Prewhitening and normalisation strategies for fast-ripple representation in intracerebral EEG

Nicolas ROEHRI[1], Jean-Michel BADIER[1], Fabrice WENDLING[3], John MOSHER[4], Fabrice BARTOLOMEI[1,2], Christian BÉNAR[1]

[1]Institut de Neurosciences des Systèmes, INSERM UMR1106, Aix-Marseille Université, Faculté de Médecine, 27, Boulevard Jean Moulin, 13005 Marseille France

[2]Service de Neurophysiologie Clinique, AP-HM, 13385 Marseille Cedex 5, France

[3]Laboratoire Traitement du Signal et de L'Image, INSERM 1099, Université de Rennes 1, 35042 Rennes Cedex, France

[4]Cleveland Clinic, S51 9500, Euclid Avenue Cleveland, USA

nicolas.roehri@etu.univ-amu.fr

Résumé – En EEG intracérébral (SEEG), les oscillations hautes fréquences (HFOs) au delà de 250Hz, plus connues sous le nom de Fast Ripples (FRs), sont considérées comme étant fortement liées aux tissus cérébraux capables de provoquer des crises épileptiques. L'analyse visuelle des FRs est longue et difficile et peut être facilitée par la représentation en temps-fréquence. Nous avons testé 5 méthodes de pré-blanchiment des signaux et de normalisation du plan (t,f) en vue d'améliorer la représentation de ces activités. Nous avons détecté tous les maxima locaux de l'image (t,f) dans la bande des HFOs supérieurs à un seuil balayant un certain intervalle. Le critère de performance est basé sur l'aire sous la courbe des courbes de précision et rappel. Nous avons montré que le pré-blanchiment des données est plus efficace que la normalisation de la représentation (t,f) et que la différentiation rétrograde de première ordre donne les meilleures résultats.

Abstract – On intracerebral EEG (SEEG), High Frequency Oscillations (HFOs) above 250Hz, also known as Fast-Ripples (FRs), are considered to be highly representative of brain tissues capable of producing epileptic seizures. The visual review of FRs is time-consuming and tedious, and can be improved by time-frequency analysis. We tested 5 methods of data prewhitening and (t,f) normalisation in order to improve the time-frequency representation of fast ripples. We detected all local maxima of the (t,f) image above a range of thresholds in the HFO band. The performance criterion was based on the area under the curve of the Precision and Recall curves. We showed that data prewhitening was more efficient than (t,f) normalisation and that overall the first-order backward differencing exhibited the best results.

1 Introduction

Over the past decade, High Frequency Oscillations (HFOs) in brain areas have been the subject of numerous studies in neuroscience. HFOs are thought to be a biomarker of the epileptogenicity of brain tissues [1, 2]. They are divided into two groups: ripples (80–250Hz) and fast-ripples (FR)(250–500Hz). Ripples are supposed to be physiologic whereas FRs are sometimes presumed to be pathological. Manual marking of FRs in stereoelectroencephalography (SEEG) signals is time-consuming and inevitably subjective because of their short time duration and low amplitude. Improving the representation of the SEEG signals by using an appropriate time-frequency representation [3, 4] would be useful. More recently, automatic HFO detectors have incorporated time-frequency representations as a key feature [5, 6]. Because SEEG signals have a spectrum with a $1/f^{\alpha}$ decay (f being the frequency), data preprocessing or (t,f) image normalisation is required.

We tested 5 commonly used methods – two methods of data prewhitening and three methods of (t,f) normalisations – on their precision to represent FRs. These methods were applied to simulated data with real background activity recorded in SEEG.

2 Methods

2.1 Simulated Data

In order to compare the different methods, simulated signals corresponding to five event types were generated. The different types are the following: $\{s_1[n]\}$ background activity, $\{s_2[n]\}$ background activity with artificial artefact, $\{s_3[n]\}$ background activity with a simulated epileptic spike, $\{s_4[n]\}$ background activity with a simulated FR and finally $\{s_5[n]\}$ background activity with a simulated spike and simulated FR. The spike, the fast-ripple and the artefact occur at $t_{\text{EP}} = 50ms$, $t_{\text{FR}} = 155ms$ and $t_{\text{ART}} = 375ms$ respectively.

The piece of human background activity was randomly selected from a collection of recordings (sampling frequency: 2048Hz) which was previously labeled as background, i.e signal without one of these elements of interest, from several patients and several brain areas. These recordings were perfor-

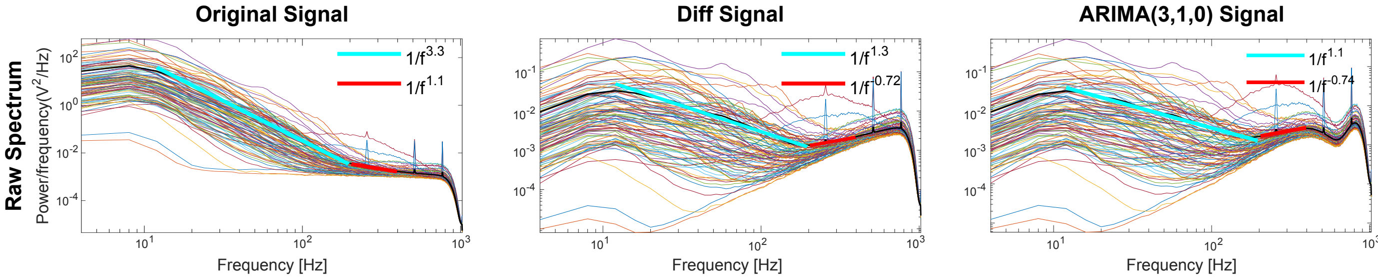

FIGURE 1 – Effect of the prewhitening methods applied to a patient recording
All the prewhitening methods were applied to each electrodes of a patient. The spectra are displayed in loglog. The thick black, cyan and red lines correspond to the average spectrum, the fit with a power-law function $(1/f^{\alpha})$ for the lower frequencies and the HFO band respectively. The slope was obtain by linear regression. The difference in the slope of the original spectrum compared to the spectra of the prewhiten signal indicates the effects of the filters. It is noteworthy that the spectrum has two different slopes, one describing the lower frequencies and another describing the FR band.

med on patients undergoing pre-surgical evaluation of drug resistant epilepsy with SEEG. For standardisation, the collection of backgrounds were normalised by dividing each signal by its own standard deviation (STD) and multiplied by the median STD of the collection to resemble real data. Unlike previous studies, the STDs were not computed on raw data but on data which were digitally bandpass-filtered (4^{th}-order Butterworth) in the fast-ripple band. The Signal-to-Noise Ratio (SNR) was also calculated on the filtered data on the time duration of the FR. This approach is motivated by the fact that SEEG signals have a spectrum with a $1/f$ decay in the FR band (cf. Fig. 1). Each event was generated in a 500-ms window. Epileptic spikes were simulated using the spline function of MATLAB which interpolates the curves between specific points taken from a real epileptic spike. The width of the spike randomly changed across trials. Its amplitude was set to be proportional to the STD of the background. The fast ripple was set to 350Hz with a duration of four periods. To avoid edge effect, the spike and the FR were windowed beforehand and then added to the background. The artefact was simply generated by increasing a single point by a certain level. This level corresponds to five times the STD of the chosen background. Examples of the five events are shown in Fig. 2.

The different prewhitening methods were applied in the time domain.

- The Diff method consists in a first-order backward differencing [7]. Let $\tilde{s}$ be the prewhiten signal.
$$\tilde{s}[n] = s[n] - s[n-1] \tag{1}$$
- The autoregressive integrated moving average (ARIMA) prewhitening computes the coefficients of a p^{th}-order AR model (lpc function in MATLAB) on the q^{th}-degree differentiated signal and filters the signal with the coefficient of the AR model. Several parameters were tested and this following set (1,1,0) gave the best results.

The Time-Frequency representation (referred to as $\{tf[n,m]\}$, with n and m corresponding to the time index and frequency index respectively) is obtained by applying a wavelet transform on the prewhiten signal and taking its square modulus. The wavelet used is a common Gabor wavelet with an oscillation parameter of 10.

Normalisation methods were applied to the (t,f) image.

- The z-score was applied to the square modulus using the mean μ_i and the STD σ_i of either a baseline or the event itself over time and for each frequency taken separately. The two types of z-score will be further named as $z_{baseline}$ and z_{event}. The baseline was taken in the same background but in a time-shifted window.
$$tf_{z_i}[n,m] = \frac{tf[n,m] - \mu_i[m]}{\sigma_i[m]} \tag{2}$$
- The Teager-Kaiser Normalisation computes on the modulus the Teager-Kaiser Operator Energy (TKEO) over time and for each frequency taken separately. $\bar{.}$ denotes the complex conjugate.
$$tf_{TKEO}[n,m] = tf[n,m]\overline{tf}[n,m] + \tag{3}$$
$$\frac{1}{2}tf[n-1,m]\overline{tf}[n+1,m] + \frac{1}{2}\overline{tf}[n-1,m]tf[n+1,m]$$

The methods are illustrated in Fig. 2. An illustration of the impact of the filters is represented in Fig. 1.

2.2 Method Quantification

To capture how relevant the representations are, we want to quantify how the oscillations are separated from the background activity. It is known that oscillations appear as blobs in the (t,f) image. While analysing visually such representations, we pay attention to the local maxima rising above the noise level. The method proposed here is to detect all local maxima in the HFO band, spanning a range of thresholds. 30 events of each type were generated. All peaks were normalised between 0 and 1 for each method. The peaks were labeled as True Positive (TP), False Positive (FP), True Negative (TN) and False Negative (FN).

TPs are local maxima which are above the threshold and are our peaks of interest, i.e local maxima of all signals s_4 and s_5 which are above the threshold and are in the confidence zone. The confidence zone was set as being the zone of the image where the blob of the FR should theoretically appear. It is a square zone centered in (162ms, 350Hz) with a time width of

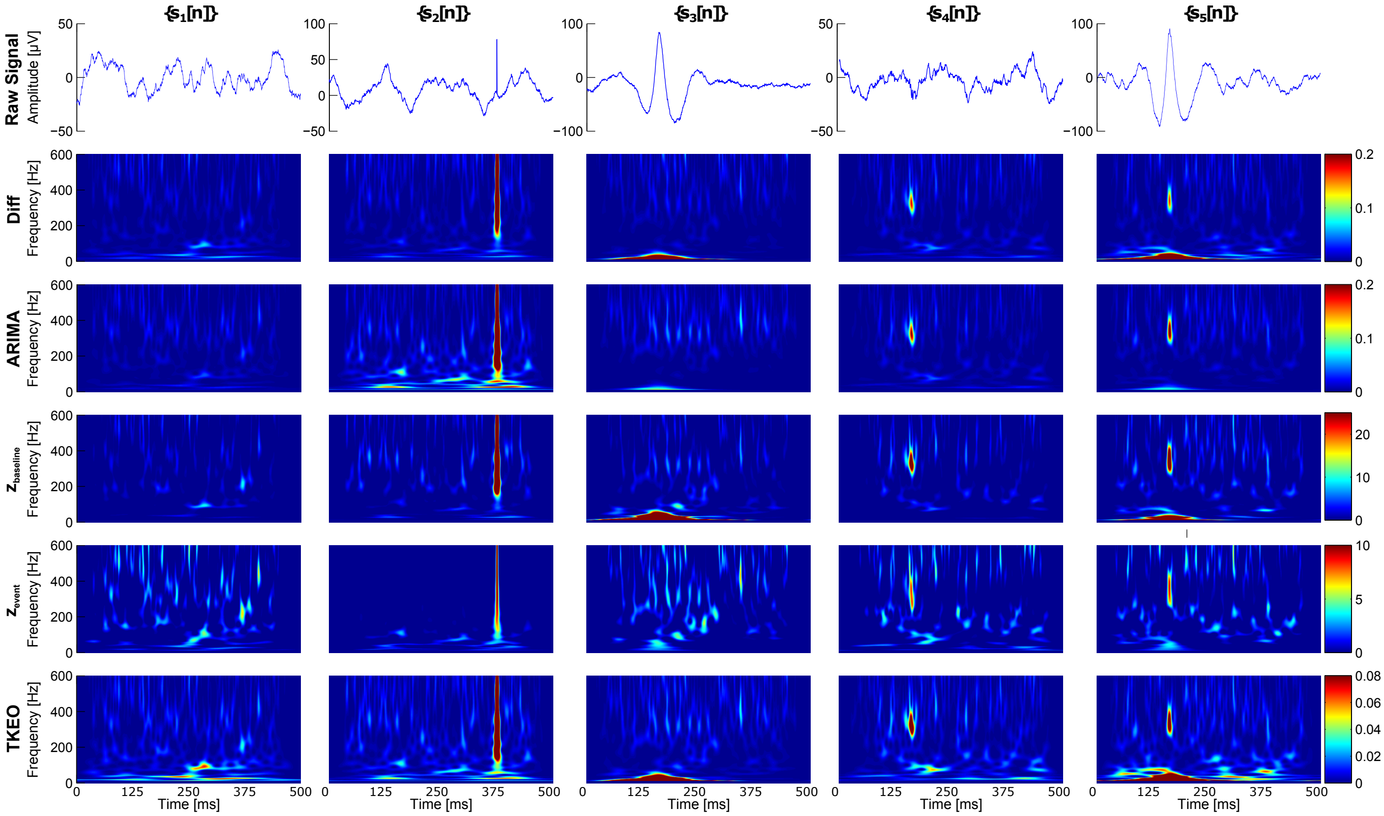

FIGURE 2 – Examples of simulated events and their different (t,f) representations.
Each column represents an event type and each row a prewhitening or (t,f) normalisation method. The colourmaps were set from 0 to the value of the highest peak of the set of events for each technique. AR prewhitening, z_{event} and TKEO normalisation seem to be more sensitive to noise since it generates higher blobs from the background. The artefacts generate long lines whose height increases along the frequency but no local maxima. Only the Diff method, the $z_{baseline}$ and TKEO normalisation display triangular shapes corresponding to the spikes in the events s_3 and s_5.

σ_t and a frequency width of σ_f. σ_t was calculated using the expression: $\xi = 2f\sigma_t$ with ξ the oscillation parameter and f the frequency of the oscillation. σ_f was heuristically set to 30Hz as being the accepted error on the frequency of the oscillation. FPs are local maxima which are above the threshold but are not our peaks of interest, i.e local maxima of all signals s_1, s_2 and s_3 which are above the threshold plus those of all s_4 and s_5 above the threshold which are not in the confidence zone. TNs are local maxima which are not above the threshold and are not our peaks of interest, i.e local maxima of all signals s_1, s_2 and s_3 which are not above the threshold plus those of all s_4 and s_5 under the threshold which are not in the confidence zone. FNs are local maxima which are not above the threshold but are our peaks of interest, i.e local maxima of all s_4 and s_5 which are not above the threshold but are in the confidence zone.

Receiver Operating Characteristic (ROC) and Precision and Recall (PR) curves are obtained by calculating the True Positive Rate (TPR) or Recall, the False Positive Rate (FPR) and the Precision or Positive Predictive Value (PPV).

The Area Under the Curve (AUC) of the PR curves was used as a ranking criterion. This method was repeated 30 times for each SNR. The different SNRs were chosen according to the range seen in real data. These SNRs were calculated on events marked using automatic detector [7]. The STD of the oscillation was obtained by decomposing the signal using the Empirical Mode Decomposition (EMD) [8] and taking the mode corresponding to the fast ripple. The obtained signal was checked on (t,f) representation before and after decomposition. The STD of the noise was computed on two pieces of filtered background before and after the FR occurrence with overall length of the oscillation. The SNR of the real data were found to lie between 0 and 17dB with a median value of 9dB.

3 Results and Discussion

In Fig. 1, FRs hardly stand out of the noise. This observation is consistent with our motivation: signal processing is needed to visualise FRs. Methods such as the Coarse Graining Spectral Analysis could be used to separate the harmonic/oscillatory from the fractal/$1/f^{\alpha}$ components of the spectrum [9] but only on the sections of recordings already marked as containing FRs because of their short duration and scarcity. Moreover, the original spectrum fits two power laws of coefficients 3 and 1 for the frequency range of 10-200Hz and 250-500Hz – the FR band – respectively. The two filters tends to flatten the spectrum and inverse the slope of the FR band.

Because of the high number of negative events (N) the ROC curves are pushed to the left part of the graph and are not discriminative. In contrast, the PR curves highlight differences between the methods [10]. In a clinical setting, it seems interesting to address the proportion of TP within all detection regardless of N. PR curves are therefore preferred for further analysis.

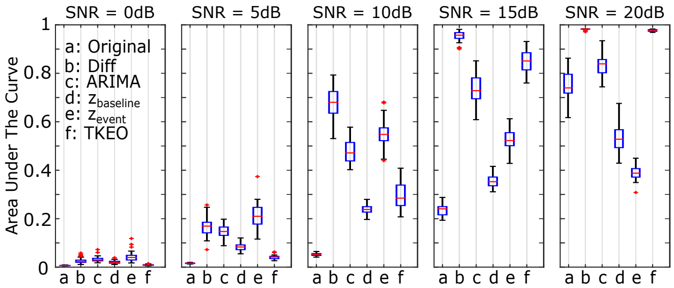

FIGURE 3 – Box and whisker plot of the AUC of the original signal and the five techniques for several SNRs.
Generally, all methods show better results when the SNR increases. All methods exhibit poor performances for SNRs below 5dB without having one method being significantly better than another one. The z_{event} shows a decrease in performance for SNR = 20dB. In most cases, the Diff method exhibits the best results followed by the ARIMA prewhitening.

Box and whisker plots of the AUC of the original signal and the 5 methods are represented for 5 different SNRs in Fig. 3. Fig. 3 a which corresponds to the normal TF representation without normalisation nor prewhitening preprocessing shows the worst performance overall except for the ideal case, SNR=20dB. This is consistent with the aim of this study. All methods exhibit poor performances for SNRs below 5dB without having one method being significantly better than another one. This is not the case for larger SNRs. The Diff method demonstrates the highest performance for SNRs higher than 10dB followed closely by the ARIMA prewhitening. It is noteworthy that there is an inversion for the two z-score methods. The $z_{baseline}$ is less efficient than z_{event} for an SNR of 15dB but more efficient for SNRs higher than 20dB. The TKEO normalisation seems to improve as well when the SNR increases. It is interesting to note that the prewhitening methods achieve better results than (t,f) normalisation approaches. Moreover, one asset of the Diff method compared to the ARIMA method is that it is not dependent of the data and could be directly applied to a whole recording.

4 Conclusion

The current study aims at finding the most relevant techniques of representing FR in time-frequency analysis. PR curves were adopted because they gave more meaningful results. Overall, the Diff method exhibited the best results. More generally, the prewhitening methods were more efficient than the commonly used time-frequency normalisation. One should better prewhiten data before producing a time-frequency representation than normalising a posteriori the (t,f) image. Future work will take into account the shape of the blobs as well as the representation of the spikes.

Références

[1] Julia Jacobs, Pierre LeVan, Rahul Chander, Jeffery Hall, François Dubeau, and Jean Gotman. Interictal high-frequency oscillations (80-500 Hz) are an indicator of seizure onset areas independent of spikes in the human epileptic brain. *Epilepsia*, 49(11):1893–1907, 2008.

[2] Julia Jacobs, Pierre Levan, Claude Douard Chtillon, Andr Olivier, Franois Dubeau, and Jean Gotman. High frequency oscillations in intracranial EEGs mark epileptogenicity rather than lesion type. *Brain*, 132(4):1022–1037, 2009.

[3] C. G. Bénar, L. Chauvière, F. Bartolomei, and F. Wendling. Pitfalls of high-pass filtering for detecting epileptic oscillations: A technical note on "false" ripples. *Clinical Neurophysiology*, 121(3):301–310, 2010.

[4] Lotfi Senhadji and Fabrice Wendling. Epileptic transient detection: Wavelets and time-frequency approaches. *Neurophysiologie Clinique*, 32(3):175–192, 2002.

[5] Gwénaël Birot, Amar Kachenoura, Laurent Albera, Christian Bénar, and Fabrice Wendling. Automatic detection of fast ripples. *Journal of Neuroscience Methods*, 213(2):236–249, 2013.

[6] Sergey Burnos, Peter Hilfiker, Oguzkan Sürücü, Felix Scholkmann, Niklaus Krayenbühl, Thomas Grunwald, and Johannes Sarnthein. Human intracranial high frequency oscillations (HFOs) detected by automatic time-frequency analysis. *PLoS ONE*, 9(4), 2014.

[7] Andrew B. Gardner, Greg a. Worrell, Eric Marsh, Dennis Dlugos, and Brian Litt. Human and automated detection of high-frequency oscillations in clinical intracranial EEG recordings. *Clinical Neurophysiology*, 118(5):1134–1143, 2007.

[8] Norden E Huang, Zheng Shen, Steven R Long, Manli C Wu, Hsing H Shih, Nai-chyuan Yen, Chi Chao Tung, and Henry H Liu. The empirical mode decomposition and the Hilbert spectrum for nonlinear and non-stationary time series analysis. *Proceedings of the Royal Society A: Mathematical, Physical and Engineering Sciences*, 454(1971):995, 903, 1998.

[9] Biyu J. He, John M. Zempel, Abraham Z. Snyder, and Marcus E. Raichle. The temporal structures and functional significance of scale-free brain activity. *Neuron*, 66(3):353–369, 2010.

[10] Tom Fawcett. ROC Graphs: Notes and Practical Considerations for Data Mining Researchers ROC Graphs : Notes and Practical Considerations for Data Mining Researchers. page 27, 2003.