Automatic Detection of Epileptic Spikes in Intracerebral EEG with Convolutional Kernel Density Estimation

Ludovic Gardy[1,2,3][a], Emmanuel J. Barbeau[1,2][b] and Christophe Hurter[3][c]
[1]*University of Toulouse, UPS, Centre de Recherche Cerveau et Cognition, Toulouse, France*
[2]*CNRS, CerCo, Purpan Hospital, Toulouse, France*
[3]*French Civil Aviation University, ENAC, Avenue Edouard Belin, Toulouse, France*

Keywords: Electroencephalography, EEG, Time Series Visualization, Signal Processing, Kernel Density Estimation, Convolution, Noisy Signal, Event Detection, Epilepsy, Accessibility.

Abstract: Analyzing the electroencephalographic (EEG) signal of epileptic patients as part of their diagnosis is a very long and tedious operation. The most common technique used by medical teams is to visualize the raw signal in order to find pathological events such as interictal epileptic spikes (IESs) or abnormal oscillations. More and more efforts are being adopted to try to facilitate the work of doctors by automating this process. Our goal was to analyze signal density fields to improve the visualization and automatic detection of pathological events. We transformed the EEG signal into images on which we applied a convolution filter based on a Kernel Density Estimation (KDE). This method that we propose to call CKDE for Convolutional Kernel Density Estimation allowed the emergence of local density fields leading to a better visualization as well as automatic detection of IESs. Future work will be necessary to make this technique more efficient, but preliminary results are very encouraging and show a high performance compared to a visual inspection of the data or some other automatic detection techniques.

1 INTRODUCTION

Epilepsy is the name of a brain disorder characterized predominantly by recurrent and unpredictable interruptions of normal brain function, called epileptic seizures (Fisher et al., 2005). Treating this disease sometimes requires the patient to undergo a record of his brain activity by Electroencephalography (EEG) in order to characterize the epileptogenic network, i.e., the brain area(s) involved in the seizures. EEG results from the electric signal generated by the cooperative action of brain cells (Blinowska and Durka, 2006). When epilepsy is drug-resistant, the solution to cure the patient is to surgically remove the area of his brain that causes seizures. To locate this area, it is often necessary to go through a stereoelectroencephalography (SEEG) consisting of the deep intracerebral implantation of electrodes. The depth EEG of the patient is recorded 24 hours a day for 6 to 15 days and then examined later by epileptologists. The electrophysiological markers and criteria for determining whether a cerebral area is impaired are still being defined (Valero et al., 2017; Roehri et al., 2017; Frauscher et al., 2017; Roehri et al., 2018). However, some markers such as interictal epileptic spikes (IESs) are characteristic of the epileptogenic network (Talairach and Bancaud, 1966). They appear spontaneously between periods of seizures and are of high amplitude for a duration ranging from 30 to 100 milliseconds (De Curtis and Avanzini, 2001) followed by a slow component for around 150 to 200 milliseconds (Staley and Dudek, 2006). IESs are generated by synchronous discharges of a group of neurons in a region referred to as the irritative zone (Latka et al., 2003). While some would argue that the neural network that produces IESs is not always identical to the seizure onset zone, IESs are useful to support the diagnosis of epilepsy (Staley and Dudek, 2006). Other markers, more recent and not used in clinical practice yet such as fast-ripples, are being studied by several teams around the world and could be essential markers of the seizure onset zone (Staba et al., 2002; Ibarz et al., 2010). There is currently no official tool that can be used in clinical practice to detect these discrete and transient events, such as IES or fast-ripples.

[a] https://orcid.org/0000-0002-2977-8831
[b] https://orcid.org/0000-0003-0836-3538
[c] https://orcid.org/0000-0003-4318-6717

Gardy, L., Barbeau, E. and Hurter, C.
Automatic Detection of Epileptic Spikes in Intracerebral EEG with Convolutional Kernel Density Estimation.
DOI: 10.5220/0008877601010109
In *Proceedings of the 15th International Joint Conference on Computer Vision, Imaging and Computer Graphics Theory and Applications (VISIGRAPP 2020) - Volume 2: HUCAPP*, pages 101-109
ISBN: 978-989-758-402-2; ISSN: 2184-4321

Moreover, their characteristics can differ from one patient to another and vary in shape, duration, or frequency, making them very difficult to detect by an automatic tool. Many attempts have been made to create such devices, but they've had a relatively low impact and have not passed the gates of research laboratories. However, we address that question with a completely new approach that could provide an efficient solution. The amounts of data to be analyzed are so huge; we estimate it at around 317 billions of electrophysiological values for a 15-day, or 360 hours, recording in one patient. We can no longer let clinicians manually look at the signal and search inside for pathological events without help. The technique we propose to visualize and automatically tag pathological events in this massive amount of noisy EEG signal is based on image processing. Our tests show that IESs have a particular signature in the field of densities. We transformed the signal into an image using Kernel Density Estimation (Silverman, 2018) and applied a convolution onto this image to build density fields based on the spacing of pixels. The brief and rapid amplitude changes during spikes lead to a larger gap between activated pixels which is characterized by a low density after convolution. These low densities are the ones that can be visualized and even automatically recorded. We analyzed the intracerebral EEG recordings of a patient treated in the epilepsy department of CHU Purpan in Toulouse, France. Our method allowed us to obtain an improved visualization of the EEG signal enabling a fast localization of the IESs but also automatic detection of these pathological events. There is still much effort to be made to generalize this approach and make it functional for clinical implications, but the preliminary results we obtain using it are very encouraging. In this paper, we will define epilepsy and diagnostic problems before presenting the related works about EEG visualization and automatic pattern detection, then present the results we have obtained and discuss them.

2 RELATED WORKS

This work builds upon recent studies covering time-series visualization (Wang et al., 2017) as well as the automatic search for pathological events such as interictal epileptic spikes (IESs) in the EEG signal (Roehri et al., 2018). The question of IESs as markers of the epileptogenic network has been widely studied, but no study has yet made it easier to visualize them or detect them automatically. These techniques are either not reliable enough or too long or difficult to use.

2.1 EEG Visualization

EEG recordings are most of the time represented as curve-shaped amplitudes varying over time (figure 1). These line graphs are a quick and easy way to describe and understand brain activity. Clinicians and neurologists, in particular, are very attached to this visualization because they are used to it and understand it well.

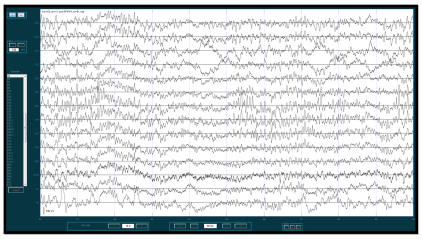

Figure 1: Classical representation as a line graph of an EEG signal. Each line represents a channel from an intracerebral recording.

Time-frequency representation (figure 2) is another way to display the signal, seldom used in clinical practice but appreciated by neuroscientists. The frequency spectrum is a good indicator of ongoing cognitive processes and possibly epileptic events such as pathological oscillations (Bragin et al., 2002; Bragin et al., 1999a; Höller et al., 2015). The promising results of a time-frequency analysis of intracerebral EEG signals in epilepsy will probably make this a not to be missed step soon from a medical point of view as well.

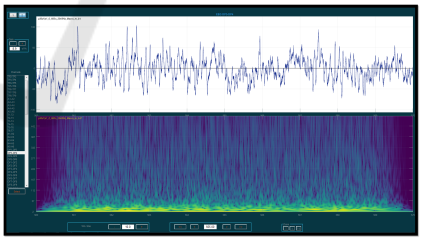

Figure 2: Additional time-frequency representation for one channel. Top graph: raw data, bottom graph: the frequency values are represented along the y-axis and the power in these frequencies on a color scale.

2.2 Time Series Visualization

Many variants of time series representations have been proposed to synthesize or improve visualization (Saito et al., 2005; Javed and Elmqvist, 2010; Van Wijk and Van Selow, 1999; Weber et al., 2001; Lin et al., 2004; Kincaid and Lam, 2006; Hao et al., 2007; Zhao et al., 2011) but their effectiveness has been discussed, and the classical representation is still

favored in practice. However, a recent study (Wang et al., 2017) proposed the application of Kernel Density Estimation (KDE) to transform a signal into a density field (figure 3). They showed that it leads to a new type of signal, and in some cases, the visualization is improved compared to the original one. We think that the visual aspect is not the only one to be interesting, but that the whole notion of signal density is.

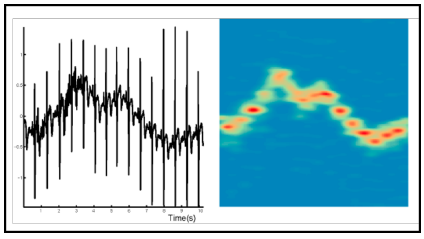

Figure 3: Density representation of a time series. Figure from (Wang et al., 2017).

2.3 Event Detection

Manually searching for pathological events such as interictal epileptic spikes (IESs) in the EEG signal is a very long and tedious operation for epileptologists. During the past decades, many methods were proposed to detect theses events automatically (Birot et al., 2013; Gotman, 1999). The noise makes it difficult for an algorithm to be efficient in this task. Furthermore, nowadays technology and storage capacities, allowing several days of 24/7 recordings on more than a hundred channels simultaneously, yield a considerable amount of data. Some algorithms work quite fast but are just as much sensitive to noise and no longer work when the pattern to research differs from the input signal. Some others are relatively efficient, but the computation time for large amounts of data is discouraging.

2.3.1 Dynamic Time Warping

In time series analysis, dynamic time warping (DTW) is one of the algorithms for measuring similarity between two temporal sequences, for instance, two time series of the same length (Keogh et al., 2009; Ding et al., 2008). The difference with a pure Euclidean Distance is that the whole sequence is taken into account to calculate the similarity between the pattern and the input signal, not just the sum of the distances between each point of the two sequences. DTW has been used for some biological applications (Rakthanmanon et al., 2012; Chadwick et al., 2011) or gesture recognition (Alon et al., 2008; Wobbrock et al., 2007) but the computation time on a massive amount of data as well as the difficulty to detect an event when the input signal differs from the pattern can make it barely efficient. An improved version of the Trillion algorithm from the UCR (University of California, Riverside) suite ((Rakthanmanon et al., 2012)) have been developped and tested (Jing et al., 2016) on a hundred patients, allowing a good recognition of IESs. Nevertheless, the necessity of having a pattern to research is still a problem. A user still needs to specify a template, and there is a large variability of spike waveforms within and between patients among other factors.

2.3.2 Machine Learning

The past decade has seen the rise of machine learning in EEG signal processing, giving birth to a rich literature. Work in this domain has focused as much on the automatic search for epileptic seizures (Song et al., 2012) as on that of epileptic markers such as pathological oscillations or IESs (Jrad et al., 2016; Birot et al., 2013). Many problems remain, starting with the fact that feature engineering is a time-consuming and challenging task. Furthermore, preprocessing and cleaning the EEG signal requires to manipulate tools that are not easy to use, especially for clinicians. Deep learning methods have been more recently built with the promise to overcome these issues or at least lighten them as it can learn good feature representations from raw data (Roy et al., 2019). It is essential to follow carefully this area of literature which is promising but not yet functional in practice.

2.3.3 Time-frequency

As shown in figure 4, sharp transients events present in depth-EEG signals (typically, the spike component of interictal epileptic spikes - IESs) are associated with an abrupt increase of the signal energy in the lower and higher frequency bands (Bénar et al., 2010).

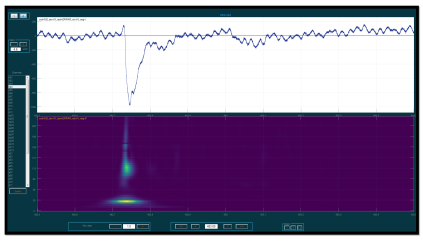

Figure 4: Example of an interictal epileptic spike (IES) in a one second time window. Top: raw signal, bottom: time-frequency representation.

An up-and-coming tool for the automatic detection of IES and pathological oscillations, based on

time-frequency analysis, is Delphos (Roehri et al., 2018; Roehri et al., 2016). However, we believe that a density analysis of the signal could lead to new possibilities and compete or cooperate with the existing techniques in the challenge toward automatic detection. Many false positives currently make the exploitation of time-frequency data difficult, while this 2-dimensional signal may benefit from a density analysis to sort the events detected by a threshold in the frequency-domain.

3 ESTIMATING DENSITIES

By converting a 1-dimensional EEG signal composed of a list of ordered values into 2-dimension, we obtain an image, which is an area of pixels. Thus, when the signal varies in amplitude or frequency, this area of pixels is affected. Two-dimensional convolution is a technique commonly used in image processing to apply effects such as blurring, sharpening, or edge detection. We used this technique, that affects pixels whose value is different from 0, on our EEG signal to emerge density fields that could witness the occurrence of pathological events. Sharp amplitude variations during IESs have the effect of spacing the points, and therefore the pixels representing the signal on the image, from each other. It is this notion of spacing between points that we can exploit to identify IESs in EEG. Typically the electrophysiological changes of the brain signal are gradual and homogeneous, but during an IESs they become huge in a short time. When convolution is applied, non-pathological variations appear under the form of high densities and IESs under the form of low density because of the fast spacing between the points in the same amount of time.

3.1 Kernel Density Estimation

It was necessary to transform the 1-dimensional EEG signals into 2-dimensional images in order to apply a convolution. Using KDE allowed to convert each value (a float or an integer) of the 1-dimensional EEG signal into a vector representing a Gaussian-shaped density probability of finding this value within a range of values. The aggregation of these vertically transposed vectors along the time axis constitutes a 2-dimensional image of the original 1-dimensional EEG signal (figure 5).

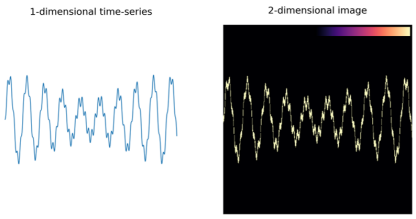

Figure 5: Left: A randomly simulated 1-dimensional signal where each timestamp is associated with a single value. Right: The same signal converted into a 2-dimensional image using KDE. Each timestamp is associated with a vertical vector representing a Gaussian-shaped density probability.

3.2 Convolution of the Imaged Signal

Convolution consists of applying a kernel on each of the pixels of the image. This technique has the effect of modifying the value of the current pixel by considering the value of the neighboring pixels. Only pixels with a value different from 0 are affected. This process of adding each element of the image to its local neighbors, weighted by a kernel, leads to an improved visualization with additional density field. Let d_{ij} denote the pixel value of an image and V its value after processing, the convolution can be modeled by

$$V = \left| \frac{\sum_{i=1}^{q} (\sum_{j=1}^{q} f_{ij} d_{ij})}{F} \right|$$

Where:

- f_{ij} = the coefficient of a convolution kernel at position i,j (in the kernel);
- d_{ij} = the data value of the pixel that corresponds to f_{ij};
- q = the dimension of the kernel, assuming a square kernel (if q = 3, the kernel is 3*3);
- F = either the sum of the coefficients of the kernel or 1 if the sum of coefficients is 0;
- V = the output pixel value;

The obtained density field, looking like an improved color-scaled line graph (figure 6), is affected both by variations in the amplitude and frequency of the original signal. If two pixels of value superior to 0 are side by side, then the two kernels overlap, and the original pixels are strengthened. If the pixels are distant, then they are not strengthened by their neighbors. The closer they are to each other, the higher the local density.

We called Convolutional Kernel Density Estimation (CKDE) the technique we used here, which aims to transform the time series into images and to apply a two-dimensional convolution on it.

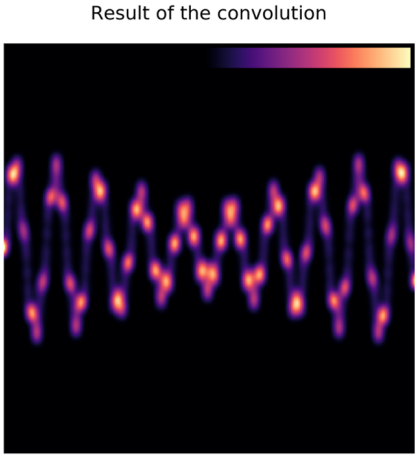

Figure 6: After the application of a Gaussian kernel of size 11 and standard deviation 3 on the image, pixels that are close to each other are strengthened. On the contrary, pixels that are distant to each other are barely reinforced.

4 USER INTERFACE

4.1 Implementation

We have built a user interface employing PyQt5 in Python 3.6 to allow the user to visualize and interacting live with the data. The top panel of the main window displays the 1-dimensional original signal and bottom panel the 2-dimensional imaged-signal (figure 7). Graphical characteristics and window settings can be modified by the user using text boxes, combo boxes, toolbars, and menus on the top and sides of the window. Some possible actions are, for instance, panning, zooming, changing colors, moving along the x and y axes, or saving the figures.

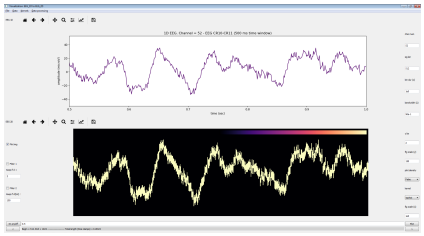

Figure 7: Main window of the GUI. The two panels at the center of the main window represent the 1-dimensional and the 2-dimensional signals. Live interactions are possible with both.

A user menu is also available for more sophisticated options such as creating a kernel for image convolution. Opening the kernel window (figure 8) allows the user to generate a Gaussian kernel with or without customizing its parameters (size and standard deviation). He can alternatively create a wholly customized kernel by filling a grid of the size he wants the values he wants.

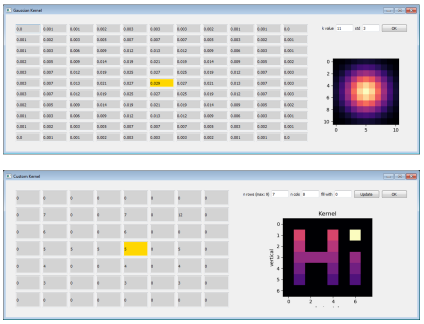

Figure 8: The kernel window allows the setting and drawing of the kernel that will be employed for image convolution. Top: Gaussian kernel, bottom: custom kernel.

The user can travel forward or backward in the time dimension of the signals by using his keyboards' left or right arrows or those located at the bottom of the window. Otherwise, it is possible to directly type a time value in seconds in the text box between the arrows.

4.2 User Feedback

The only user of the GUI described is the first author of this paper, accustomed to analyzing EEG signals on different clinical or research software. The GUI was designed to visualize the original signal and its associated image to identify possible errors in the algorithm, which is still under development. The main idea being a proof of concept that density analysis of EEG can be useful, only one recording channel at a time is displayed, to avoid missing any important detail (but all channels are processed). Navigation over time is instantaneous, as is the navigation from one channel to another or the enabling and disabling of the convolution, allowing a fast and efficient interaction. An upcoming more sophisticated interface will be developed soon with the ability to visualize multiple channels at once and a more straightforward design so that the platform can be used instinctively by other users.

5 RESULTS

We have evaluated the efficiency of EEG signal 2-dimensional convolution to visualize and automatically detect interictal epileptic spikes (IESs). The data used are those of a patient who was hospitalized in 2015 and we know well. The EEG signal from the

same patient were used in a previous study for which the purpose was different (Despouy et al., 2019). For this last study, the EEG signal was carefully examined and tagged. We ran the current tests on a 10 minutes part of this tagged signal and compared previous manual detection of IESs to automatic detection using our new method. This data set was composed of a hundred intracerebral macroelectrodes recorded at 2048 Hz that we downsampled at 512 Hz.

5.1 Visualization of Events

The visual inspection of densities (figure 9) allowed an easy identification of IESs, which are characterized by low densities due to the larger spacing between pixels.

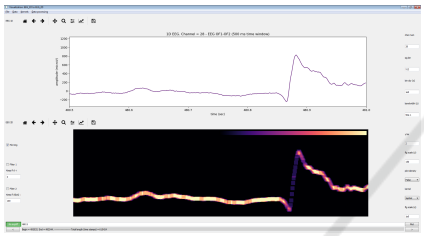

Figure 9: Convolution applied on one channel of the imaged EEG signal, which appears as a color-scaled line graph. Example of density decrease during an IES caused by the significant spacing between pixels during this sharp amplitude changing.

On the previous example, the size of the image was 512 (horizontal length) * 150 (vertical length), and the applied kernel was of size 7 * 7 with custom values, as follows:

$$\begin{pmatrix} 9 & 9 & 9 & 9 & 9 & 9 & 9 \\ 9 & 9 & 9 & 9 & 9 & 9 & 9 \\ 9 & 9 & 9 & 9 & 9 & 9 & 9 \\ 9 & 9 & 9 & 10 & 9 & 9 & 9 \\ 9 & 9 & 9 & 9 & 9 & 9 & 9 \\ 9 & 9 & 9 & 9 & 9 & 9 & 9 \\ 9 & 9 & 9 & 9 & 9 & 9 & 9 \end{pmatrix}$$

5.2 Automatic Detection of Events

A low pass filter was applied to the density field in order to remove everything from the image except the IESs (figure 10). This means that only the densities forming the IES are conserved since all the others are set to 0. The densities resulting from IESs thus become high densities. By summing the densities of each pixel of the resulting image, we discern if an IES is present or not. If no IES is present, the total density

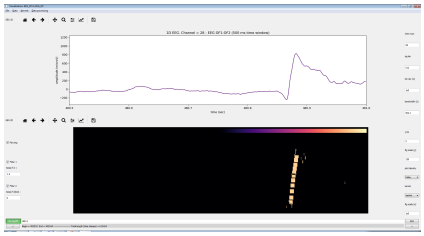

Figure 10: Image after application of a low pass filter. All the high densities are removed to display only the IESs.

on the image will be around 0. If there is one, it will be higher, between 400 to more than 1000.

15 IESs were automatically identified in the portion of the analyzed signal. Among them, 13 were true IESs, while 2 were false positives (figure 11). 100% of the events that were tagged during previous visual inspection were automatically identified.

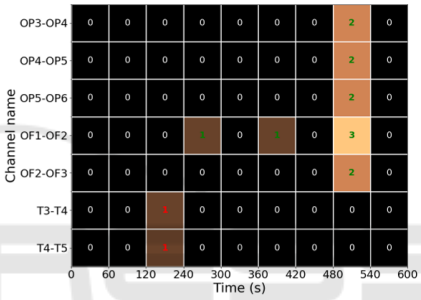

Figure 11: Map of detected events. The green text color indicates the correctly detected IESs, the red color the false positives. The names of the channels on which an event has been detected are represented along the y-axis. Time is represented in seconds along the x-axis. The more events detected in a given time period, the lighter the square corresponding to this time period for a given recording channel.

An IES is detected when the total density on the remaining image after removal of high densities by filtering exceeds a certain threshold. It works well to detect pathological events but also can lead to false positives, which are mainly due to two things (figure 12). Firstly, an accumulation of residual densities accompanying rapid micro-changes in signal intensity. Secondly, an accumulation of low densities related to the borders of the density field not being eliminated during the filtering. We will expose in the Discussion a way to solve these problems.

The main objective was to ensure the efficiency of detection. Thus, minimal effort was allocated to increase the speed of computation which currently lasts 90 minutes for a 10 minutes signal. Table 1 summarizes the parameters used for image generation from the original signal, kernel creation, and convolution, as well as the characteristics of the automatic detection process.

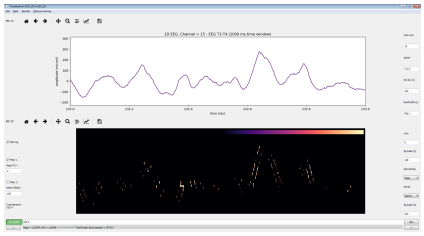

Figure 12: Example of false detection. The total density on the image is high, as it is the case when an IES is detected, but this is only related to the accumulation of low scattered local densities. On the contrary, when it comes to a spike, the densities occur during a short duration.

Table 1: Parameters and results table.

SIGNAL PARAMETERS	
Type	SEEG
Duration	10 minutes
Sampling frequency	512 Hz
N intracerebral channels	109
IMAGE PARAMETERS	
X size	512
Y size	150
KERNEL PARAMETERS	
Type	Custom
Shape	Square
X size	7
Y size	7
AUTOMATIC DETECTION	
Density filter	Low pass
Process duration	90 minutes
N detected events	15
N good detections	13
N false detections	2

6 INTEREST OF THE CKDE APPROACH

With this proof-of-concept, we have identified several interesting or novel aspects that are worth assessing in future work:

- Unlike other automatic detection methods, density changes are neither affected by the signal orientation (positive or negative) nor by prominent but slow changes in amplitude, nor by unwanted oscillations.
- Using the parameters we proposed, only very abrupt variations are detected, like those caused by IESs, thus avoiding false detections driven by rise or fall of slow and non-pathological amplitudes.
- Furthermore, no training on the data is necessary to the algorithm, and only a few or no preprocessing at all has to be done.
- From a visualization point of view, the representation of densities in EEG is straightforward for the user to understand given that the data look a lot like a line graph.
- The preliminary results in automatic detection are encouraging with a 100% identification (13/13) of IESs and only two false positives inside real intracerebral recordings.

7 LIMITATIONS AND FUTURE WORK

The main objectives of this study were to develop an efficient method to visualize SEEG data and automatically detect pathological electrophysiological signals. We aim to compete with existing methods that still suffer from many gaps, but another possibility could also be to use CKDE in cooperation with other routines to improve their efficiency. Future work will need to focus on a more precise and robust definition of the parameters such as the size and values of the kernel chosen for convolution as well as the low pass filter value. It is important to note that the parameters used here were hyper optimized after a preliminary visual analysis of the signal. In a future version, these parameters should be automatically determined so that the user does not have to spend time adjusting them. Furthermore, our tests have so far been carried out only on one patient implanted with a hundred intracerebral recording channels sampled at 512 Hz over 10 minutes. The first results lead us to be confident about the functionality of the technique and its potential performance, but we have to replicate them on a much more substantial amount of signal. This approach is currently underway with data recorded from more than 60 epileptic patients implanted for SEEG examinations between 2013 and 2019. In addition, the detection of other types of pathological markers such as high-frequency oscillations (Bragin et al., 2002; Bragin et al., 1999b) and more specifically fast-ripples (Ibarz et al., 2010; Zelmann et al., 2009; Roehri et al., 2017) should be evaluated and compared with other detectors. The problem of false positives can be addressed by reducing the time window for automatic signal analysis. False positives are related to the accumulation of small local and scattered residual densities over a relatively long period, whereas the IESs are characterized by small densities as well, but stacked over a much shorter duration. By reducing the time window on

which the densities are summed from 1 second to 100 or 200 milliseconds, this problem should disappear. However, the calculation time should be increased.

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