

New Methods of Time Series Analysis of Non-Stationary EEG Data: Eigenstructure Decompositions of Time Varying Autoregressions

Andrew D. Krystal, Raquel Prado and Mike West *

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*Andrew Krystal is Assistant Professor in the Department of Psychiatry and Behavioral Sciences and Director of the Quantitative EEG Laboratory at Duke University Medical Center, Durham NC 27710, USA. Raquel Prado is Assistant Professor, Departamento de Cómputo Científico y Estadística, Universidad Simón Bolívar, Caracas, Venezuela. Mike West is Arts & Sciences Professor of Statistics and Decision Sciences, and Director of the Institute of Statistics and Decision Sciences, Duke University, Durham, NC 27708-0251, USA. The work reported here was carried out in the Department of Psychiatry and the Institute of Statistics and Decision Sciences at Duke University. The authors acknowledge partial financial support under grants NIMH K20MH01151, R29MH57532 and NSF/DMS-9704432. *Address for correspondence:* Dr. A. D. Krystal, Box 3309, Duke University Medical Center, Durham NC 27710. *tel:* (919) 681-8742, *fax:* (919) 681-8744.

Abstract

OBJECTIVE: Those who analyze EEG data require quantitative techniques that can be validly applied to time series exhibiting ranges of non-stationary behavior. Our objective is to introduce a new analysis technique based on formal non-stationary time series models. This novel method provides a decomposition of the time series into a set of “latent” components with time-varying frequency content. The identification of these components can lead to practical insights and quantitative comparisons of changes in frequency structure over time in EEG time series. **DESIGN and METHODS:** The technique begins with the development of time-varying autoregressive models of the EEG time series. Such models have been previously used in EEG analysis but we extend their utility by the introduction of eigenstructure decomposition methods. We review the basis and implementation of this method and report on the analysis of 2 channel EEG data recorded during 3 generalized tonic-clonic seizures induced in an individual as part of a course of electroconvulsive therapy for major depression. **RESULTS:** This technique identified EEG patterns consistent with prior reports. In addition, it quantified a decrease in dominant frequency content over the seizures and suggested for the first time that this decrease is continuous across the end of the seizures. The analysis also suggested that the seizure EEG may be best modeled by the combination of multiple processes, whereas post-ictally there appears to be one dominant process. There was also preliminary evidence that these features may differ as a function of ECT therapeutic effectiveness. **CONCLUSIONS:** Eigenanalysis of time-varying autoregressive models has promise for improving the analysis of EEG time series.

Key Words: EEG, nonstationary processes, seizures, time series analysis, time-varying autoregressive modeling

1 Introduction

EEG data has been shown to exhibit non-stationary behavior in a variety of contexts (e.g., Kawabata, 1973, Ferber, 1987, Geva et al., 1995, Pijn et al., 1997), suggesting the need for analysis methods that can be validly applied to non-stationary data. In such contexts, traditional time series methods, including Fourier-based spectral methods, are invalid unless analysis is restricted to short quasi-stationary data segments (Kawabata, 1973, Barlow, 1985, Ferber, 1987, Pijn et al., 1997). Such “windowed” analyses can provide useful insights, though are statistically inefficient and scientifically incomplete representations of the EEG generating process. Hence there is a need for globally non-stationary models and flexible methods for data analysis and investigation of how the characteristics of EEG signals changes with time (Thakor et al., 1993). Direct data representation methods, such as variants of singular-value decompositions and wavelet approaches, can often be useful in re-representing EEG series and providing preliminary insights into data structure (Thakor et al., 1993, Schiff et al., 1994, Durka and Blinowska, 1995). Such methods, however, have some inherent limitations when applied to the analysis of EEG data.

Wavelet-related methods are based on orthogonality principles for purely mathematical reasons. This orthogonality imposes the restriction that the resulting decomposition yields a series of components in different frequency bands (or in terms of basis functions with differing frequency content) which are not correlated with each other. However, EEG data is correlated across frequency bands and so we need analysis techniques that reflect this. In addition, wavelet and related analyses are direct data decomposition techniques that do not correspond to a model of the data-generating process. The data is simply decomposed into components within a series of fixed frequency bands (basis functions). As a result, in these analyses the time:frequency structure is obscured by “smearing” activity with distinct time:frequency behavior across frequency bands. This results in the need for additional post-hoc analyses to resolve components and requires ad-hoc assumptions

in the definition of frequency bands (such as that there is a distinct theta frequency band spanning 4-8 Hz). There is generally little information upon which to base the definition of frequency bands for a given new data set. However, this definition is crucial since it determines the ranges of frequencies within which distinct components cannot be resolved. Such definitions essentially arbitrarily assume that all of the data within each defined band is one physiological process. Thus, while wavelet-related analyses are mathematically attractive and can shed light on patterns of change in frequency structure (Thakor et al., 1993, Schiff et al., 1994, Durka and Blinowska, 1995), the resulting multi-resolution reconstructions lead to decompositions of EEG data into latent components at discrete and artificially constrained frequency levels; their interpretation is often obscure as a result.

EEG analysis would be improved through the use of model-based approaches which allow for the separation of complex signals into possibly correlated components on the basis of their time:frequency behavior, each of which may have behavior varying across the continuum of frequencies. One such class of models, time-varying (parameter) autoregressions, or TVAR models, have been successfully applied in a number of EEG studies (Bohlin, 1977, Gersch, 1985 and 1987, Kitagawa and Gersch, 1996). This is the class of models we utilize here. As will be seen, we go beyond the traditional uses of such models to more deeply exploit their mathematical structure in isolating non-stationary latent processes underlying EEG signals. This is based on new time series decomposition methods and provides illuminating representations of the time-frequency structure of EEG signals.

In the standard autoregressive framework, a discretely sampled EEG signal is modeled by representing the voltage level at time t as a linear combination of voltage levels at times $t-1, t-2, \dots, t-p$, say, for some maximum integer lag $p > 0$, plus a random (driving noise or “innovation”) component. The relationship is assumed to be fixed over time in that the regression parameters defining the linear combination are constant for the entire period of recording. In TVAR models these parameters vary over time, adapting to

changes evidenced in the series, and so potentially cater for the kinds of time-evolving structure evident in many non-stationary series. In particular, such models can respond to and adequately capture the forms of change in the frequency structure of oscillations in EEG data often encountered. TVAR models have been used in the past to model non-stationary time series in various fields, including seismology, geology and economics, and have proven utility as flexible empirical models. In connection with EEG studies, Gersch (1985,87) and Kitagawa and Gersch (1996) have applied TVAR models to the analysis of non-stationary human epileptic EEG data. The methods we describe naturally extend this prior work. We develop the TVAR models in the context of the broader class of *state-space models* in which new theory of model decompositions leads to data analysis methods that significantly deepen the applied relevance of TVAR models. This approach, based on instantaneous, time-evolving eigenstructure analyses of matrices arising in the state-space representation, has been detailed theoretically in Prado and West (1997), West (1997), and West et al. (1999). Figures 2, 4 and 6 illustrate how EEG signals can be decomposed as linear combinations of underlying, hidden or latent time series, each of which generally takes an oscillatory form in a characteristic frequency range, but with frequency structure that changes as it represents non-stationarities in the data. Such decompositions, and corresponding investigations of the time evolution of amplitudes, frequencies and other characteristics of these component series, are particularly well suited to separating out components in the EEG that may have distinct physiological generators. However, as mentioned above, unlike wavelet and other direct data decomposition techniques, the components recovered in TVAR models may be correlated, the dependencies inducing changes in form that are related across components; this is an important distinction as EEG structures in different frequency bands may be inherently related due to common underlying physiological activity. Our new perspective on EEG data analysis is based on exploration and study of these time-varying latent components, and involve EEG characterization through graphical representation of time-

frequency structure evidenced by such decompositions.

The remainder of this article reviews the basis of TVAR models, describes their implementation, and illustrates the use of this general approach to time:frequency analysis of non-stationary signals (Prado and West, 1997, West, 1997, West et al., 1999) through its application to the decomposition of EEG data recorded during generalized tonic-clonic seizures. This analysis had the objectives of exploring and quantifying patterns of the change over time of EEG frequency content during the seizures. The identification of latent components at unrestricted and often intersecting frequency ranges represents a first modeling approach to isolating EEG components that reflect the physical superposition of activity of multiple neural generators (Geva et al., 1995). The data we study here were recorded during generalized tonic-clonic seizures elicited during electroconvulsive therapy (ECT), which remains the most effective treatment known for severe major depression (Krystal and Weiner, 1994). We chose this particular data set to illustrate analysis with TVAR models because prior analysis of ECT seizure EEG data suggests that analysis of signal frequency content may be important for understanding the mechanism of action of ECT and for serving as a useful clinical tool, but has been dependent upon the use of the Fourier transform in a setting where aspects of the signal (including the dominant frequency) are known to change with time (Weiner et al., 1991, Krystal et al., 1993, 1995, 1996, Zoldi et al., 1996). We compared seizures elicited by 3 different types of ECT that differ in antidepressant potency and side-effects, with the hopes that, in addition to providing an introduction to TVAR modeling, this analysis would provide novel insights into both scientific issues related to generalized tonic-clonic seizures and clinical ECT issues (Sackeim et al., 1991 and 1993, Krystal et al., 1995).

2 Materials and Methods

2.1 The basis and implementation of TVAR models and time series decompositions.

A univariate time series $x_t, (t = 1, 2, \dots,)$ follows a time-varying autoregressive model of order p , or TVAR(p), if $x_t = \sum_{j=1}^p \phi_{t,j} x_{t-j} + \epsilon_t$, where $\phi_t = (\phi_{t,1}, \dots, \phi_{t,p})'$ is the instantaneous autoregressive parameter vector at time t and ϵ_t are zero-mean innovations assumed uncorrelated and normal, $\epsilon_t \sim N(0, \sigma_t^2)$ with possibly time-varying variances σ_t^2 . The model has the form of a standard autoregression at each time t , but the autoregressive parameters and innovations variance may change through time subject to model constraints on the evolution of these parameters. Higher-order TVAR models have proven useful (e.g., Gersch, 1987, Kitagawa and Gersch, 1996) in modeling series exhibiting non-stationary patterns of time-varying periodicities such as are displayed in EEG traces.

The TVAR model is completed by specifying evolution model components for ϕ_t and σ_t^2 . We adopt a traditional random walk $\phi_t = \phi_{t-1} + \xi_t$ model that assumes zero-mean innovations ξ_t that are uncorrelated and normal, $\xi_t \sim N(0, \mathbf{W}_t)$ (e.g., West et al., 1999). Similarly, the changes of σ_t^2 over time are modeled using a standard multiplicative random walk (West and Harrison, 1997 chapter 10) $\sigma_t^2 = \sigma_{t-1}^2(\delta/\eta_t)$, where η_t are independent Beta variates $\eta_t \sim Be(a_t, b_t)$, also independent of the innovations ϵ_t and ξ_t . Time variation of the TVAR parameters ϕ_t is adjusted using a standard discount factor method that weights the degree to which these parameters are allowed to vary in time using a parameter $\beta \in (0, 1)$ (West and Harrison, 1997). The idea is to specify the form and magnitude of the variance matrix that controls the evolution of the parameter at time t as a function of how much information we have about the parameters at time $t - 1$. In this, “information” is measured by the (inverse of the) variance-covariance matrix for the parameters. Hence, this variance matrix is “inflated” between times $t - 1$ and t by a multiple of $100(1 - \beta)/\beta\%$ where β is the constant discount

factor, taking a value on $(0, 1)$ and generally close to 1. Evidently, low values of β are consistent with high variability in the ϕ_t parameters over time, while high values – typically in the range 0.9 - 0.999 – are typically relevant in this applied area. The beta parameters (a_t, b_t) are defined at each time t by a further discount factor δ completely analogous to β . In application, we treat the model order p and the discount factors β and δ , as tuning parameters chosen to maximize the agreement between the model and the data by maximizing the joint log-likelihood function of the data time series and the predictions of the model (see details in West et al., 1999). Standard sequential updating and retrospective filtering/smoothing algorithms (West and Harrison, 1997) are applied to obtain posterior distributions for the parameters ϕ_t and σ_t^2 .

Once the EEG series are modeled via TVAR models, the focus is on exploring the time:frequency structure of latent processes underlying the signals using new theory of dynamic model decomposition based on the eigenstructure of the TVAR evolution matrix. The basic decomposition result for the class of TVAR models states that

$$x_t = \sum_{j=1}^{p_z} z_{t,j} + \sum_{j=1}^{p_y} y_{t,j}$$

where p_z is the number of pairs of complex characteristic roots of the instantaneous AR characteristic polynomial defined by ϕ_t at time t , and p_y is the number of real characteristic roots, such that $2p_z + p_y = p$. Each $z_{t,j}$ process has basically the form of a time-varying ARMA(2,1). This process can be conceptualized as a *damped sinusoid of time-varying amplitude, phase and frequency characteristics*; between consecutive time points, the amplitude of the $z_{t,j}$ process is “damped” by a randomly time-varying modulus $r_{t,j}$, and the overall amplitude, phase and frequency $\omega_{t,j}$ (wavelength or period $2\pi/\omega_{t,j}$) are also randomly time-varying. Each $y_{t,j}$ is essentially a time-varying AR(1) process that will usually represent high-frequency noise and model approximation (see discussion in West et al., 1999). This decomposition of the original signal x_t into latent processes $z_{t,j}$ then leads to a time-domain analysis of the time:frequency structure of x_t via exploration of

each of the latent processes and their parameters as they vary over time. The forms of each of these latent processes $z_{t,j}$ may be graphed against time, as may their time-varying characteristic frequencies $\omega_{t,j}$ and moduli $r_{t,j}$; such graphs present analogue displays of patterns of time-variation in the spectral characteristics of x_t . Assessment of changes over time in these parameters can be viewed as a novel approach to exploring time-variation in spectral density functions, and the corresponding decomposition analysis represents a form of spectral decomposition in the time domain.

The sequential updating and retrospective smoothing algorithms for calculating the TVAR models and their dynamic model decompositions have been implemented in software that is freely available from the ISDS web site at Duke University¹. The software comes in two versions, one in Matlab and one in Fortran90. The Matlab version is free standing, the Fortran version utilizes a few functions from the public domain library *LAPACK* (Anderson et al., 1995) and requires S-Plus graphics for output display. Our implementation in Fortran/S-Plus is described in Prado (1998), and both software and documentation are available to interested readers from the web site. We have tested all software on currently available Pentium II machines running public domain unix, and on DEC/AlphaStations under Digital UNIX 4.0B. The code is very fast. A typical ECT seizure EEG record of a seizure episode over about 2 minutes and sampled at 43Hz generates a data series of about 4,500 points. Running time of the Fortran code for the entire analysis is about 1 minute on the above platforms.

As an example, Figure 1 displays four sections of 500 consecutive observations from near the start, two central sections and near the end of the recording period of one example signal from an ECT induced seizure EEG. We refer to this series as the *treatment 2* seizure, the terminology being further explained below. The original signal is digitized at 256Hz, but we typically subsample to reduce data length and computation time. We subsample every sixth observation to deliver 4,523 observations, about 106 seconds at

¹<http://www.stat.duke.edu/~mw/tvar.html>

a rate of 42.67 observations per second. Subsampling in the present application was justified in that we carried out analysis with the original data and found no discernible difference in results. It should be noted, however, that subsampling can affect the capacity to resolve higher frequency content, which could be a factor in the analysis of other data sets. The figure clearly illustrates the intense oscillatory nature of the data and the changes over the seizure course in amplitude and frequency characteristics. Optimization of the agreement between the model and the original data set (maximizing the joint likelihood function of the model and the data) and the requirement that one set of parameters be used to model all 3 seizures resulted in a choice of order 12 for the time-varying autoregressive models (TVAR(12)) and discount factors $\beta = 0.994$ and $\delta = 0.95$ that were utilized to generate the results described below. It should be noted that different data sets will generally lead to different maximum likelihood estimates of these three parameters. For the 3 time series studied the maximum likelihood values are very close, so we are justified in compromising on the choice of common values for the three individual analyses. Other values will be relevant for other data sets, and the software mentioned earlier provides utilities for computing the likelihood function and the resulting maximizing values in analysis of any specific data set. The latent component decomposition of the treatment 2 seizure data appears in Figure 2 and the trajectories of the characteristic frequencies of these components are represented in Figure 3. The “breaks” in Figure 3 exhibited by the highest frequency components are a consequence of the fact that the number of complex and the number of real roots of the instantaneous characteristic AR polynomial, defined by ϕ_t at each time t , also change over time. For short time periods, a pair of complex roots may be substituted by two distinct real roots and in a similar way, two distinct real roots may “switch back” to a pair of complex roots. However, this event has little impact on the interpretation and understanding of the component structure given that the low frequency bands components are dominant.

2.2 Application to the analysis of generalized tonic-clonic seizure EEG data recorded during electroconvulsive therapy.

TVAR modeling was applied to EEG data from three successive ECT treatments in an individual with major depression who gave informed consent. This subject received right unilateral ECT electrode placement as described by d'Elia (Krystal et al., 1995). Pharmacologic agents in use were: methohexital 1 mg/kg, succinylcholine 1mg/kg, and 100% oxygen by mask. The administration of succinylcholine at this dosage eliminated any movement during the seizure that would otherwise result in an extreme amount of movement artifact obscuring the data. As a result, ECT represents a unique, movement-artifact-free, opportunity to study the EEG recorded during generalized tonic-clonic seizures.

Seizure threshold was estimated at treatment 1 by starting with a stimulus intensity, in terms of charge, that was so low that it was unlikely to elicit a seizure and then gradually increasing the stimulus intensity (at 50% increments) until a seizure duration of 25 seconds was achieved (Coffey et al., 1995). This final stimulus intensity that was associated with a greater than 25 second seizure was defined as the seizure threshold (1.0T). For the next three treatments the subject received a 1.5 times threshold (1.5T) stimulus at treatment 2, a 4 times threshold (4.0T) stimulus at treatment 3 and a 2.5 times threshold stimulus at treatment 4 (2.5T). Treatments were administered 3 times per week on Monday, Wednesday, and Friday. For each of these 3 seizures 2 channels of EEG data were recorded from left and right prefrontal-to-ipsilateral mastoid derivations using Ag/AgCl electrodes with a MECTA SR1 ECT device (MECTA Corp. Lake Oswego, Or) and with a low frequency cutoff of 1.0 Hz and a high frequency cutoff of 70 Hz (Krystal et al., 1995). EEG data was digitized at 256 Hz and 12 bits accuracy using a computer based EEG acquisition and analysis system (EEGSYS, Friends of the Medical Science, Inc.). Manual artifact rejection of EEG data was

performed blind to subject and treatment characteristics by A.D.K.. Data from the right hemisphere appears in the figures.

3 Results

3.1 General observations

Figure 1 displays various segments of the EEG series recorded during treatment 2, the full series appearing also at the bottom of Figure 2. The TVAR decomposition of the treatment 2 data appears in Figure 2 and illustrates the series of latent components into which the signal was separated. It is of particular note that these components are not orthogonal and their frequency compositions vary with time. The components are plotted with the vertical scale set as the range of the data, so that their relative amplitudes are easily assessed, and they are ordered by increasing frequency with component (1) corresponding to the lowest characteristic frequency. The amplitudes of the components reflect the well-described phenomenon of increasing amplitude in the immediate post-stimulus period with maximal amplitude in the middle portion of the seizure followed by dissipation and postictal suppression (that occurs just prior to time $t = 70$) (Weiner et al., 1991, Weiner and Krystal, 1993). The latent components in this decomposition are dominated by TVARMA(2,1) quasi-periodic structures with characteristic frequencies $\omega_{t,j}$, and the estimated time trajectories of these frequencies are displayed in Figure 3. Each component manifests an apparent decreasing frequency over time, consistent with a decrease in the dominant frequency content from the beginning to the end of the seizure. The lowest frequency component lies in the 2-5 Hz frequency range for most of the recording period, that is the characteristic range of slow-waves manifested in the EEG during the middle and late phases of ECT seizures (Niedermeyer, 1993, Staton et al., 1981, Weiner and Krystal, 1993). As shown in Figure 2, the slow wave activity dominates in amplitude and appears as a smooth version of the data series. The second

component, slightly higher in frequency range, is much lower in amplitude but represents a significant component process. Higher frequency components also appear in the decomposition but are lower in amplitude than the lower frequency components. Thus, this decomposition is an explicit representation of expected phenomena: the seizure EEG is dominated by 2-5 Hz frequency slow-waves, that decrease in frequency as the seizure progresses (Staton et al., 1981, Weiner et al., 1991, Weiner and Krystal, 1993). The decrease in slow-wave frequency, evident in Figure 3, represents the first time that this phenomenon has been quantified for ECT seizure EEG data.

Figures 4, 5, 6 and 7 display the latent components and the trajectories of the characteristic frequencies associated with such components in the decompositions of the EEG data sets recorded at treatment 3 and treatment 4. Similar to the treatment 2 EEG series, the treatment 3 and 4 series seem to be composed of a low-frequency wave, a slightly higher frequency wave, at least one and sometimes two 8-13 Hz waves and at most a couple of higher frequency components. Figures 8, 9 and 10 compare the trajectories of the lower frequency components for the three treatments. It is important to note that when comparing components across treatments that all 3 seizures end at different times; the seizure of treatment 2 ends just prior to $t = 70$, the treatment 3 seizure ends at $t = 42$, and the treatment 4 seizure ends at $t = 46$.

It is notable that the latent components of the EEG data from seizure 3 manifest the interesting behavior that, for a brief period during the seizure, the component that is lowest in frequency for the majority of the recording period becomes higher in frequency than the component that is generally next highest in frequency ($t = 10$ to $t = 22$). This finding highlights the capacity of TVAR decompositions to identify components that may have physiologic relevance and retain their separate identity even though their frequency content varies continuously over the data segment studied.

3.2 Physiology of Generalized Tonic-Clonic Seizures

One unexpected finding of this decomposition, that may have relevance for understanding the physiology of generalized tonic-clonic seizures, is evident in Figures 3,5,7,8,9, and 10. These figures demonstrate that, for nearly all of the components, the characteristic frequency tends to decrease continuously and this process appears to continue unimpeded even after the seizure ends. It is remarkable that while the amplitudes of these components diminish drastically at the end of the seizure and the onset of the postictal suppression (see Figures 11-13), it is not even possible to identify where the seizure ends from the Figures of the characteristic frequencies of the components (see Figures 3,5,7,8,9,10). This finding not only reinforces the capacity of TVAR decomposition to identify components that maintain their identity over time despite substantial changes in the original time series, but also suggests that there may be a physiologic process that is manifest in slowing of the dominant frequency that is initiated at the start of the seizure and continues after the end of the seizure in the EEG as indicated by the onset of postictal suppression.

A related finding is that multiple components appear to contribute to the model during the seizure, however after the seizure ends, all of the components are essentially of 0 amplitude, except for component 1, the lowest frequency component (see Figures 2, 4, 6). This is consistent with the possibility that there may be multiple physiologic processes interacting during the seizure, however, post-ictally, all but one of these turn off and there is one dominant process which has a decreasing dominant frequency over time.

3.3 Findings of Clinical Relevance to ECT

An additional related finding of this analysis may have relevance to understanding the mechanism of action of ECT and may be of clinical utility. Figures 8 and 9 indicate that the characteristic frequency of the low frequency components of treatment 2 start out higher and remain higher than

that for treatments 3 and 4 during the course of their seizures. This finding is particularly interesting given that treatment 2 was only 1.5 times threshold UL ECT, in view of past evidence that suggests that this treatment may be less efficacious than the higher level treatments 3 and 4 (Sackeim et al., 1991 and 1993, Krystal et al., 1995). Further, the treatment which would be expected to be the most efficacious and have the most side-effects (4.0T of treatment 3) manifests a much lower characteristic frequency immediately after the stimulus and maintains the lowest average dominant frequency of these components over the course of the seizure (see Figures 8 and 9). These findings are consistent with the hypothesis that more effective forms of ECT and those with more cognitive side-effects elicit an earlier and more intense seizure inhibitory response as reflected in the earlier and more intense onset of ictal low-frequency (2-5 Hz) waves (Nobler, 1993, Krystal et al., 1993, 1995, 1996, 1997 and 1998).

4 Discussion

We have presented discussion and analytic studies that underpin the prospects for deeper and more scientifically incisive analyses of EEG data using TVAR decomposition methodology. This methodology is practical from a computational standpoint, and is particularly well-suited to EEG analysis as it directly caters for ranges of observed non-stationarities such as are evident in the EEG; the results are often interpretable decompositions of series into multiple, non-orthogonal latent components with varying frequency content over time. We have found that this technique can be applied readily to the analysis of non-stationary EEG data recorded during generalized tonic-clonic seizures where the amplitude and frequency content were time-varying (see also West et al., 1999). The methodology is very promising for EEG analysis and particularly for seizure EEG data with inherent temporal evolution (Zoldi et al., 1996, Pijn et al., 1997).

The present analysis suggests that TVAR decomposition may be of par-

ticular utility because it is able to identify physiologic components that retain their identity despite substantial changes in the signal and in the components over time. This type of result is not possible with wavelet-related analyses because of the absence of an underlying model and the requirement of orthogonality of components. In the present analysis, the capacity to model the EEG time series in terms of time-varying latent components was apparent. We were able to identify components that retained their identity over time despite substantial shifts in frequency which occasionally even led to the trajectories of dominant frequencies of separate components intersecting. This attribute of TVAR analysis made it possible for us to develop new insight regarding the time:frequency behavior of generalized tonic-clonic seizure EEG data. We were able to quantitatively identify that the characteristic frequencies of components of generalized tonic-clonic seizures not only diminished during the seizure but, for the first time, observed that the frequencies continued to smoothly diminish and remain low following the end of the seizure. In addition, this analysis also indicated for the first time that during the seizure the EEG data is best modeled as comprised of a number of distinct components, whereas following seizure termination all but one of these components is suppressed and the signal is best modeled as a single process.

While a continuous decrease in dominant frequency across the seizure end-point has not been previously reported, this observation is consistent with the notion that EEG characteristic frequency may be an index of the degree of the strength of seizure inhibitory processes elicited by the seizure. These processes have been associated with low-frequency activity involved in the termination of spontaneous generalized-tonic seizures (Engel, 1989, Sackeim et al., 1991) and generalized tonic-clonic seizures elicited by ECT (Krystal et al., 1995 and 1998). Further, this hypothesis is consistent with the finding that there is a rise in the seizure threshold following the onset of ECT seizures that persists long after the seizures end (Sackeim et al., 1991 and 1999, Krystal et al., 1998). Further work is needed to determine the

generality of these findings and to test the hypothesis that there are multiple processes underlying generalized tonic-clonic seizures followed by a single dominant process during the period of post-ictal suppression.

The findings of the present study must be considered to be preliminary, however, they indicate that the application of TVAR models may have potential to be of clinical relevance to the understanding and practice of ECT. The results are consistent with prior work employing segmental analysis suggesting that more effective types of ECT treatment appear to have an earlier decrease in characteristic frequency and lower characteristic frequency which has been thought to reflect that such treatments elicit an earlier and more vigorous seizure inhibitory response (Engel, 1989, Sackeim et al., 1991, Krystal et al., 1995, 1996, 1997 and 1998). This finding complements the findings of the previous paragraph and suggests that the identification of the characteristic frequency of EEG data recorded during ECT seizures with TVAR decomposition should be explored. Such studies will determine if it is useful for inferring the speed of onset and intensity of seizure inhibitory properties that are thought to relate to the therapeutic antidepressant efficacy of ECT, and therefore may be useful to clinicians for adjusting the dosing ECT treatments to maximize therapeutic benefit, while minimizing treatment adverse effects (Krystal et al., 1993, 1995, 1996, 1997 and 1998).

In conclusion, by analyzing the complete pattern of time evolution of frequency content over seizures with parametric TVAR decomposition models, we hope to enhance the scientific and clinical applicability of EEG data. Further work is needed to determine whether these models are indeed helpful for better understanding the physiology of generalized tonic-clonic seizures, elucidating the mechanisms of antidepressant action of ECT and serving as a useful clinical tool for the dosing of ECT treatments. Our experience with the present data suggests that such studies will be fruitful.

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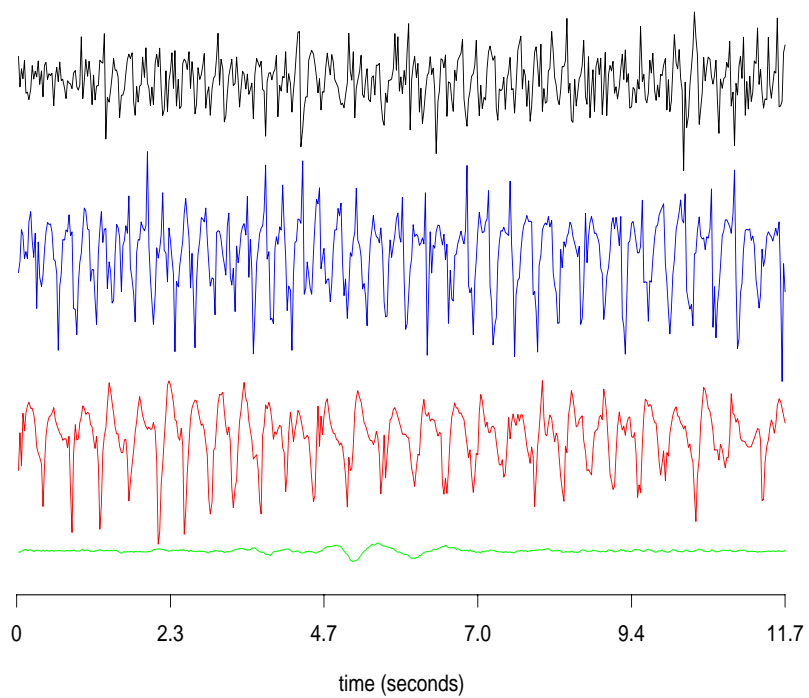


Figure 1: Sections of EEG voltage levels from treatment 2 EEG data. From the top down, the graph displays four sections of 500 observations from the full 4,200, taken at the start, early central, late central and final sections of the full series. Note that 500 samples represents about 11.7 seconds.

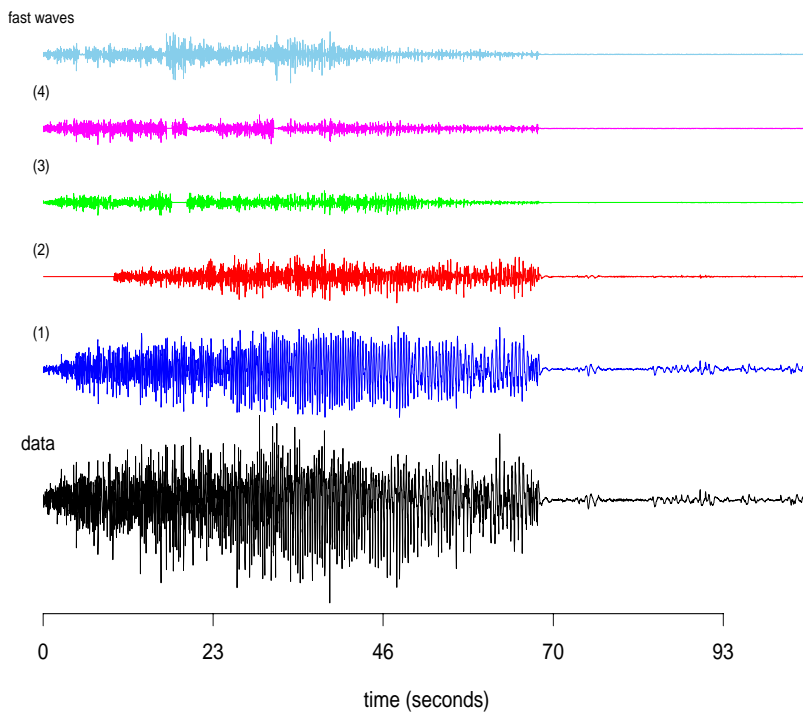


Figure 2: Data and estimated latent components in the treatment 2 (1.5T) decomposition. From the bottom up, the graph displays the time series followed by the estimated components in order of increasing characteristic frequencies. The latent components (1), (2), (3) and (4) are individual quasi-periodic TVARMA(2,1) processes, and the final “fast component” is the sum of all remaining, very high frequency components representing both rapid neural oscillations, neural and experimental noise.

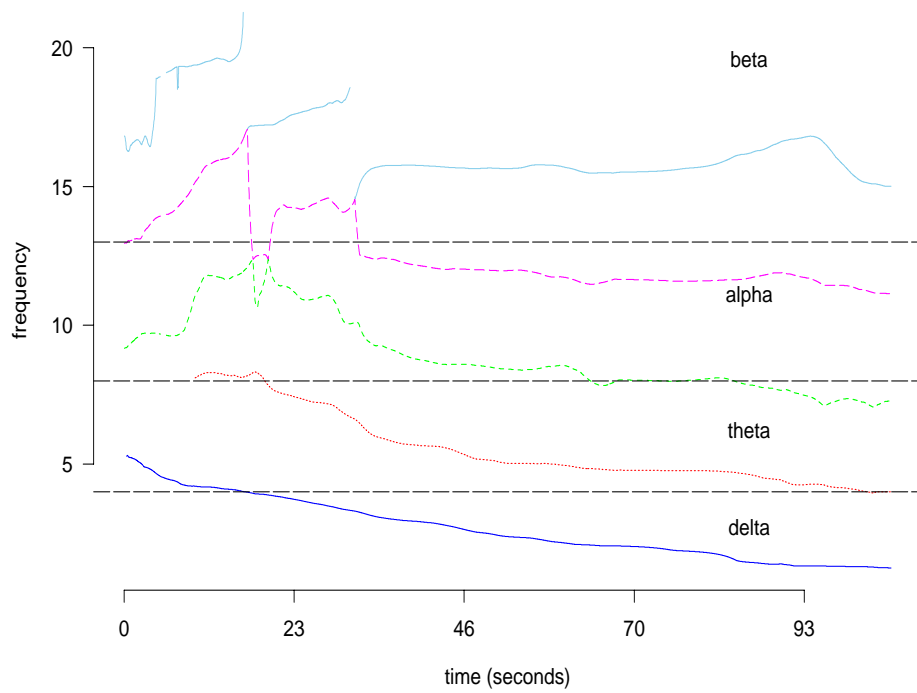


Figure 3: Trajectories of estimated characteristic frequencies of all latent components in the treatment 2 (1.5T) EEG series.

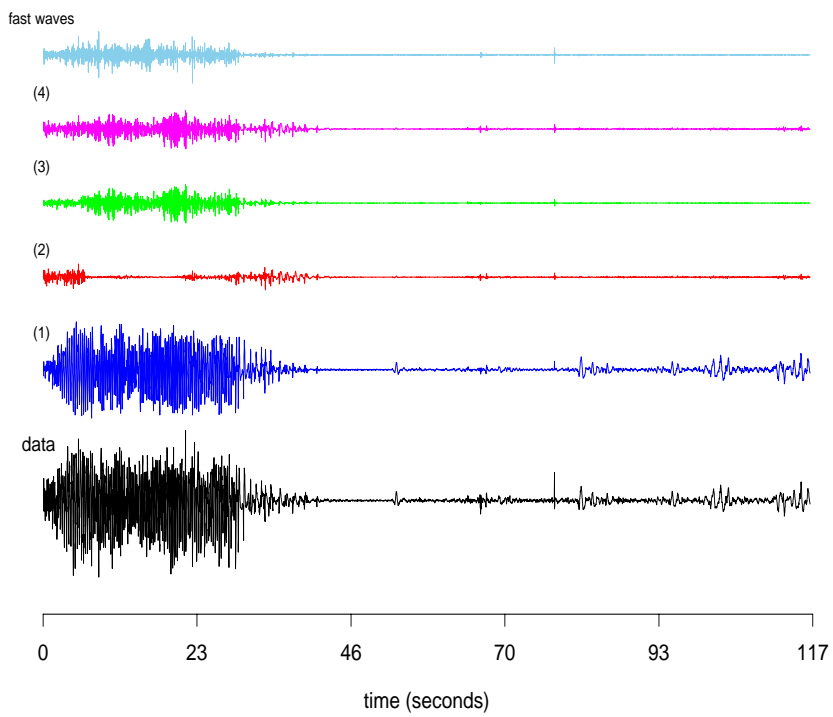


Figure 4: Data and some estimated latent components in the decomposition of EEG series for treatment 3 (4.0T), in a format as in Figure 2.

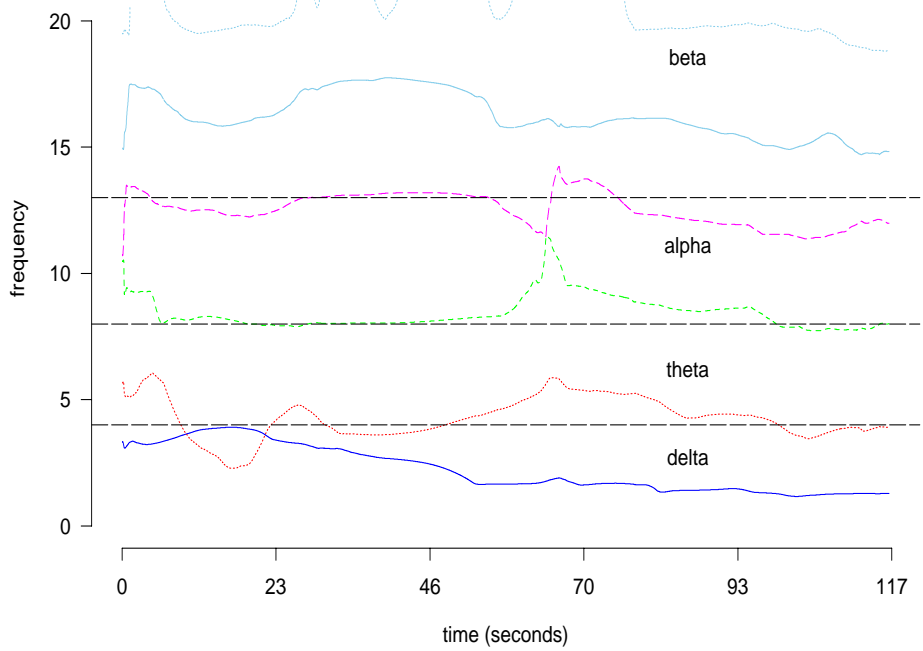


Figure 5: Trajectories of estimated characteristic frequencies of all latent components in the EEG series of treatment 3 (4.0T).

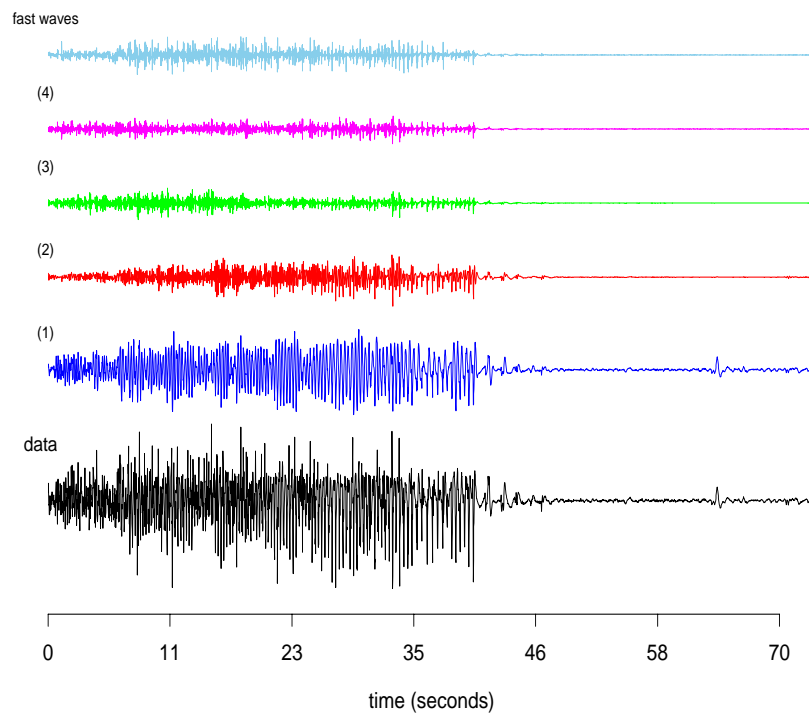


Figure 6: Data and some estimated latent components in the decomposition of the treatment 4 (2.5T) EEG series, in a format as in Figure 2.

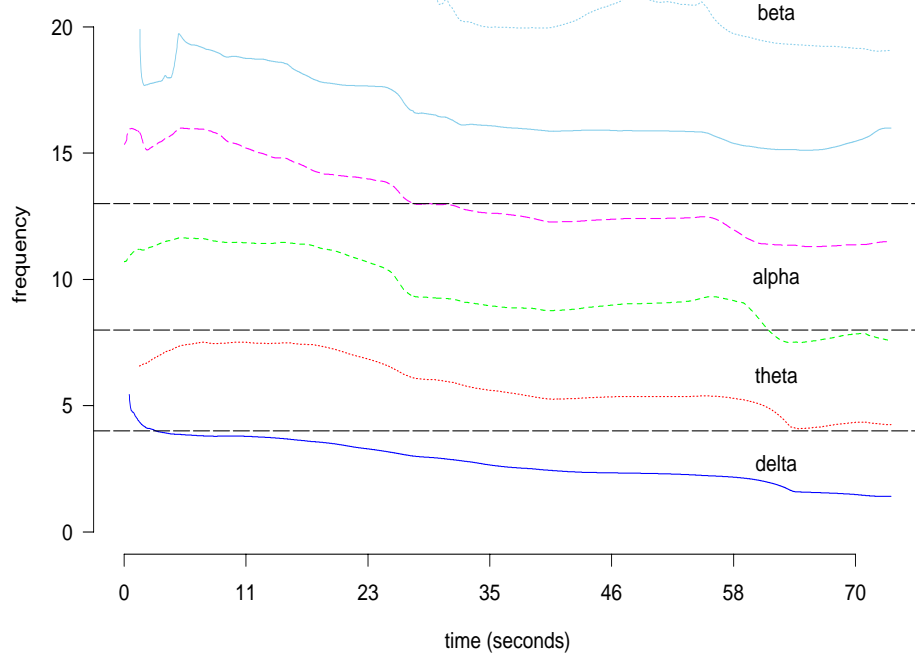


Figure 7: Trajectories of estimated characteristic frequencies of all latent components in treatment 4 (2.5T) EEG series.

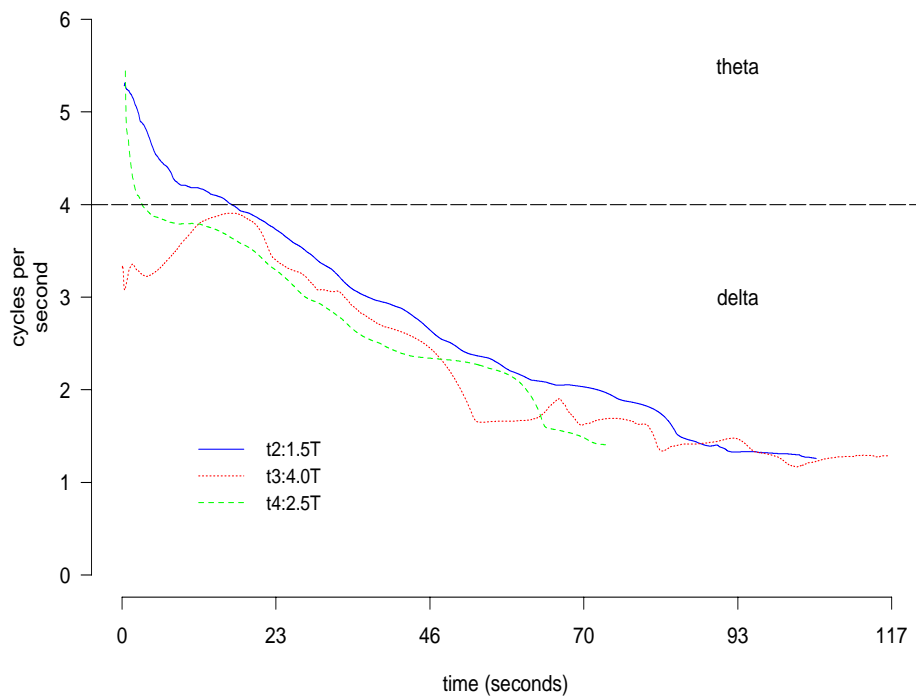


Figure 8: Trajectories of estimated characteristic frequencies of the lowest frequency components in decompositions of treatment 2 (1.5T), treatment 3 (4.0T) and treatment 4 (2.5T) EEG series.

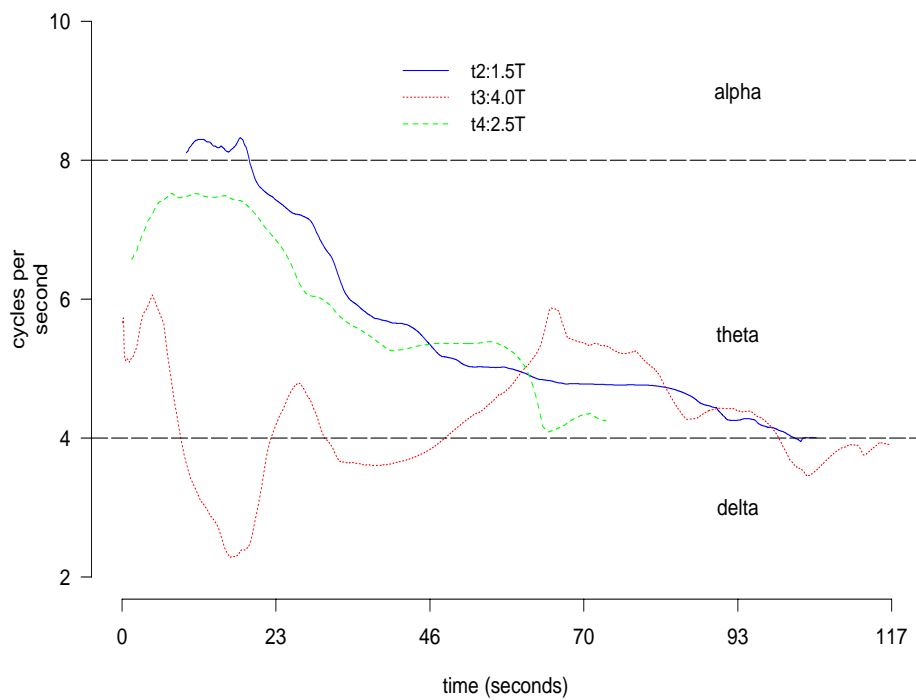


Figure 9: Trajectories of estimated characteristic frequencies of the second lowest frequency components in decompositions of EEG series of treatments 2 (1.5T), 3 (4.0T), and 4 (2.5T).

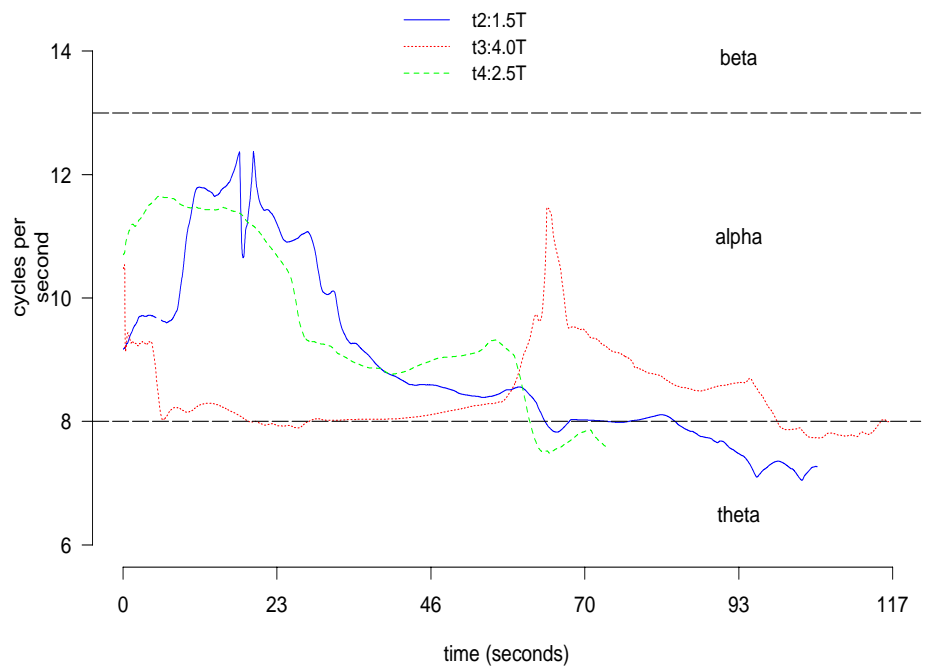


Figure 10: Trajectories of estimated characteristic frequencies of the third lowest frequency components in decompositions of the treatment 2 (1.5T), 3 (4.0T), and 4 (2.5T) EEG series.

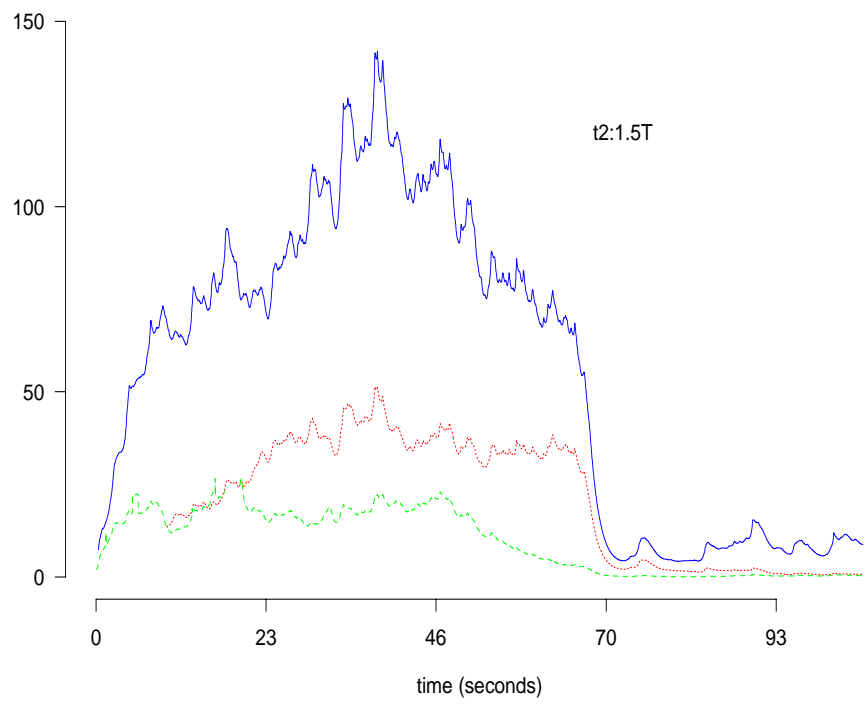


Figure 11: Trajectories of estimated amplitudes of low frequency components in decomposition of treatment 2 (1.5T) EEG series.

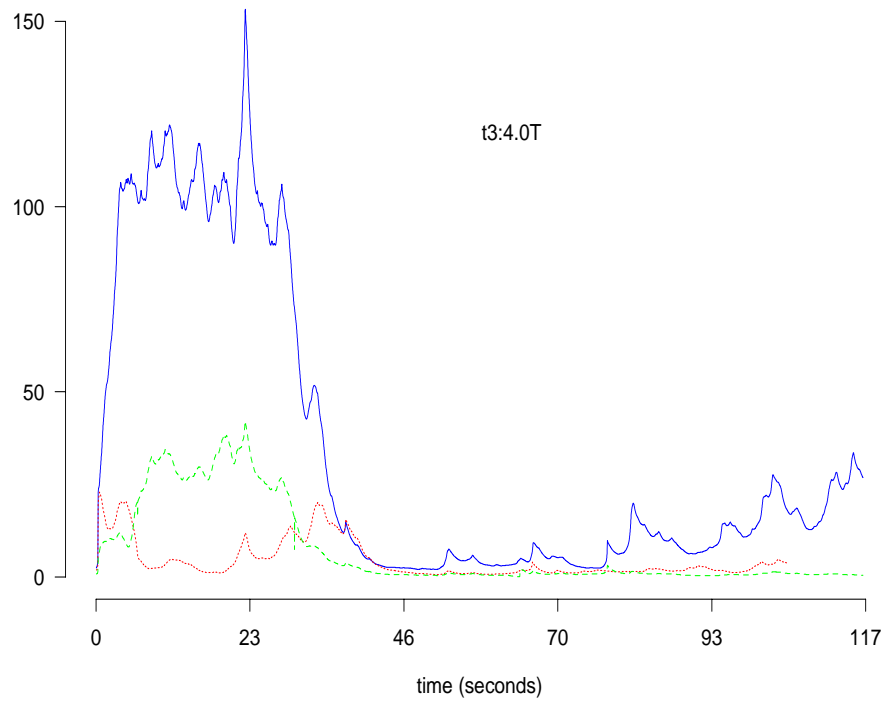


Figure 12: Trajectories of estimated amplitudes of key low frequency components in decomposition of the EEG series of treatment 3 (4.0T).

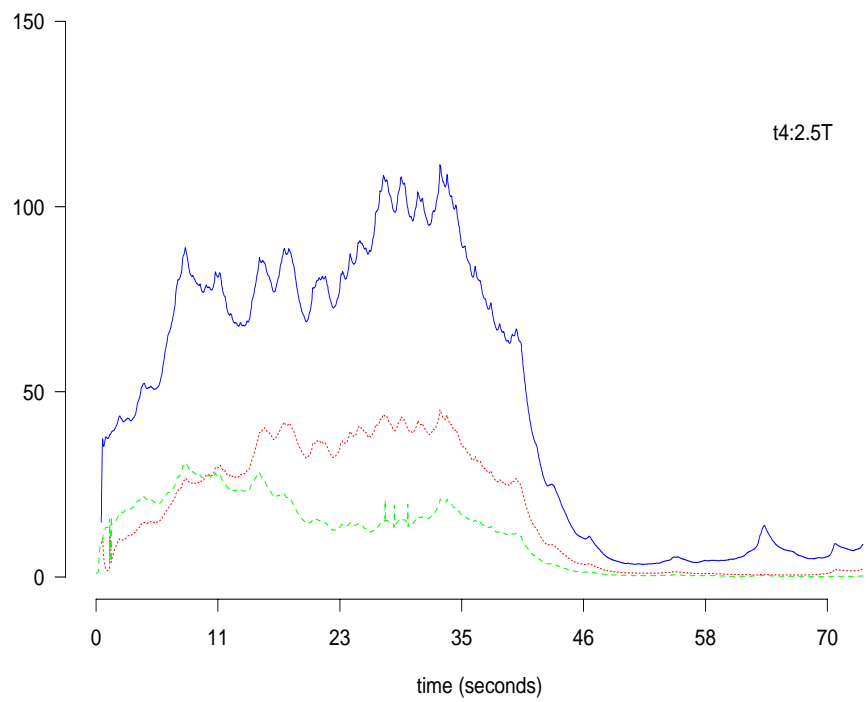


Figure 13: Trajectories of estimated amplitudes of key low frequency components in decomposition of the EEG series of treatment 4 (2.5T).