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Volterra-Hansen theory of event-related transients modulated by inter-event intervals

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Abstract. Cognitive neuroscientists often conduct trial-based experiments, having two or more events (e.g., sensory stimulus and motor response) per trial, conjointly with neurophysiological time series acquisition and analysis of event-related transient brain activity. Hansen decomposition [Hansen, 1983] is a frequency-domain technique for separating multiple overlapping event-related transients. However, the theory assumes that the brain is a linear system and, consequently, that event clusters within a trial are not associated with interactive (e.g., sensorimotor integrative) brain processes. The Volterra theory of nonlinear systems includes linear systems as a first approximation, adding higher-order correction terms to accommodate interactions. This paper presents an event-related specialization of Volterra models, and formulates how the kernels which characterize such models may be estimated from multi-trial data via Hansen's computationally efficient approach. Volterra-Hansen estimation of primary event-related transients and secondary inter-event modulations makes demands on experimental design, which may be evaluated prior to physiological acquisition. Methods for analysis and source estimation of event-related transients may also be applied to inter-event modulations, thereby facilitating the study and localization of integrative processes in the brain.

Keywords: Trial-Based Cognitive Paradigm; ERP; ERF; Overlapping Waveform Separation; Nonlinear System Identification

1. Introduction

Experimental paradigms designed with multi-event trials (e.g., cue-stimulus-response) are commonly used in cognitive neuroscience in conjunction with brain physiology measures such as event-related electric potentials (ERPs) and magnetic fields (ERFs). Simple averaging of physiological data epochs across trials after alignment to selected events has been the primary technique for estimating transient waveforms that reflect brain activity which is coupled in phase to experimental events. However, event-related transients are likely to overlap in time within each trial (e.g., a cue-related transient may overlap with a stimulus-related transient which may overlap with a response-related transient). In addition, the brain naturally *relates* different events within a trial so that, in some sense, the events (or their representations) *interact* in the brain. For example, the brain mediates a behavioral response to a sensory stimulus in the context of an informative cue. The cognitive neuroscientist's main interest may be precisely with how the brain handles such inter-event relationships. Yet, if the brain were simply a linear system—in which case cue-related, stimulus-related, and response-related transients could be cleanly disentangled—then purely separable event-related transients would be independent, i.e., non-interacting, contrary to fact and actual scientific interest. Therefore, a combined linear-nonlinear approach is called for, in order to isolate event-related transients while also facilitating the study of how they are *modulated* in the context of other events.

Hansen [1983] proposed a linear theory of event-related transients, and devised an associated frequency domain technique for extracting underlying waveforms which overlap in multi-trial experimental data. Essentially, *Hansen decomposition* applies the discrete Fourier transform (DFT) in order to convert a system of waveform convolution equations to a series of complex scalar linear equations. These are solved independently at each frequency bin for the Fourier representation of the underlying event-related transients, which finally are reconstructed in the time domain via the inverse DFT. Hansen applied the technique to the problem of separating stimulus-related and response-related waveforms in EEG data acquired with a reaction-time task. McGill and Dorfman [1984] independently devised the method, which also has been studied by Pflieger [1991], Zhang [1998], and (more recently) Yin et al. [2009]. The related but distinct Adjar technique [Woldorff, 1993] also is based on a linear theory of transients, but operates iteratively in the time domain to resolve adjacent responses in a stream of events which are not necessarily clustered as multi-event trials.

Volterra theory [Volterra, 1930] is a series approximation approach that can extend linear systems (first-order terms) to nonlinear systems by adding higher-order terms [Schetzen, 1980]. It has been applied to evoked potential and other neurophysiological data [Sclabassi et al., 1988a] [Shi and Hecox, 1991], to fMRI data [Friston et al., 1998], and as an approach for functional multimodal integration [Pflieger & Greenblatt, 2000], but has received little attention among cognitive ERP/ERF researchers.

This paper presents a unified Volterra-Hansen theory with the dual aims of (i) separating event-related transients which cluster together on single trials, while also (ii) quantifying *inter-event modulations*, i.e., the manner in which an event-related transient may be modified in the context of other events which co-occur on the same experimental trial. Section 2 presents a specialization of Volterra theory for event-marker input time series in a trial-based setting. Section 3 connects the first-order (linear) terms of the event-related Volterra model to Hansen decomposition theory (with singularity analysis). Section 4 extends the Volterra-Hansen theory to second-order models; and the general result is presented in Section 5. It is hoped that these theoretical developments may provide cognitive neurophysiologists with a fruitful framework for novel experimental designs and analyses.

2. Trial-based event-related Volterra (ERV) model in the time domain

An ERV model for L distinct events occurring on any given trial j has the form

$$y_j(t) \approx \varepsilon_j(t) + \sum_{i_1=1}^{L} \left(\begin{array}{l} \int_{-\infty}^{\infty} h_{i_1}^{(1)}(\tau_1) x_{ji_1}(t-\tau_1) d\tau_1 + \\ \sum_{i_2=1}^{L} \left(\int_{-\infty}^{\infty}\int_{-\infty}^{\infty} h_{i_1 i_2}^{(2)}(\tau_1,\tau_2) x_{ji_1}(t-\tau_1) x_{ji_2}(t-\tau_2) d\tau_1 d\tau_2 + \cdots \right) \end{array} \right) \tag{1}$$

where $y_j()$ is a measured physiological time series; $\varepsilon_j()$ is random error; $h_{i_1}^{(1)}()$ is a first-order kernel (i.e., impulse response function); $h_{i_1 i_2}^{(2)}(,)$ is a second-order kernel; and so on. $x_{ji_1}(t) = c_{ji_1}\delta(t - t_{ji_1})$ is a time series marking the occurrence of event i_1 at time t_{ji_1}, where c_{ji_1} is an optional *response variability coefficient* (1 by default). The integrals readily drop out of Eq. (1):

$$y_j(t) \approx \varepsilon_j(t) + \sum_{i_1=1}^{L} c_{ji_1} \left(\begin{array}{l} h_{i_1}^{(1)}(t - t_{ji_1}) + \\ \sum_{\substack{i_2=1 \\ i_2 \neq i_1}}^{L} c_{ji_2} \left(\begin{array}{l} \underline{h}_{i_1 i_2}^{(2)}[t_{ji_1} - t_{ji_2}](t - t_{ji_1}) + \\ \sum_{\substack{i_3 > i_2 \\ i_3 \neq i_1}}^{L} c_{ji_3} \left(\underline{h}_{i_1 i_2 i_3}^{(3)}[t_{ji_1} - t_{ji_2}, t_{ji_1} - t_{ji_3}](t - t_{ji_1}) + \cdots \right) \end{array} \right) \end{array} \right). \tag{2}$$

Here, the order>1 kernels have been rewritten (underbars) in *oblique form* [Sclabassi et al., 1988b, figure 2, p. 21] [Shi and Hecox, 1991, figure 2, p. 838] to reveal that each event-related transient (indexed by i_1) is essentially the first-order kernel modified by higher-order kernels sharing a *common time base* and *parameterized by inter-event intervals* (IEIs) with respect to the primary event. Thus, each event-related transient is modulated within the temporal context of other events on the same trial.

The objective of ERV modeling is to estimate the kernels given multi-trial event-related data.

3. Hansen decomposition

Hansen decomposition [Hansen, 1983] may be recast in the context of Eq. (2) as solving first-order trial-based ERV models in the frequency domain. The first-order time-domain ERV model

$$y_j(t) = \varepsilon_j(t) + \sum_{i_1=1}^{L} c_{ji_1} h_{i_1}^{(1)}(t - t_{ji_1}) \tag{3}$$

may be expressed in the frequency domain as

$$\begin{aligned} Y_j(f) &= \mathrm{E}_j(f) + \sum_{i_1=1}^{L} c_{ji_1} \exp\left\{ \frac{-2\pi i f t_{ji_1}}{N} \right\} H^{(i_1)}(f) \\ &= \mathrm{E}_j(f) + \sum_{i_1=1}^{L} q^{(ji_1)}(f) a^{(i_1)}(f) \end{aligned} \tag{4}$$

where

$$q^{(ji_1)}(f) \equiv c_{ji_1} \exp\left\{\frac{-2\pi i f t_{ji_1}}{N}\right\} \tag{5}$$

and

$$H_{i_1}^{(1)}(f) = a^{(i_1)}(f)\,. \tag{6}$$

$Y_j()$, $\mathrm{E}_j()$, and $H_{i_1}^{(1)}()$ are discrete Fourier transforms (DFTs) of $y_j()$, $\varepsilon_j()$, and $h_{i_1}^{(1)}()$, respectively; and N is the number of time samples per epoch (time interval) associated with a trial. $q^{(i_1 j)}()$ incorporates both the time shift t_{ji_1} of event i_1 on trial j, which is known experimental data, and the single trial amplitude $c_{ji_1}^{-1}$, which is 1 to an initial approximation. (Hansen did not consider response variability coefficients; they may be estimated, iteratively, from the single trial epochs). Thus, the first-order kernels $h_{i_1}^{(1)}()$—i.e., the primary event-related transient waveforms—are obtained by solving for the unknown complex scalars $a^{(i_1)}(f)$ to obtain $H_{i_1}^{(1)}(f)$, followed by *inverse DFT*.

Hansen decomposition has the advantages of *computational separability* and *over-determined linearity* of the frequency-domain solution, i.e., the method solves for only L (number of events per trial) unknown complex numbers independently for each frequency f given J (number of trials) linear equations (typically, $J \gg L$). Whereas Hansen and others solved via normal equations, the solution via complex singular value decomposition (SVD) [Press et al., 1988] is:

$$\begin{gathered}
\mathbf{Q}(f) \equiv \begin{bmatrix} q^{(11)}(f) & \ldots & q^{(1L)}(f) \\ \vdots & \ddots & \vdots \\ q^{(J1)}(f) & \cdots & q^{(JL)}(f) \end{bmatrix} \quad \mathbf{a}(f) \equiv \begin{bmatrix} a^{(1)}(f) \\ \vdots \\ a^{(L)}(f) \end{bmatrix} \quad \mathbf{Y}(f) \equiv \begin{bmatrix} Y_1(f) \\ \vdots \\ Y_J(f) \end{bmatrix} \\
\mathbf{Q}(f)\mathbf{a}(f) \approx \mathbf{Y}(f) \\
\mathrm{svd}(\mathbf{Q}(f)) = \mathbf{U}(f)\mathbf{W}(f)\mathbf{V}(f)^* \\
\mathbf{a}(f) \approx \mathbf{V}(f)\mathbf{W}(f)^+\mathbf{U}(f)^*\mathbf{Y}(f)
\end{gathered} \tag{7}$$

where $\mathbf{W}(f)$ is a diagonal matrix of non-negative real singular values, and $\mathbf{W}(f)^+$ is obtained by zeroing singular values that are close to zero, but otherwise forming their reciprocals.

It is important to note that $J \gg L$ by itself does not guarantee a unique Hansen decomposition. On the contrary, $\mathbf{Q}(f)$ is identically singular when $f = 0$, $L > 1$, and $c_{ji_1} = 1$ (then each element of $\mathbf{Q}(0)$ is 1), and can be singular for $f > 0$ if the experiment has IEIs which are inadequately randomized across trials, or too-long epochs per trial (so that the smallest nonzero frequency approaches zero). Thus, although the normal equations solution is equivalent to the SVD solution (with no singularities), the latter permits (i) assessment of adequate IEI randomization before running an experiment, and (ii) a possible means for handling singularities after the fact.

If the error process spectral density $\left|\mathrm{E}_j(f)\right|$ is available, it may be used to whiten $\mathbf{Y}(f)$ and $\mathbf{Q}(f)$ by simple division, in which case the whitened $\overline{\mathbf{Y}}(f)$ and $\overline{\mathbf{Q}}(f)$ may be substituted in Eq. (7). Unless *single-trial estimates* of the error process are available, the whitened and unwhitened solutions are algebraically equivalent—although even here whitening can influence the treatment of singularities.

4. Second-order ERV models in the frequency domain

This section extends the first-order frequency-domain ERV solution (Hansen decomposition) to second-order ERV models, for which event-related transients are modulated by IEIs:

$$y_j(t) \approx \varepsilon_j(t) + \sum_{i_1=1}^{L} c_{ji_1}\left(h_{i_1}^{(1)}(t - t_{ji_1}) + \sum_{\substack{i_2=1 \\ i_2 \neq i_1}}^{L} c_{ji_2} h_{i_1 i_2}^{(2)}[t_{ji_1} - t_{ji_2}](t - t_{ji_1})\right). \tag{8}$$

Equation (8) may be expressed in the frequency domain as:

$$\begin{aligned} Y_j(f) &= \mathrm{E}_j(f) + \sum_{i_1=1}^{L} c_{ji_1} \exp\left\{\frac{-2\pi i f t_{ji_1}}{N}\right\}\left(H_{i_1}^{(1)}(f) + \sum_{\substack{i_2=1 \\ i_2\neq i_1}}^{L} c_{ji_2} \underline{H}_{i_1 i_2}^{(2)}[t_{ji_1} - t_{ji_2}](f) \right) \\ &= \mathrm{E}_j(f) + \sum_{i_1=1}^{L} q^{(ji_1)}(f) a^{(i_1)}(f) + \sum_{i_1=1}^{L} \sum_{\substack{i_2=1 \\ i_2\neq i_1}}^{L} \sum_{k_{12}=1}^{D_{i_1 i_2}} q_{k_{12}}^{(ji_1 i_2)}(f) a_{k_{12}}^{(i_1 i_2)}(f) \end{aligned} \tag{9}$$

where

$$q_{k_{12}}^{(ji_1 i_2)}(f) \equiv q^{(ji_1)}(f) c_{ji_2} d_{k_{12}}^{(i_1 i_2)}(t_{ji_1} - t_{ji_2}) \tag{10}$$

and

$$\underline{H}_{i_1 i_2}^{(2)}[\sigma_{12}](f) = \sum_{k_{12}=1}^{D_{i_1 i_2}} a_{k_{12}}^{(i_1 i_2)}(f) d_{k_{12}}^{(i_1 i_2)}(\sigma_{12}). \tag{11}$$

Here, $d_{k_{12}}^{(i_1 i_2)}(\sigma_{12})$ is one of $D_{i_1 i_2}$ a priori basis functions (indexed by k_{12}) in the parameter σ_{12}, which represents the interval from modulatory event i_2 to primary event i_1. In other words, the second-order kernel that represents i_2-modulation of the i_1-related transient is expanded, in the frequency domain, by solving for the complex coefficients $a_{\bullet}^{(i_1 i_2)}(f)$ given the complex basis functions. The latter, for example, may be complex sinusoids with the fundamental cycle spanning the range of inter-event intervals which may be found across trials in the experimental data.

In this form, it becomes clear that Eqs. (9), (10), and (11) extend Eqs. (4), (5), and (6) by adding new q and a terms, so that the columns of $\mathbf{Q}(f)$ and the rows of $\mathbf{a}(f)$ in Eq. (7) are extended accordingly. Thus, the general solution form of Eq. (7) is preserved for second-order ERV models.

Note that the number of unknown a coefficients per frequency increases from L (first order) to $L + L(L-1)D$ (for a common number D of basis functions). Thus, experimental requirements to achieve non-singular $\mathbf{Q}(f)$ (e.g., minimum number of trials, adequate IEI randomization) are more stringent for second-order models.

5. General-order ERV models in the frequency domain (with kernel selection)

By further extension, a Hansen-like solution for general ERV models (order M) per Eq. (2) follows from Eqs. (12), (13), and (14), which parallel Eqs. (9), (10), and (11):

$$\begin{aligned} Y_j(f) = \mathrm{E}_j(f) &+ \sum_{i_1=1}^{L} \beta_{i_1} q^{(ji_1)}(f) a^{(i_1)}(f) + \sum_{i_1=1}^{L} \sum_{\substack{i_2=1 \\ i_2\neq i_1}}^{L} \beta_{i_1 i_2} \sum_{k_{12}=1}^{D_{i_1 i_2}} q_{k_{12}}^{(ji_1 i_2)}(f) a_{k_{12}}^{(i_1 i_2)}(f) + \\ &\sum_{m=3}^{M} \sum_{i_1=1}^{L} \sum_{\substack{i_2=1 \\ i_2\neq i_1}}^{L} \cdots \sum_{\substack{i_m > i_{m-1} \\ i_m \neq i_1}}^{L} \beta_{i_1 i_2 \cdots i_m} \sum_{k_{12}=1}^{D_{i_1 i_2}} \cdots \sum_{k_{1m}=1}^{D_{i_1 i_m}} q_{k_{12}\cdots k_{1m}}^{(ji_1 i_2 \cdots i_m)}(f) a_{k_{12}\cdots k_{1m}}^{(i_1 i_2 \cdots i_m)}(f) \end{aligned} \tag{12}$$

where

$$q_{k_{12}\cdots k_{1m}}^{(ji_1 i_2 \cdots i_m)}(f) \equiv q_{k_{12}\cdots k_{1(m-1)}}^{(ji_1 i_2 \cdots i_{m-1})}(f) c_{ji_m} d_{k_{1m}}^{(i_1 i_m)}(t_{ji_1} - t_{ji_m}) \tag{13}$$

and

$$\underline{H}_{i_1 i_2 \cdots i_m}^{(m)}[\sigma_{12}, \ldots, \sigma_{1m}](f) = \sum_{k_{12}=1}^{D_{i_1 i_2}} \cdots \sum_{k_{1m}=1}^{D_{i_1 i_m}} a_{k_{12}\cdots k_{1m}}^{(i_1 \cdots i_m)}(f) d_{k_{12}}^{(i_1 i_2)}(\sigma_{12}) \cdots d_{k_{1m}}^{(i_1 i_m)}(\sigma_{1m}). \tag{14}$$

Here, *selection booleans* $\beta_{\bullet}$ have been introduced so that a "fully populated" ERV model of order M may be *reduced* by special considerations (pertaining to the experimental situation) for including $(\beta_{\bullet} = 1)$ or excluding $(\beta_{\bullet} = 0)$ particular kernels. For example, the sequence of events in a trial may suggest a second-order kernel for i_1-modulation of the i_2-related transient, but not vice versa. Reducing the full model facilitates tractability by decreasing the number of unknown a coefficients.

Thus, the general form of the solution shown in Eq. (7)—along with its associated singularity analysis—is preserved for ERV models of any order and with arbitrary selection of available kernels.

6. Discussion

Volterra and Hansen theories have been unified with the aim of separating temporally overlapping event-related transients (embedded in physiological time series, such as EEG or MEG) that, in turn, can be modulated by other temporally proximate events (occurring within cognitive-behavioral experiments designed with multiple events per trial). Thus, the theoretical framework in principle can handle both *linear separation* of event-related transients (ERTs) along with their *nonlinear contextual integration* via inter-event modulations (IEMs). First-order kernels are transient waveforms which resemble ordinary average ERPs or ERFs—however, with the difference that the former are estimated from (and interpreted within) an explicit ERV model. Second- and higher-order kernels are IEI-parameterized waveforms having precisely the same time base as the first-order kernels which they modify. Thus, modulation of an ERT on a particular trial depends on that trial's IEIs relative to the target/primary event.

Application of the theory depends critically on sufficiently-randomized IEI distributions. Consequently, not all multi-event trial-based experimental designs are suitable for Volterra-Hansen analysis. Importantly, the $\mathbf{Q}(f)$ matrix series of Eq. (7) depends to a first approximation (that is, with default response variability coefficients) on experimental event data only. Thus, singularity analysis via SVD may be carried out in advance of physiological data acquisition to insure that the experimental design is adequate to support estimation of specific ERV models.

As with ordinary averaging, ERV kernels are estimated separately for each data channel. Also, higher-order kernels have the same physical units (e.g., microvolts or femtotesla) as first-order transients, because the former are correction terms for the latter. Consequently, all source estimation methods which apply to multi-channel ERPs or ERFs may also be applied to multi-channel IEMs. This could be significant if an investigator wishes to estimate brain locations that process inter-event *interactions* (e.g., multi-sensory integration paradigms) rather than primary sensory or motor processes.

A limitation of the current theory is its assumption of homogeneous and independent realizations of ERT-generation processes across trials. These issues may call for hierarchical modeling.

The principal results of this paper were derived in an internal report [Pflieger, 2010]. EEG applications (using reaction time paradigms; paired-click auditory gating paradigms with randomized inter-click intervals; and Go-NoGo paradigms) are underway, to be reported separately.

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