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# Cluster-based spike detection algorithm adapts to interpatient and intrapatient variation in spike morphology

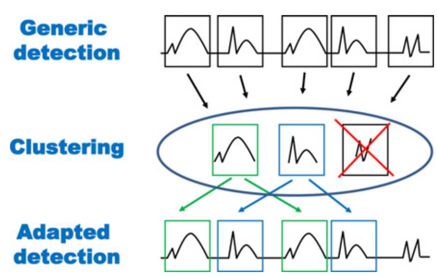
Antoine Nonclercq[a,*], Martine Foulon[b], Denis Verheulpen[b,c], Cathy De Cock[b], Marga Buzatu[b,c], Pierre Mathys[d], Patrick Van Bogaert[c]

[a] Laboratory of Image, Signal and Telecommunication Devices (LIST), CP165/51, Université Libre de Bruxelles (ULB), Avenue F. Roosevelt 50, 1050 Brussels, Belgium
[b] Department of Pediatric Neurology, Centre Hospitalier Universitaire de Charleroi, Boulevard P. Janson 92, 6000 Charleroi, Belgium
[c] Department of Pediatric Neurology, Erasme Hospital, Université Libre de Bruxelles, Route de Lennik 808, 1070 Bruxelles, Belgium
[d] Bio, Electro and Mechanical Systems (BEAMS), CP165/56, Université Libre de Bruxelles, Avenue F. Roosevelt 50, 1050 Bruxelles, Belgium

## HIGHLIGHTS

- ► An automated cluster-based spike detection algorithm is proposed.
- ► It was tested in recordings with continuous spike and waves during slow wave sleep.
- ► It performs similarly to three EEG experts.
- ► It shows little difference with an expert in spike-and-wave percentage evaluation.
- ► The algorithm adapts to different types of recording in a fully automated way.

## GRAPHICAL ABSTRACT

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## ABSTRACT

Visual quantification of interictal epileptiform activity is time consuming and requires a high level of expert's vigilance. This is especially true for overnight recordings of patient suffering from epileptic encephalopathy with continuous spike and waves during slow-wave sleep (CSWS) as they can show tens of thousands of spikes. Automatic spike detection would be attractive for this condition, but available algorithms have methodological limitations related to variation in spike morphology both between patients and within a single recording.

We propose a fully automated method of interictal spike detection that adapts to interpatient and intrapatient variation in spike morphology. The algorithm works in five steps. (1) Spikes are detected using parameters suitable for highly sensitive detection. (2) Detected spikes are separated into clusters. (3) The number of clusters is automatically adjusted. (4) Centroids are used as templates for more specific spike detections, therefore adapting to the types of spike morphology. (5) Detected spikes are summed.

The algorithm was evaluated on EEG samples from 20 children suffering from epilepsy with CSWS. When compared to the manual scoring of 3 EEG experts (3 records), the algorithm demonstrated similar performance since sensitivity and selectivity were 0.3% higher and 0.4% lower, respectively. The algorithm showed little difference compared to the manual scoring of another expert for the spike-and-wave index evaluation in 17 additional records (the mean absolute difference was 3.8%). This algorithm is therefore efficient for the count of interictal spikes and determination of a spike-and-wave index.



* Corresponding author at: Laboratory of Image, Signal and Telecommunication Devices (LIST), CP165/51, Université Libre de Bruxelles, Avenue F.D. Roosevelt 50, B1050 Bruxelles, Belgium. Tel.: +32 2 650 30 86; fax: +32 2 650 47 13.
*E-mail address:* anoncler@ulb.ac.be (A. Nonclercq).

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## 1. Introduction

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition (Fisher et al., 2005). Epilepsy has variable etiologies, may affect both children and adults, and has an active incidence of 4–8/1000. Most epileptic patients show on their scalp EEG abnormalities recognizable by trained neurologists and called "spikes" in reference to their spike-like morphology. The presence of spikes is a marker of epilepsy, being significantly associated with the occurrence of epileptic seizures. In most clinical situations, precise quantification is not mandatory. In some specific cases however, quantification of spikes is clinically relevant since the amount of spikes is related to the importance of brain dysfunction. This situation is encountered in epileptic encephalopathy (EE) with continuous spike and waves during slow-wave sleep (CSWS). EE with CSWS is an age-related epilepsy that presents with neurocognitive regression and an EEG pattern characterized by strong activation of the epileptic activity during sleep, with spikes that tend to diffuse over the whole scalp, and typically occupy more than 85% of slow-wave-sleep time (Tassinari et al., 2000). Proper diagnosis of EE with CSWS is very important, since it requires specific treatment, including corticosteroids (Buzatu et al., 2009).

Even if EE with CSWS is rather rare, two reasons justify the use of a detection algorithm: the fact that manual counting of the spikes may be very time-consuming on a recording that can show tens of thousands of spikes, and the fact that achieving an accurate manual count on a long-term recording requires a high level of expert's vigilance, which makes it a hard task and exposes to the risk of a decreased diagnosis accuracy. Hence, we decided to develop an algorithm and to test it against the scoring of EEG experts in patient's records showing EE with CSWS.

Many automated spike detection algorithms have been published (as shown in Frost (1985), Wilson and Emerson (2002) and Halford (2009) for review). Algorithms are typically based on methods such as template matching (Ji et al., 2011), mimetic analysis (Exarchos et al., 2006), power spectral analysis (Sugi et al., 2002; Adjouadi et al., 2004; Exarchos et al., 2006), wavelet analysis (Adeli et al., 2003; Indiradevi et al., 2008) and artificial neural networks (Guler and Ubeyli, 2005; Tzallas et al., 2006). Newer methods include independent component analysis (De Lucia et al., 2008) and dithering (Casson and Rodriguez-Villegas, 2011).

One of the major problems of automatic spike detection is that both spike morphology and background vary widely between patients (interpatient variation) (Wilson and Emerson, 2002) as well as within a single recording (intrapatient variation) (Wahlberg and Lantz, 2000). This is why spike detection algorithms usually give better performance when the EEG expert is asked to select samples of spikes in order to tailor the algorithm to the patient (Sankar and Natour, 1992; Aarabi et al., 2009). However, this approach is not always suitable, as (1) it is time consuming for the expert, (2) some infrequent types of spike morphology can be discarded, and (3) it reduces analysis reproducibility since results rely on these specific spikes that are scored by the expert.

In order to overcome the interpatient variation in spike morphology, a previous study by our group presented an original algorithm that automatically adapts to each patient (Nonclercq et al., 2009). Overall averaging was performed on all detected spikes to obtain the 'average spike' of the recording, which was then used to tailor the algorithm to the patient. When there is only little variation in spike morphology in the recording, such an averaging is meaningful. However, spikes found in a recording may belong to a few distinct classes corresponding to different foci (Engel, 1993). Averaging is then meaningless if performed on distinct groups of spikes. In order to overcome such a problem, spike clustering becomes necessary (Wahlberg and Lantz, 2000).

Clustering is the assignment of a set of spikes into subsets (called clusters) so that spikes in the same cluster show similar morphologies. Clustering may be performed in the temporal domain (i.e. applied to spikes present over a period of time), spatial domain (i.e. applied to spikes present in different derivations), or both.

Spikes clustering has been widely used for the reconstruction of sources that generate the epileptiform discharges (Wahlberg and Lantz, 2000; Van 't Ent et al., 2003; Van Hese et al., 2008). It has also been performed to evaluate feature extraction and classification algorithms (Exarchos et al., 2006). It has been used in the temporal domain to separate spikes from other waves, using either raw data or parameterized data (Inan and Kuntalp, 2007). Similarely, it has been used in the spatial domain to reject events that were not located in an expected site (Aarabi et al., 2009).

Out of the many clustering algorithm used in EEG, *k*-mean is one of the best known (Inan and Kuntalp, 2007; Aarabi et al., 2009). It decomposes the spikes into a set of disjoint clusters, each cluster being defined by a cluster center, called centroid. The algorithm is iterative and works in two steps. First, each spike is assigned to the nearest centroid. Second, the position of each centroid is recalculated as being the mean of all spikes belonging to the corresponding cluster. The algorithm performs those two steps continuously until the assignment of spikes among centroids no longer changes.

This paper presents an automated detection algorithm that relies on temporal *k*-mean clustering to tackle interpatient and intrapatient variation in spike morphology. It uses centroids as templates that are specific to the types of spikes belonging to the cluster, in order to analyze individual types of spike morphology from the recording.

To evaluate the ability of the algorithm to quantify interictal epileptiform activity, two studies were conducted. The first one compared performance of three experts who scored EEG samples from three patients. The objective was to compare human experts (inter-expert study) versus the algorithm in terms of sensitivity, selectivity and detection correlation coefficient. The second study compared performance of a single expert versus the algorithm on 17 EEG samples from 11 patients. The purpose was to put the method into practice in the case of spike-and-wave index (SWI) evaluation.

## 2. Materials and methods

Patients, EEG samples selection and instructions given to the experts are identical to our previous paper (Nonclercq et al., 2009).

### 2.1. Patients

A group of children showing the CSWS syndrome was retrospectively selected based on the following criteria: (1) cognitive, language and/or behavioral deterioration and (2) CSWS pattern on sleep EEG. For study 1, three children (two eight-year-old girls and one nine-year-old boy) were selected from the database of the University Hospital of Charleroi. For study 2, 11 children, seven boys and four girls (sex ratio: 1.75) aged 3–13 years, were selected from the database of the Erasme University Hospital. All patients underwent sleep scalp EEG using either 11 electrodes (FP1, FP2, C3, C4, T3, T4, O1, O2, CZ, A1, and A2) or 21 electrodes placed according to the 10–20 International System. The recordings were performed with a 200 Hz sampling frequency and 12bit resolution.

### 2.2. EEG samples selection

For study 1, an EEG expert (M.F.) selected 21 short samples (6 samples for patients A and B, and 9 for patient C), which included