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Signal subspace integration for improved seizure localization

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***Abstract*— A subspace signal processing approach is proposed for improved scalp EEG-based localization of broad-focus epileptic seizures, and estimation of the directions of source arrivals (DOA). Ictal scalp EEGs from adult and pediatric patients with broad-focus seizures were first decomposed into dominant signal modes, and signal and noise subspaces at each modal frequency, to improve the signal-to-noise ratio while preserving the original data correlation structure. Transformed (focused) modal signals were then resynthesized into wide-band signals from which the number of sources and DOA were estimated. These were compared to denoised signals via principal components analysis (PCA). Coherent subspace processing performed better than PCA, significantly improved the localization of ictal EEGs and the estimation of distinct sources and corresponding DOAs.**

I. INTRODUCTION

Accurate spatial localization of epileptic seizures from scalp EEGs is a difficult problem. The precision of scalp-based localizations is limited by the spatial resolution of the electrode array, typically of the order of several cm in clinical systems. Also the inherent structure and complexity of scalp EEG signals, which measure aggregate neural activity from multiple cerebral and non-cerebral sources with overlapping spectral contents, also limits the localization accuracy. Typically, clinicians visually examine ictal EEGs to identify the electrode(s) at which seizure-related waveforms first appear, and estimate the corresponding brain area covered by this electrode as the region of ictal onset. However, in many cases focal seizures may be lateralizable to a cerebral hemisphere but may not be localizable to a smaller brain area. These are sometimes referred to as broad-focus seizures. A number of source separation methods have been proposed for decoupling contributions from multiple sources in scalp signals, e.g., [2], [5], [4], [6], [8], [11], [14]. Some of these methods aim to separate cerebral from non-cerebral contributions, particularly muscle- and eye-blink related artifacts that often contaminate scalp signals. The problem of decoupling multi-path seizure propagation from either multiple foci or broad regions of the brain has received relatively less attention, despite its clinical relevance. In particular, pediatric patients often have heterogeneous seizures with significant intra-patient variability, which are difficult to localize.

This study investigated signal decomposition and subspace processing for improving source localization, and identifying individual source directions of arrival in scalp EEGs recorded during broad-focus seizures. Signal subspace methods use an empirically derived signal basis to construct the subspace, and have been proposed for narrow- and broad-band processing [7], [13], [22], [18]. Despite many similarities, these methods are not identical to principal (PCA) or independent component (ICA) analyses. The assumption of statistical source independence may hold for multifocal seizure with multiple distinct focis, but not for broad-focus seizures with a spatially diffuse focus, for which ICA-based methods may not be appropriate. Also, PCA aims to re-express these signals as a sum of uncorrelated components, which may be geometric abtractions and may not correspond to individual, but correlated seizure sources. Thus, to preserve the original data correlation and still eliminate components corresponding to noise, subspace signal processing may be more appropriate. Multiple Signal Classification (MUSIC), which is also a subspace processing method is widely used for DOA estimation [17].

II. METHODS

A. Electrophysiological Data

Two scalp EEG datasets were analyzed, from 3 adult patients (age 33-50) and 3 pediatric patients (age 18-20), respectively, all with diagnosed focal epilepsy and multiple ictal segments that were not localizable to a single electrode or well defined brain region via standard EEG examination and analysis. The National Institutes of Health (NIH) define children as individuals under the age of 21. Adult data were recorded in the Clinical Neurophysiology Laboratory of the Comprehensive Epilepsy Center at Beth Israel Deaconess Medical Center. A standard international 10-20 clinical EEG system was used, and signals were remontaged to a common average reference. All EEGs were sampled at 500 Hz. Pediatric data were collected at Children's Hospital Boston, in the Clinical Neurophysiology Laboratory of the Epilepsy Center, using a clinical 10-20 EEG system (with additional electrodes FT9 and FT10). Signals were sampled at 1024 Hz and remontaged to a common average reference. Note that there is a slight difference in EEG nomeclature in the adult and pediatric datasets. Table I summarizes patient demographics and data details.

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TABLE I
CLINICAL/DATA INFORMATION

Patient	Age	# Ictal segments	Localization by visual EEG inspection
1	33	7	R hemisphere
2	50	2	-
3	42	11	R/L hemispheres
4	20	4	R Frontal/Central/Parietal
5	18	2	R Anterior quadrant
6	18	4	R Frontal/Central/Parietal

B. EEG Preprocessing

A stopband filterbank of 3rd order elliptical filters centered at the 60 Hz-harmonics of powereline noise, was applied to to data, in the range 60-250 Hz for adult EEGs and 60-512 Hz for pediatric EEGs, with a 1 Hz bandwidth, 20 dB attenuation in the stopband, and 0.5 dB ripple in the passband. Signals were filtered in both forward and reverse directions to eliminate phase distortions due to the non-linear phase of the filter. Eye blinking and muscle artifacts were suppressed using a matched-filtering approach [19].

C. Subspace signal processing

Algorithms for source separation include decomposition methods, such as principal and independent component analysis, statistical methods based on ARMA and nonlinear regression models, and various beamforming approaches, e.g., [1], [3], [12], [16], [23], [25]. Some of these methods may not appropriate for decomposing correlated sources [16]. In broad-focus seizures, contributions from individual sources may be correlated.

1) Model preliminaries: We consider an N-channel EEG array that measures signals $x(t)$ from p wideband seizure sources in the presence of noise. We define the ictal source vector as $\vec{s} = [s_1(t), ..., s_p(t)]^T$. The observed signals are then represented as a weighted superposition of individual source contributions, with relative delays τ_j, and noise:

$$x(t) = \sum_{j=1}^{p} b_j s_j(t+\tau_j) + v(t) \quad (1)$$

where b_j are the source weights. We assume an uncorrelated to the sources and normally distributed noise field, $\vec{v}(t) \sim \mathcal{N}(0, \Sigma^2)$. Given the non-stationarity of EEG signals, a processing window [t, t+T] is defined, in which stationarity may be assumed. In previous studies we have estimated that at least in adults, the dynamics and statistics of ictal EEGs vary with a periot of ∼3-4 s [20]. Therefore, in this study we used a processing window of length T = 4s.

2) Signal decomposition into dominant components: Empirical mode decomposition (EMD) is a flexible, data-driven method for estimating the dominant components (modes) of a non-stationary signal [10]. EEGs were decomposed into their dominant modes, each with a distinct characteristic frequency f_i. An example is shown in Figure 1. All analyzed seizures were not localizable by means of standard clinical methods of visual EEG examination and interpretation. EEGs were decomposed into their dominant modes and each modal matrix was subsequently decomposed into mutually orthogonal signal and noise subspaces. Once individual modes were denoised, new wideband signals with increased signal-to-noise (SNR) ratio were synthesized. The gain in SNR was in the range of 2.8-10.4 dB. Directions of arrival were estimated from the latter signals.

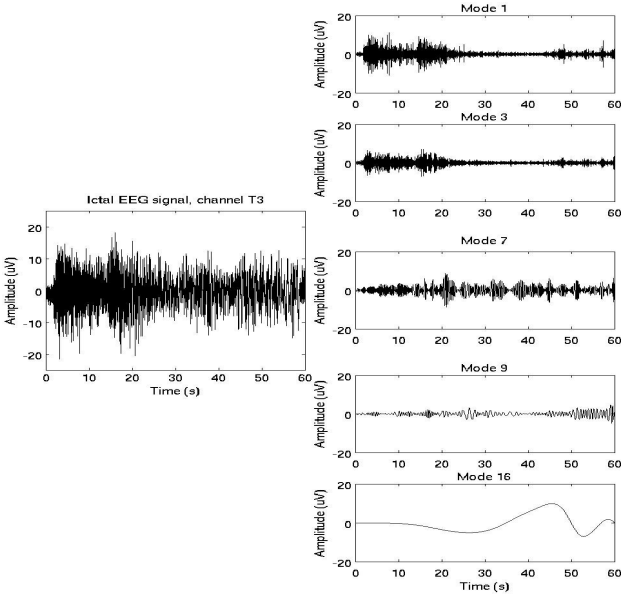

Fig. 1. Raw EEG signal (at channel T3) and 5 estimated dominant modes. In this example the entire non-stationary signal was decomposed.

3) Construction of modal signal subspaces: The coherent subspace processing method introduced by [24], which is widely used for estimation of arrival angles from multiple sources, was used here using individual EEG modal signals. It involves a transformation of narrowband data using a focusing matrix, so that within the common bandwidth of sources $s_1, ..., s_d$, the direction (or array manifold) matrix $A(\theta, f_i) = [\vec{a}(\theta_1, f_i), ..., \vec{a}(\theta_p, f_i)]$ is constant. $\vec{a}(\theta_k, f_i)$ is the direction of the kth source at frequency f_i with respect to some fixed reference point. Therefore, the following transformation of decomposed mode signals $x_m(t)$ is necessary:

$$y_m(f_i, t) = T(f_i) x_m(f_i, t) \quad (2)$$

$$T(f_i) A(\theta, f_i) = A(\theta, f_c) \quad (3)$$

where f_c is a constant frequency. The focusing matrix T is not a priori known and its estimation requires an initial guess of the arrival angles. If this deviates significantly from the true angles, this results in significant estimation bias. In this study, we estimated T using the minimization [9]:

$$min_T \| A(\theta, f_c) - T(f_i) A(\theta, f_i) \|_F \quad (4)$$

where $\| \cdot \|_F$ denotes the Frobenius norm. Note that for coherent integration of all frequencies in the broadband signal, this focusing is necessary [23]. The transformed and resynthesized wideband signals are given by

$$\vec{y}(t) = \sum_{m=1}^{M} T(f_m) \vec{x}_m(t) \quad (5)$$

Spatial spectra of $\vec{y}(t)$ were estimated in order to identify the peaks corresponding to individual source contributions and DOAs. The adaptation of the Pisarenko framework [15], for estimation of spatial spectra from the eigenvalues/eigenvectors of the sample covariance matrix, was used for this purpose [21]. Table II compares clinical seizure localizations to those obtained via signal subspace processing.

TABLE II
SEIZURE LOCALIZATIONS

Patient	Localization (raw EEG)	Localization (processed)
1	R hemisphere	T2, T4
2	-	F8,T2,T4,T6
3	R/L hemispheres	T3 (7 SZ), T2, T4 (4 SZ)
4	R Frontal/Central/Parietal	F4, Fp2
5	R Anterior quadrant	T4
6	R Frontal/Central/Parietal	F4, F8

III. RESULTS

In addition to signal subspace decompositions, EEGs were also denoised using PCA. The first 3 principal components were used to resynthesize filtered signals, as they explained on average $\sim$80% of the data variance. Figures 2-3 and 5 show examples of raw, subspace- and PCA-filtered EEGs from two adult and one pediatric patient, respectively. All ictal segments are from the first 10 s of each seizure.

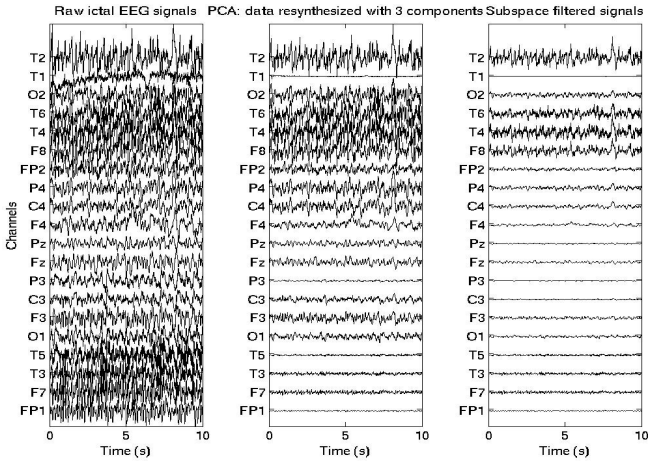

Fig. 2. Raw (left panel), PCA-filtered (middle panel) and subspace-filtered EEG signals (right panel), from patient #2.

Source locations are not identifiable in raw EEGs in Figure 2. In PCA-filtered signals, activity in a large area of the right hemisphere is estimated, which includes frontal, temporal, parietal and central channels. In subspace-processed signals the activity is further constrained to channels F8 T4, T6, T2.

In raw EEGs in Figure 3, bilateral activations make it difficult to estimate the seizure onset zone. Subspace processing enhanced activation in channel T3, with smaller contributions from channels T2, T4 and F8, and attenuated activity in all other channels. The corresponding spatial spectrum with a peak approximately in the direction of channels T3 is shown in Figure 4. Note that the midline corresponds to the $0-180^o$ axis, and increasing azimuth is counterclockwise.

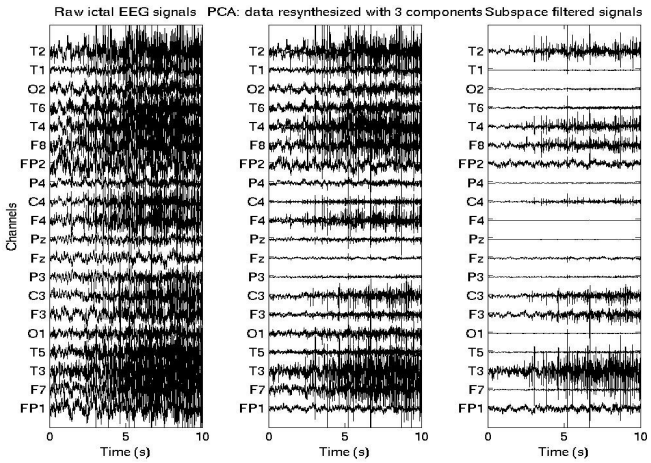

Fig. 3. A second example (from patient #3), of raw (left panel) and processed ictal EEG signals (middle and right panels).

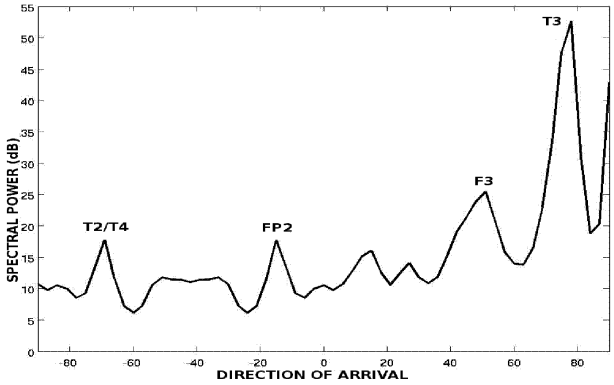

Fig. 4. Estimated DOA for the ictal segment in Figure 3. The highest spectral peak corresponds to the direction of channel T3, with additional peaks ($\sim$25-30 dB lower), in the directions of channels F3, FP2, and T2/T4.

In subspace-filtered signals in Figure 5, only activations in channels F4 and Fp2 are enhanced. The corresponding spatial spectrum of the subspace processed data is shown in Figure 6. Two peaks with spectral power $\sim$120 dB and $\sim$80 dB, respectively, and DOAs $\sim$-30^o and $\sim$-10^o, are clearly identifiable. These approximately correspond to arrivals in the direction of channels F4 and Fp2.

IV. DISCUSSION

We have proposed a signal subspace integration method that combines mode decomposition with transformations (focusing) of individual modal signals and their corresponding subspaces, to denoise scalp EEGs and improve the localization of multiple correlated seizure source contributions. In contrast to previous studies that have applied subspace methods to eliminate artifactual contributions or decouple independent sources in EEGs, here we applied this method to decouple correlated ictal contributions in broad-focus seizures. Specifically, two sets of ictal EEGs were analyzed,

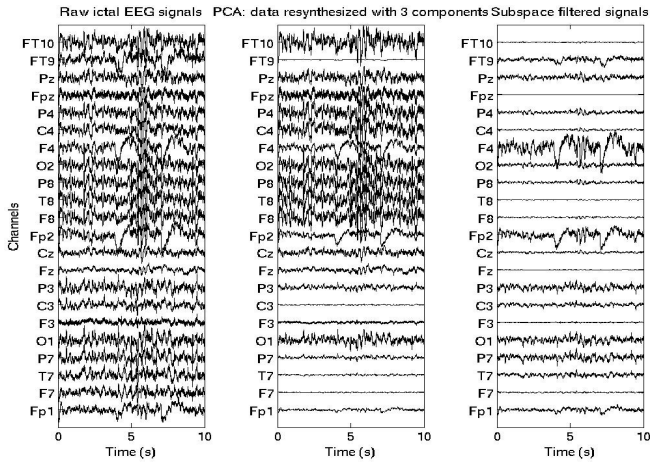

Fig. 5. Example from one pediatric patient (# 6 in Table 1): Raw (left panel) and and denoised ictal EEG signals (middle and right panels).

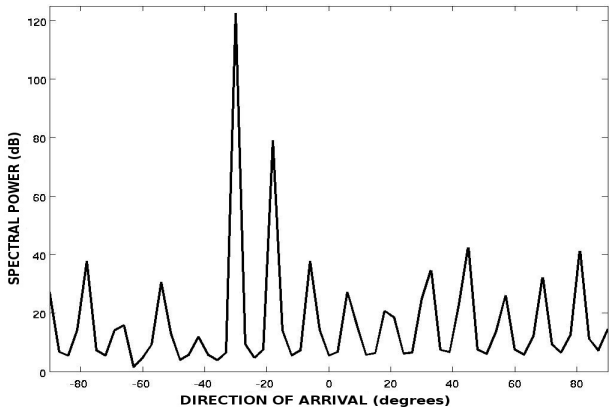

Fig. 6. Estimated DOA for the ictal segment in Figure 5. The highest spectral peak corresponds to the direction of channel T4, and a second peak ($\sim$40 dB lower), occurs in the directions of channel Fp2.

from adult and pediatric patients with focal epilepsy, and non-localizable seizures via clinical EEG examination. We compared denoising via subspace processing to PCA-based filtering. Subspace processing improved the specificity of the localization significantly both in comparison to raw EEG analysis and PCA. Furthermore contributions from individual sources (localizable to EEG electrodes) and their directions of arrival were identifiable in spatial spectra of subspace processed signals. Thus, this approach is promising for scalp EEG denoising, and may be used in conjuction with other localization algorithms, e.g., time-delay based, or even visual examination of filtered signals. Evidently this is only a preliminary study and does not include a rigorous comparison with other subspace decomposition methods, simulations or application to large EEG datasets. Furthermore, comparison seizure freedom after resection of the presumed epileptogenic zone, which is the ultimate gold standard of localization will validate the accuracy of the proposed approach. To assess the specificity and performance of the method, an extensive study that includes these comparisons is necessary.

REFERENCES

[1] J. Anemuller, T. J. Sejnowski, and S. Makeig, Complex independent component analysis of frequency-domain electroencephalographic data, *Neural Networks*, vol. 16(9), 1311-1323, 2003.

[2] A. Bell and T. Sejnowski, An Information-Maximization approach to blind separation and blind deconvolution, *Neural Comput*, 7(6):1129-1159, 1995.

[3] J. F. Bohme, On parametric methods for array processing, *Proc. EVSIPCO'83 Conf.*, 12-16, 1982.

[4] A. Cichocki, S.L., Shishkin, T. Musha, et al., EEG filtering based on blind source separation (BSS) for early detection of Alzheimer's disease, *Clin Neurophysiol*, 116(3):729-37, 2005.

[5] J. Corsini, L. Shoker, S. Sanei, G. Alarcon, Epileptic xseizure predictability from scalp EEG incorporating constrained blind source separation, *IEEE Trans Biomed Eng*, 53(5):790-799, 2006.

[6] M. De Vos, A. Vergult, L. De Lathauwer, W. De Clercq, et al., Canonical decomposition of ictal scalp EEG reliably detects the seizure onset zone, *NeuroImage*, 37(3):844-854, 2007.

[7] K. Hermus, P. Wambacq, H. Van Hamme, A review of signal subspace speech enhancement and its application to noise robust speech recognition, *EURASIP J Adv Sig Proc*, 0455821:1-15, 2007.

[8] C.W. Hesse, C.J. James, Tracking and detection of epileptiform activity in multichannel ictal EEG using subspace correlation of seizure source scalp topographies, *Med Biol Eng Comput*, 43(6):764-770, 2005.

[9] H. Hung, M. Kaveh, Focusing matrices for coherent signal-subspace processing, *IEEE Trans Acoust Speech Sig Proc*, 36:1272-1281, 1988.

[10] N.E. Huang et al. (1998), Empirical Mode Decomposition and Hilbert spectrum for non-linear, non-stationary time series analysis, *Proc. R. Soc. Lond. A*, 454:903-995.

[11] . N. Jmail, M. Gavaret, F., Wendling, et al., A comparison of methods for separation of transient and oscillatory signals in EEG, *J Neurosci Methods*, 199(2):273-289, 2011.

[12] S. Li and T. J. Sejnowski, Adaptive separation of mixed broadband sound sources with delays by a beamforming Herault-Jutten network, *IEEE J. Ocean. Eng*, 20(1):73-79, 1995.

[13] W. S. Liggett, Passive sonar: Fitting models to multiple time series, *Signal Processing*, J.R. Griffith et al., Eds. New York Academic, 1973.

[14] B., Mijovic, M. De Vos, I., Gligorijevic, et al., Source separation from single-channel recordings by combining empirical-mode decomposition and independent component analysis, *IEEE Trans Biomed Eng*, 57(9):2188-2196, 2010.

[15] V.F. Pisarenko, On the estimation of spectra by means of non-linear functions of the covariance matrix, *Geophys J Royal Astr Soc*, 28:511-531, 1972.

[16] B. Porat, B. Friedlander, Estimation of spatial and spectral parameters of multiple sources, *IEEE Trans. Inform. Theory*, 29: 412-425, 1983.

[17] R.O. Schmidt,"Multiple Emitter Location and Signal Parameter Estimation," IEEE Trans. Antennas Propagation, Vol. AP-34 (March 1986), pp.276-280.

[18] G. Su and M. Morf, Signal subspace approach for multiple wideband emitter location, *IEEE Trans Acoust, Speech, Signal Proc*, vol. ASSP-31:1502-1522, 1983.

[19] C. Stamoulis, B.S. Chang, Application of matched-filtering to extract EEG features and decouple signal contributions from multiple seizure foci in brain malformations, *Proc 4th Int IEEE Conf Neural Eng*, 514-517, 2009.

[20] C. Stamoulis, L.J. Gruber, D.L. Schomer, B.S. Chang, High-frequency neuronal network modulations encoded in scalp EEG precede the onset of focal seizures, *Epilepsy Behav*, 2012.

[21] P. Stoica, J. Li, X. Tan, On spatial power spectrum and signal estimation using the Pisarenko framework, *IEEE Trans Sig Proc*, 56(10):5109-5119, 2008.

[22] D. W. Tufts, R. Kumaresan, Estimation of frequencies of multiple sinusoids: Making linear prediction perform like maximum likelihood, *Proc. IEEE*, 70, 1982.

[23] W. Wang, S. Sanei, J. A. Chambers, Penalty function-based joint diagonalization approach for convolutive blind separation of nonstationary sources, *IEEE Trans Sig Proc*, vol. 53(5), 1654-1669, 2005.

[24] H. Wang, M. Kaveh, Coherent signal-subspace processing for the detection and estimation of angles of arrival of wideband soures, *IEEE Trans Acoust Speech Sig Proc*, ASSP-33(4):823-831.

[25] M. Wax, T. Kailath, Optimum localization of multiple sources by passive arrays, *IEEE Trans Acoust. Speech, Signal Proc*, ASSP-31:1210-1218, 1983.