*

- Freeman,W.J. 1978. Models of the dynamics of neural populations. *Electroencephalogr. Clin. Neurophysiol.* [Suppl] 34:9-18.
- Friston KJ. Brain function, nonlinear coupling, and neuronal transients *Neuroscientist*. 2001 Oct;7(5):406-18.
- Friston KJ. Transients metastability and neuronal dynamics *NeuroImage* 1997;5:164-171
- Galambos,R. 1992. in *Induced Rhythms in the Brain* (Basar, E. and Bullock, T.H., eds), pp. 201–216, Birkhauser.
- Kiebel,S.J., Tallon-Baudry,C., and Friston,K.J. submitted. Analysis of oscillatory activity as measured with EEG/MEG using Statistical Parametric Mapping. *NeuroImage*.
- Klimesch,W., Schack,B., Schabus,M., Doppelmayr, M., Gruber, W., and Sauseng, P. 2004. Phase-locked alpha and theta oscillations generate the P1–N1 complex and are related to memory performance. *Brain Res. Cogn. Brain Res.* 19:302-316.
- Lopes da Silva,F.H., Hoeks,A., Smits,H., and Zetterberg,L.H. 1974. Model of brain rhythmic activity. The alpha-rhythm of the thalamus. *Kybernetik*. 15:27-37.
- Makeig,S., Westerfield,M., Jung,T.P., Enghoff,S., Townsend,J., Courchesne,E., and Sejnowski,T.J. 2002. Dynamic brain sources of visual evoked responses. *Science*. 295:690-694.
- Maunsell, J. H. & van Essen, D. C. 1983. The connections of the middle temporal visual area (MT) and their relationship to a cortical hierarchy in the macaque monkey. *J Neurosci* 3, 2563-86
- McAdams,C.J., and Maunsell,J.H.R. 1999. Effects of attention on orientation-tuning functions of single neurons in macque cortical area V4. *J. Neurosci*. 19:431:441.
- Murphy, P. C., Duckett, S. G. & Sillito, A. M. 1999. Feedback connections to the lateral geniculate nucleus and cortical response properties. *Science* 286, 1552-4.
- Pfurtscheller,G., and Lopes da Silva,F.H. 1999. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clin. Neurophysiol*. 110:1842-1857.
- Robinson,P.A., Rennie,C.J., Wright,J.J., Bahramali,H., Gordon,E., and Rowe,D.L. 2001. Prediction of electroencephalographic spectra from neurophysiology. *Phys. Rev. E*. 63:021903.
- Salinas,E., and Their,P. 2000. Gain modulation: a major computation principle of the central nervous system. *Neuron*. 27:15-21.
- Sherman,S.M., and Guillery,R.W. 1998. On the actions that one verve cell can have on another: Distinguishing “drivers” from “modulators”. *Proc. Nat. Acad. USA*. 95:7121-7126.

- Singer,W., and Gray,C.M. 1995. Visual feature integration and the temporal correlation hypothesis. *Annu. Rev. Neurosci.* 18:555-586.
- Smith,M.R., Nelson,A.B., and Du Lac,S. 2002. Regulation of firing response gain by calcium-dependent mechanisms in vestibular nucleus neurons. *J. Neurophysiol.* 87:2031-2042.
- Stam,C.J., Pijn,J.P.M., Suffczynski,P. and Lopes da Silva,F.H. 1999. Dynamics of the human alpha rhythm: evidence for non-linearity? *Clin. Neurophysiol.* 110:1801-1813.
- Tallon-Baudry C, Bertrand O, Delpuech C, Pernier J. 1996. Stimulus specificity of phase-locked and non-phase-locked 40 Hz visual responses in human J Neurosci. 16(13): 4240-9
- Tallon-Baudry,C., and Bertrand,O. 1999. Oscillatory gamma activity in humans and its role in object representation. *Trends Cogn. Sci.* 3(4):151-162.
- Treue,S., and Martinez-Trujillo,J.C. 1999. Feature-based attention influences motion processing gain in macaque visual cortex. *Nature.* 399:575:579.
- Truccolo,W.A., Ding,M., Knuth,K.H., Nakamura,R., and Bressler,S.L. 2002. Trial-to-trial variability of cortical evoked responses: implications for the analysis of functional connectivity. *Clin. Neurophysiol.* 113:206-226.
- Turrigiano,G.G., and Nelson,S.B. 2004. Homeostatic plasticity in the developing nervous system. *Nat. Rev. Neurosci.* 5:97:107.
- Varela,F.J. 1995. Resonant cell assemblies: A new approach to cognitive functions and neural synchrony. *Biol. Res.* 28:81-95.
- Wendling,F., Bellanger,J.J., Bartolomei,F., and Chauvel, P. 2000. Relevance of nonlinear lumped-parameter models in the analysis of depth- EEG epileptic signals. *Biol. Cybern.* 83:367-378.