Detection of Interictal Spikes and Artifactual Data through Orthogonal Transformations

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Abstract

This study introduces an integrated algorithm based on the Walsh transform in order to detect interictal spikes and artifactual data in epileptic patients using recorded EEG data. The algorithm proposes a unique mathematical use of Walsh-transformed EEG signals to identify those criteria that best define the morphological characteristics of interictal spikes. EEG recordings were accomplished using the 10-20 system interfaced with the Electrical Source Imaging System with 256 channels (ESI-256) for enhanced preprocessing and on-line monitoring and visualization. The merits of the algorithm are: (a) its computational simplicity, (b) its integrated design that identifies and localizes interictal spikes while automatically removing or discarding the presence of different artifacts such as EMG, EKG, and eye blinks, and (c) its potential implication to other types of EEG analysis, given the mathematical basis of this algorithm which can be patterned or generalized to other brain dysfunctions. The mathematics that were applied here assumed a dual role, that of transforming EEG signals into mutually independent bases and in ascertaining quantitative measures for those morphological characteristics deemed important in the identification process of interictal spikes. Clinical experiments involved 31 patients with focal epilepsy. EEG data collected from 10 of these patients were used initially in a training phase to ascertain the reliability of the observable and formulated features that were used in the spike detection process. Spikes were annotated independently by three EEG experts. On evaluation of the algorithm using the 21 remaining patients in the testing phase revealed a Precision (Positive Predictive Value) of 92% and a Sensitivity of 82%. Based on the 20 to 30-minute epochs of continuous EEG recording per subject, the false detection (FD) rate is estimated at 1.8 FD per hour of continuous EEG. These are positive results that support further development of this algorithm for prolonged EEG recordings on ambulatory subjects and to serve as a support mechanism to the decisions made by EEG experts.

Keywords: Epileptogenic data, Focal epilepsy, Walsh transform, Signal processing, Interictal spike detection, and Artifact removal.
I. Introduction

The focus of this study is placed on the design of an integrated algorithm for the detection of interictal activity in EEG attributed to focal epilepsy. The detection process is designed such as to allow physicians to make evaluative assessments of epileptic seizures, which in turn will enable targeted treatment. The use of the Walsh transform in analyzing epileptogenic data, and the application of its associated mathematical derivations proposed show promise not only for detecting interictal spikes, but also in characterizing them with quantitative measures. The proposed algorithm is augmented with cautionary measures that identify or filter out artifactual data associated with eye blinks, muscle movement (EMG), and heartbeat (EKG). Processes and methods for the automated detection of interictal activity as presented respond to the diagnostic value of interictal epileptiform activity (Fish, 2003)

Epileptiform activity was assessed in earlier studies (Gotman, 1985; Glover, 1989, Birkemeier, 1978; Jayakar, 1989; and Gevins, 1987) combining an extensive clinical experience. Rule-based detection algorithms have elicited two characteristics that are considered as most reliable in the detection of spikes, and they are the fast rise and decay of the spike, and the sharpness of its peak. The spatio-temporal context is taken into account in several studies using different approaches: context-based detection (Jayakar, 1991; Dingle et al., 1993), state-based detection (Gotman, 1992), neural networks (Hellmann, 1999; Ko and Chung, 2000; Kurth et al., 2000; and Tarassenko, 1998), principles of the wavelet theory (Popescu, 1998; and Calvano et al., 2000, Latka, 2003), and expert systems (Davey et al., 1989; Dingle et al., 1993), to cite a few. An earlier implementation example of the Walsh transform to stereo vision in 2-D images is provided by Adjouadi and Candocia (1994). Also, Barreto et al. (1993) describe a study for the detection of interictal spikes using electrocorticographs and Lagrange derivatives.
The approach considered in this study is to take EEG data from 10 of the 31 subjects in the study, and use them in a training phase to adjust the mathematical parameters (decision criteria) specifically designed for the task at hand. This phase is used to confirm or slightly redress the criteria established. The testing phase involving EEG data from the other 21 subjects is then performed in order to assess the performance merit of such criteria.

II. Methods

2.1 Participants

Thirty one (31) children with focal epileptic seizures served as subjects for this study. The epileptic patients recorded were either: (a) inpatients at the hospital for long-term EEG monitoring, or (b) outpatients for short-term EEG monitoring sessions. Patients were selected for the study if they were identified by a doctor (MD) as having focal epilepsy. The patients were awake during the recording sessions. However, data in this study were selected randomly, and contained awake, drowsy and also sleep sections. To be able to judge the algorithm's accuracy, the data had body movement, muscle artifacts, eye movement artifacts, and physiologic but non epileptic waveforms such as sleep spindles.

All of the procedures followed strict protocols pursuant to the ethical guidelines and regulatory requirements regarding research involving human subjects.

2.2 The Integrated Recording System

EEG data was recorded employing the 10-20 electrode placement system interfaced with the Syn-Amps of the Electric Source Imaging system with 256 channels (ESI-256), all under expert clinical supervision at Miami Children’s Hospital. The Syn-Amp amplifiers of the ESI-256 machine were used to allow for optimal online processing of signals for digital filtering,
amplification and digitization of the EEG signals, and the transferring of the digitized data to the host computer. The EEG data was collected in continuous mode using a 500 Hz sampling frequency with 0.1-70 Hz bandpass filter settings and 22 bits A/D converter. The EEG recording time for each patient varied between 20 to 30 minutes. The EEG sections selected for analysis were those in which artifacts created by the patients physical activity was minimal. Artifacts due to electrical interference by the recording system are not significant with the setup provided by the interface of the ESI-256 machine. Other artifacts, such as eye blinks, EMG, and EKG were recorded. However, by using the ear reference electrodes, recording of EKG artifacts was reduced for most patients.

2.3 Clinical Criteria Characterizing Interictal Spikes

A simulated spike waveform is shown in Figure 1 in order to provide key assessments of its characterizing features, with an excellent overview provided in (Gevins and Remond, 1987). With the help of medical experts, the following list of criteria was established as necessary to declare the existence of an interictal spike, defined as a waveform $RPF$, with two half waves $RP$ and $PF$:

1. Sharpness of a spike is continuous in both narrow and wide intervals of observation.

2. The rising and falling slopes of the spike are both steep. As illustrated in Figure 1, the rising slope $m_{RP}$ is measured from the first trough $R$ to the peak of the spike, and the falling slope $m_{PF}$ is measured from the peak to the second trough $F$.

3. A sharp peak $P$ characterizes the spike, which is due to a sudden change in polarity of the voltage signal recorded. This sharpness may occur in both the time and spatial domains.
4. A spike is estimated to have a total duration of 20 to 70 milliseconds (ms). The total duration of the spike, $\Delta_t$, is measured from $R$ to $F$, as the sum duration of the two half waves. $P_x$, $R_x$, and $F_x$ denote the respective latencies in the $x$-axis for points $P$, $R$, and $F$.

\[
\Delta_t = \Delta_{RP} + \Delta_{PF}, \quad \text{Where } \Delta_{RP} = P_x - R_x \text{ and } \Delta_{PF} = F_x - P_x
\]  

(1)

5. The two half waves are observed to satisfy the condition that their absolute difference is less than or equal to their calculated average (Jayakar, 1989). This implies that the duration of the shorter half wave must be at least one third of that of the longer half wave.

\[
|\Delta_{RP} - \Delta_{PF}| \leq \frac{(\Delta_{RP} + \Delta_{PF})}{2}
\]  

(2)

6. The amplitude of a spike is greater than 20 microvolts (µV). The amplitude $A_a$ is defined as:

\[
A_a = (A_1 + A_2)/2
\]

with $A_1 = P_y - R_y$, and $A_2 = P_y - F_y$

And where, $P_y$, $R_y$, and $F_y$ denote the respective latencies in the $y$-axis for points $P$, $R$, and $F$.

In addition, the downward deflection voltage $A_2$ is usually larger than the upward deflection voltage $A_1$, and satisfying the condition:

\[
\frac{1}{4} \leq \frac{A_1}{A_2} \leq 2
\]  

(4)

7. The maximum amplitude of a spike is at least 1.5 times larger than that of the background signal, where the background signal may be defined as the EEG activity lasting twice the duration of the spike (assumed in this case to be 140 ms) at either side of a potential spike.

8. Multi-channel activity may be reported, where one spike observed in a given channel may also be observed in another neighboring channel. In other words, spikes do not occur in isolation. This can be assumed provided that the inter-electrode spacing of the recording system used is small. Neighboring channels are identified as those that are of closest physical proximity, in direct relation to the system’s electrodes configuration used (Ochi et al., 2001).
9. The existence of artifacts (spike-like transients) undermines the identification of spike, and therefore such artifacts must be accounted for automatically by the devised algorithm, in order to minimize the false detection rate.

10. A slow wave may follow a spike. This characteristic, not always present, may be used only to augment the certainty in identifying a spike, but not to undermine it.

2.4 Algorithm Development Process

The interesting aspect in this study is that Walsh operators satisfy the important concept of orthogonality and yet an analogy to discrete mathematical derivatives can be generalized in terms of their functional behavior. The mathematical steps considered in the development of this algorithm are detailed in the Appendix.

Figures 2 and 3 provide comparative results in the functionality of the Walsh operators versus those of the common mathematical derivatives. Figure 4 assesses the error signals in the functionality difference between the Walsh operators and their respective derivative operators. These functional equivalencies are mentioned here to show that Walsh operators just like derivatives can indeed be used to extract sharp transitions and pinpoint through zero-crossings the location of a given peak, but yet, through orthogonality (independence between these operators), we can simultaneously use them in a unique way to extract specific features as those outlined for a spike. Thus, if we are to make the generalization that the first-order Walsh operator \((\omega_1^N)\) is functionally equivalent to the first-order derivative \(d^1\), and the second-order Walsh operator \((\omega_2^N)\) is functionally equivalent to the second-order derivative \(d^2\) for any \(N\), it should be with the knowledge that this functional equivalence is more accurate for smaller values
of \( N \). In other words, by varying \( N \), different characteristics of the input signal may be appreciated at different scales (or resolutions or degrees of fuzziness).

After further analysis of the behavior of \( W_N^r \) \((r=1,2)\) in relation to interictal spikes, and using Figure 5 for visual appreciation, the following set of rules are established through experimental evaluation:

- The results from \( W_N^1 \) yield two peaks for each spike. The first peak is associated with the rising slope, and the second with the falling slope. The amplitude of each peak in \( W_N^1 \) is an indicator of the steepness of the slope, where a higher peak means a steeper slope.

- The results from \( W_N^2 \) yield a peak associated to the spike’s peak location. The amplitude of this peak in \( W_N^2 \) relates to the sharpness of the corresponding spike, where a higher peak means a sharper spike.

2.5 The Implementation Steps

The following steps are presented in the same sequence that they are implemented in the algorithm described in the Appendix. Intermediate results for each step are revealed to assess both the validity of such steps and the merit of each step for identifying interictal spikes and for rejecting artifacts.

**Step 1- Satisfying Criterion 1: Sharpness of a spike is continuous**

Continuity in sharpness in a spike means that it is sharp in narrow as well as in wider intervals of observation. This implies that high values must result for the peaks in \( W_N^1 \) and \( W_N^2 \), with \( N = 4, 8, \) and 16 used as the respective number of points analyzed simultaneously in the input data. For wider intervals of observation, the algorithm developed takes the results at different scales
(resolutions) and adds them together to detect all potential transitions under different scaling. In other words, sharpness/steepness of the signal identified in any of the $W^r_4, W^r_8$, and $W^r_{16}$, ($r=1,2$) signals, resulting in high-amplitude peaks, should yield a steep and sharp signal in $W^r$.

Furthermore, interictal spikes must also exhibit high local sharpness and steepness. The best way to measure this observation is through convolutions with the first and second order Walsh operators, which will provide a high peak and a zero crossing, emphasizing and localizing that part of the signal that meets sustained steep slopes and sharp peak.

**Step 2- Satisfying Criterion 2: Rising and falling slopes of the spike are both steep**

To ensure that the rising and falling slopes of the spike are both very steep, we consider the two peaks resulting in $W^1$ and the one peak resulting in $W^2$ in direct association with the steep slopes of the spike. A maximum duration of 20 ms for the “valley” created between these two peaks, defined as $\Delta_{PP}$ confirms the steepness of the slopes. The 20 ms condition is obtained empirically through the so-called training set used in the study. In this implementation step, if the separation $\Delta_{PP}$ is greater than that set duration, then the first peak is eliminated and the check is made again for the second peak, and so on. The result of this procedure is that $W^1$ would contain only peaks that are related to signals that have both a steep rising slope and a steep falling slope.

**Step 3- Satisfying Criterion 3: A sharp peak characterizes the spike**

The criterion that a sharp peak $P$ characterizes the spike is resolved through set dynamic thresholds both in the temporal and spatial domains, and through verification in the peak resulting in $W^2$. This implementation step yields the following observations:
Dynamic thresholds in temporal and spatial domains are found effective given the variations in the signal’s background activity. With the choice of windows of 3s intervals, these thresholds are set at one standard deviation about the mean of all the peaks found in these 3s windows.

The amplitude of the peak in $W^2$ is proportional to the sharpness of the peak in the input signal that has satisfied the threshold conditions. This peak in $W^2$ occurs in an interval corresponding to $\Delta_{pp}$ in $W^1$.

It is noted that Walsh signals are reviewed to evaluate spatial sharpness with regard to both the order of complexity (that is $r=1, 2$) and the different degrees of fuzziness ($N=4, 8, \text{ and } 16$, which is the size of the Walsh operator used).

**Step 4- Satisfying Criteria 4 - 7: Characterizing spike’s duration, half waves and amplitude**

Since criteria 4, 5, and 6 are based on conditions already established using specific measured bounds, this implementation step was to assess and potentially modify such measured bounds through empirical observation using the training set consisting of the 10 patients. In fact, we consider criteria 4, 5, and 6 to be added measures of certainty to the detection of spikes beyond satisfying criteria 1, 2, and 3.

In this implementation step, the following changes were considered in the final algorithm:

- If we consider the fact that a sharp transient has a total duration between 70 to 200 ms, the total duration of an interictal spike can then extend anywhere between 20 to 200 ms. The training set using the 10 patients revealed that a change of range in this duration from 50 to 215 ms would be more appropriate to minimize artifactual activity on the lower bound and to incorporate wider spikes as detected by medical experts on the higher bound. This was a sensible compromise between missing out on artifacts and the possibility of missing out on
detecting narrow spikes, since the automated process for artifact removal was consistently successful with the integrated algorithm.

- The ratio of amplitude between a potential spike and the background activity can be made to be greater than 1.5 (e.g. 1.6) in order to overcome the potential effects of EKG data, based on empirical observation of the training set. We however opted for eliminating EKG artifacts based on their periodicity, rather than subjectively increasing this aspect ratio.

**Step 5- Satisfying Criteria 8 - 10: Multi-channel activity, spike-like transients, and slow wave following a spike**

Criteria 8 and 10 are defined as support observations used to increase the certainty in identifying a spike but not to undermine it. Criterion 9 is established to ensure that the effects of artifactual data are either identified as such or filtered out to yield a minimized false detection rate.

It is noted however that prior to determining whether the established criteria are satisfied or not, the first performed preprocessing step is that of filtering out or reducing background signal from potential events. In order to eliminate the background signal, we compared the heights of the peaks in each of $W_1$ and $W_2$ within a window of 3 seconds and if the heights of the peaks in that time range were below the computed threshold which is set as one standard deviation about the mean of all the peaks found in these 3s windows, then such behavior is associated with the background signal, and thus eliminated from further consideration in the transformed signals.

The purpose of criteria 8 (multi-channel activity), especially when dealing with neighboring electrodes with close proximity, is to simply increase the validity in assuming that a potential spike is indeed an actual spike based on the fact that spikes do not occur in isolation, although criteria (1 through 7) established in the algorithm are already stringent in identifying a spike in any one channel. Of course inter-electrode spacing of the recording system used should be
considered in defining neighboring channels; and the proximity of these channels is important in the case where such electrode spacing is necessary for accurate 3-D localization of epileptic interictal spikes (Mirkovic et al., 2003).

Criteria 9 involve spike-like transients (artifactual data) which were dealt with automatically through cautionary measures integrated into the algorithm. Implementation details for identifying or eliminating the effects of eye blinks, EKG and EMG are provided in Section 3.2

The purpose of criteria 10 (slow wave following spike) is also to increase the certainty of identifying an actual spike (a true positive): a slow wave is identified in the $W^1$ signal, where two peaks follow the peaks associated with a spike. These peaks correspond to the rising and falling slopes of the slow wave whose duration is estimated between 100 and 200ms. In addition, they are separated with a “valley” corresponding to the small slope (close to zero) of the slow wave.

It is important to note that all of these checks in all these steps were performed through the use of the $W^r$ signals (for $r = 1, 2$), as opposed to using the original EEG signal itself. Such a fact, which exploits the orthogonality property, will be demonstrated through the results obtained.

III. Results

The spike detection algorithm was run on epileptogenic EEG using the testing set (10 of the 31 subjects). The “gold standard” is: identification of spikes by both medical advisors scoring the files. The following terms are thus defined:

- TRUE POSITIVE (TP): The algorithm and at least one of the medical advisors declare the presence of a spike.
- FALSE POSITIVE (FP): The algorithm identifies a spike that none of the medical advisors did.
- FALSE NEGATIVE (FN): at least one medical advisor identifies a spike that the algorithm did not.
The standard measures of sensitivity and precision (Eberhart et al., 1990) are used for the evaluation of the algorithm:

- **Sensitivity (S)** is “the likelihood that an event will be detected given that it is present” [21], defined as:

\[
S = \frac{TP}{TP + FN}
\]  
(6)

- **Precision (P) or positive predictive value** is “the likelihood that a signal of an event is associated with the event, given that a signal occurred” [21], defined as:

\[
P = \frac{TP}{TP + FP}
\]  
(7)

### 3.1 Implementation Results and Analysis

The results of the algorithm display automatically the detected spikes to facilitate manual observation. These results are given in Tables 1 and 2.

Figures 6-9 provide different results on different patients illustrating interesting detection outcomes. In these figures, it should be noted that the actual size consists of 1 sec/div, 30 mm/sec with a Gain of 30 uV/mm, LFF=1 Hz, HFF=70 Hz, and Notch of 60 Hz. The figures have been reduced in size to fit in the manuscript. In the presentation of these results, for each patient, an EEG record is first provided where the algorithm has identified automatically a TP, a FP or a FN. This EEG record is then followed by the intermediate steps as outlined in the algorithm provided in the Appendix, and as portrayed in the examples of the results obtained in Figures 6-9 for interictal spike detection and in Figures 10-12 for artifact identification and removal. Figure 13 illustrates an example where multi-channel activity was detected.
3.2 Resolving Contentious Issues of Artifactual Data

The algorithm developed included in its implementation cases of spike-like transients (artifactual data) that needed to be identified as such automatically to minimize any false detection, which was accomplished in this case, as preprocessing steps for EKG, Eye blinks, and EMG data. For the removal of EKG artifacts, the periodicity of the EKG behavior was exploited. After applying the Walsh transform to the EEG signal and obtaining the $W^1$ and $W^2$ signals, and after filtering out the background signal they are checked for periodicity as follows: If five consecutive peaks satisfying the set thresholds in the $W^1$ and/or $W^2$ signals are found within 500 ms to 1 s apart from each other, then those waves are classified as periodic and may be associated with EKG waves, and certainly not as potential spike waves. Note that with the choice of windows of 3s intervals, the chosen thresholds are set at one standard deviation about the mean of all the peaks found in these 3s windows. As an additional measure of caution, note also that the criteria defining a spike are violated in the thresholded $W^1$ and/or $W^2$ signals as shown in Figure 10.

For the artifacts of eye blinks and EMG, as illustrated in Figures 11 and 12, one or more of criteria (1, 2, 3, or 5) were not satisfied through the analysis of W1 and W2 signals. Interesting results obtained when dealing with “Eye Blink” artifact showed reversed characteristics sought by the search criteria using the Walsh operators in W1 and W2 (with one peak in W1 instead of 2 and 2 peaks in W2 instead of 1).

3.3 Discussion

In retrospect, the related studies we have reviewed including those included in the review article (Wilson and Emerson, 2002), and taking into consideration the use of existing algorithms such as: Gotman spike detector (GSD), two-stage spike detector (2SSD), multiple monotonic neural
network (MMNN), wavelet spike detector (WSD), to name a few, show the following varied results:

Sensitivity: being the most commonly used performance metric varied between low values ranging between 15% to 52% and high values ranging between 70% and 97%.

Selectivity, Precision, and Specificity: These metrics are used intermittently from study to study. We also determined that the performance metric Selectivity was used with different definitions: sometimes as the False Positive rate FP/(FP+TN), sometimes as the negative prediction value or Specificity TN/(TN+FN) and still at other times as the positive prediction value or Precision TP/(TP+FP). The reported values ranged between 40% and 92%. The high 92% was accomplished with a limited example data set of 73 events. In related studies where events were much higher (300 events or more), the sensitivity/selectivity varied between 70%/65% to 80%/40% which is more like the mean of what other studies report.

In all of these performance values, it can be said that the good results were accomplished when the number of patients was relatively small ranging from 2 to 18, or when the number of events is small (less than 100). For example, for the case where the low values were obtained was for the specific study where the patient count was 50. Studies involving higher number of patients (greater than 50) did not unfortunately provide these performance metrics.

It should be made clear that given the many different research aspects used in the related studies along with the variety and inconsistent use of metrics such as (precision, specificity, sensitivity, selectivity), number of patients used (or number of events considered), the lack of providing performance metrics in others, did not permit for a clear cut comparison and made it difficult to produce a fair assessment of all the results.
Conclusion

In this study we formulated and evaluated characterizing features of interictal spikes using orthogonal operators that were designed based on the Walsh transformation. We translated each of the observable characteristics into mathematical expressions such that each and every one of the characteristics is implemented in the development of our algorithm. The uniqueness of this algorithm is in the establishment of a mathematical foundation capable of extracting potential spikes from background EEG signal using mutually independent Walsh signals which served as an orthogonal basis for analysis.

When three experts annotated the spikes, and with the 31 subjects used, the results based on the test samples only (21 patients out of the 31) reveal a precision of 82% and a sensitivity of 92%, with a false positive (FP) detection rate of about 1.8 FP per hour of EEG recording, given a 20 to 30- minute epochs of continuous EEG recording per subject. Given the complex nature of EEG recordings, these results, which are supported by clinical experimentation, are most encouraging. The integrated algorithm proposed is computationally efficient, fully automated, and integrated in a way that it uses only Walsh operators in a unique way for the extraction of interictal spikes. Artifacts due to EMG, EKG or eye blinks were discarded automatically by virtue of cautionary processing steps embedded in the algorithm.

The use of such an algorithm is foreseeable in automated techniques that combine EEG and other sensory modalities for 3-D localization of epileptic foci (Ebersole et al., 1993; Barkley and Baumgartner, 2003; Mirkovic et al., 2003). Further developments of the EEG analysis component of the algorithm can also extend into the scrutiny of the transitional aspects between interictal and ictal phases to integrate nonlinear mechanisms for anticipating seizures (Lehnart et
al., 2001; Le Van Quyen, 2001, and Yaylali, 1996). This last task will constitute the next important objective of our research group.

References


Appendix

The use of the Walsh transform is viewed as an integrated approach to transforming the original EEG signal into orthogonal (mutually independent) Walsh transformed signals under the different sequency orders of the Walsh kernel (Gonzalez and Woods, 1993). An example is given for 8x8 and 4x4 Walsh matrices (kernels) where the basis functions satisfy orthogonality in the row and column vectors. The sequency in these ordered forms (ascending sequency) denotes the number of sign changes in each row vector as shown in parenthesis following the last column of each kernel.

\[
\begin{array}{c|cccccccc}
0 & +1 & +1 & +1 & +1 & +1 & +1 & +1 & (0) \\
1 & +1 & +1 & +1 & -1 & -1 & -1 & -1 & (1) \\
2 & +1 & +1 & -1 & -1 & -1 & +1 & +1 & (2) \\
3 & +1 & +1 & -1 & -1 & +1 & -1 & -1 & (3) \\
4 & +1 & -1 & -1 & +1 & -1 & -1 & +1 & (4) \\
5 & +1 & -1 & -1 & +1 & -1 & +1 & -1 & (5) \\
6 & +1 & -1 & +1 & -1 & -1 & +1 & -1 & (6) \\
7 & +1 & -1 & +1 & -1 & +1 & -1 & -1 & (7) \\
\end{array}
\]

(a) 8x8 Walsh Matrix (Kernel)  \hspace{1cm} (b) 4x4 Walsh Matrix (Kernel)

\[\frac{1}{\sqrt{N}} \quad (N=8 \text{ or } N=4 \text{ in these cases}) \text{ can be used with each kernel to yield an orthonormal basis.}\]

These \((\pm 1)\) elements of the Walsh transform can be generated for any \((n \times n)\) size matrix by using the relation \(W(x, u) = \prod_{i=0}^{n-1} (-1)^{b_i(x)h_{n-1-i}(u)}\), where \(b_i(k)\) is the \(i^{th}\) binary bit of \(k\), and the matrix can be ordered with ascending sequency.

For the ordered Walsh kernel matrix, the Walsh operator \(\omega^r_N\) of \(r^{th}\) order and length \(N\) is defined based on the sequency value (number of sign changes in its \(\pm 1\) elements) and the dimension \(N\) considered. The order \(r\) is given by the sequency of the operator, and refers to the type of
differences (derivatives) used between sample points. The dimension \( N \) (\( N=2n \)) refers to the width of the operator, function of the number of points considered. Considering the digitized input signal, \( f(t) \), the Walsh transform defined by \( W_N^r \) is given by the convolution (\( \ast \)) of \( \omega_N^r \) with \( f(t) \) as:

\[
W_N^r = \omega_N^r \ast f(t)
\]  

The Walsh operator of 1\(^{\text{st}}\) order and length 2, \( \omega_2^1 \), is functionally equal to the 1\(^{\text{st}}\) derivative, \( d^1 \):

\[
\omega_2^1 = [1 -1] = d^1 = \frac{\partial}{\partial x}
\]  

The Walsh operator of 2\(^{\text{nd}}\) order and length 4, \( \omega_4^2 \), is functionally equivalent to the 2\(^{\text{nd}}\) derivative, \( d^2 \):

\[
\omega_4^2 = [1 -1 -1 1] \approx d^2 = \frac{\partial^2}{\partial x^2} = [1 -2 1]
\]

The results of the algorithm display automatically the detected spikes to facilitate manual observation. The mathematical steps considered in the development steps of the proposed algorithm are as follows:

**Implementation Steps of the Algorithm**

- After Walsh transforming each EEG channel, and in order to enhance identification of the sharp and steep transitions of potential spikes, the Walsh results at different scales (resolutions of \( N=4, 8, \) and 16) are added together to detect all potential transitions under different scaling (as revealed through higher amplitudes), expressed mathematically as:

\[
W_4^r + W_8^r + W_{16}^r \quad \text{for} \quad r = 1, 2
\]  

- Following these two graphs (for \( r=1 \) and \( r=2 \)), and since the interictal spike must exhibit high degrees of sharpness in narrow and wider intervals, the resulting measures of sharpness/steepness in these intervals can be extracted through the functional equivalence of performing first and second order derivatives on the results obtained in the previous step.
This is achieved with a point-by-point multiplication between the equivalent first and second order Walsh operators and the addition of the Walsh operators of different lengths $N$, given by $W_4^r + W_8^r + W_{16}^r$ ($r = 1, 2$). In other words the following operations are performed in this step to emphasize that part of the signal that meets sustained steep slopes and sharp peak:

$$W_1 = \omega_2^r \cdot W^r = \omega_2^r \cdot [W_4^r + W_8^r + W_{16}^r] \quad \text{when } r = 1,$$

and

$$W_2 = \omega_{2+r}^r \cdot W^r = \omega_{2+r}^r \cdot [W_4^r + W_8^r + W_{16}^r] \quad \text{when } r = 2$$

(5)

Note in the results of this step that potential spikes will be predominant with the respect to the background.

- Dynamic thresholding is assumed next yielding $W_{T1}$ and $W_{T2}$ as thresholded version of $W_1$ and $W_2$ from the previous step. In order to extract that part of the signal deemed important from background activity, the threshold ($T$) was computed as one standard deviation above the mean of all the peaks found in 3s windows.

- The next step yields the signals denoted by $W_{T1}^*$ and $W_{T2}^*$ containing only those components of the signals in $W_{T1}$ and $W_{T2}$ that satisfy all the established criteria as described in Section 2.5. Note the two peaks in $W_{T1}^*$ which are indicative of the steepness of the rising and falling slopes of the spike, and the one prominent peak in $W_{T2}^*$ which accurately depicts the spike’s peak location, and whose amplitude is related to the sharpness of the spike.
**Table 1:** Results for both training and testing sets for spike identification when spikes are annotated by two experts.

<table>
<thead>
<tr>
<th>Set</th>
<th>NS</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>S₁</th>
<th>S₂</th>
<th>S₃</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Training</strong></td>
<td>51</td>
<td>46</td>
<td>1</td>
<td>5</td>
<td>19</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>(10 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Testing</strong></td>
<td>186</td>
<td>148</td>
<td>23</td>
<td>38</td>
<td>100</td>
<td>89</td>
<td>58</td>
</tr>
<tr>
<td>(21 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Both Training</strong></td>
<td>237</td>
<td>194</td>
<td>24</td>
<td>43</td>
<td>119</td>
<td>109</td>
<td>78</td>
</tr>
<tr>
<td>and Testing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2:** Results for both training and testing sets for spike identification when spikes are annotated by three experts.

<table>
<thead>
<tr>
<th>Set</th>
<th>NS</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>S₁</th>
<th>S₂</th>
<th>S₃</th>
<th>S₄</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Training</strong></td>
<td>51</td>
<td>46</td>
<td>1</td>
<td>5</td>
<td>19</td>
<td>20</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(10 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Testing</strong></td>
<td>319</td>
<td>261</td>
<td>23</td>
<td>58</td>
<td>100</td>
<td>89</td>
<td>133</td>
<td>58</td>
</tr>
<tr>
<td>(21 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Both Training</strong></td>
<td>370</td>
<td>307</td>
<td>24</td>
<td>63</td>
<td>119</td>
<td>109</td>
<td>133</td>
<td>58</td>
</tr>
<tr>
<td>and Testing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: In Tables 1 and 2: NS = total number of spikes identified. S₁, S₂, and S₃ = spikes identified, by 1st, 2nd, and 3rd EEG expert, respectively. Note that NS= TP+FN. Note also that (-) in the table means that spikes identified by the third expert were not used in the training phase to stay consistent with Table 1. Only the testing phase results were important in this case.

**Table 3.** Sensitivity (S) and Precision (P) measurements for the phases of training and testing when two experts annotated the spikes. Recall that $S = TP/(TP + FN)$ and $P = TP/(TP + FP)$.

<table>
<thead>
<tr>
<th>Set</th>
<th>Sensitivity</th>
<th>Precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training</td>
<td>0.90</td>
<td>0.98</td>
</tr>
<tr>
<td>Testing</td>
<td>0.80</td>
<td>0.87</td>
</tr>
<tr>
<td>Both</td>
<td>0.82</td>
<td>0.89</td>
</tr>
</tbody>
</table>

**Table 4.** Sensitivity (S) and Precision (P) measurements for the phases of training and testing when three experts annotated the spikes. Recall that $S = TP/(TP + FN)$ and $P = TP/(TP + FP)$.

<table>
<thead>
<tr>
<th>Set</th>
<th>Sensitivity</th>
<th>Precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training</td>
<td>0.90</td>
<td>0.98</td>
</tr>
<tr>
<td>Testing</td>
<td>0.82</td>
<td>0.92</td>
</tr>
<tr>
<td>Both</td>
<td>0.83</td>
<td>0.92</td>
</tr>
</tbody>
</table>
Figure 1: Simulated Spike and its Morphological Features
Figure 2: Contrasting the functionalities of the first-order Walsh operator and the first-order derivative.
Figure 3: Contrasting the functionalities of the second-order Walsh operator and the second-order derivative

(a) Input EEG signal at electrode F3

(b) Results of the convolution of the second-order Walsh operator with signal in (a): \( W_2 = W_3^2 = \omega_3^2 \ast F3 \)

(c) Results of the convolution of the second-order derivative with signal in (a): \( D_2 = D^2 = d^2 \ast F3 \)

(c) Difference in the convolution results of the second-order Walsh operator versus the second-order derivative: \( W_2 - D_2 = W_3^2 - D^2 \)
(a) Contrasting the differences in the convolution results of the first-order Walsh operator versus the first-order derivative: $W^1_N - D$ with $N = 4, 8, \text{ and } 16$

(b) Contrasting the differences in the convolution results of the second-order Walsh operator versus the second-order derivative: $W^2_N - D^2$ with $N = 4, 8, \text{ and } 16$

Figure 4: Comparative results contrasting the errors (by difference) in functionality between the Walsh operators and their analogous mathematical derivatives
Figure 5: Simulation of Interictal Spike with Anticipated Results in $W_N^1$ and $W_N^2$
Figure 6: Examples of results illustrating the detection of spikes for patient 15 in channels C3
Figure 7: Examples of results illustrating the detection of spikes for patient 5 in channels F3
Figure 8: Examples of results illustrating the detection of spikes for patient 3 in channels FP2
Figure 9: Examples of results illustrating the detection of spikes for patient 10 in channels FZ
Figure 10: Results obtained when dealing with EKG data – Note the periodicity in EKG and how the characteristics sought by the search criteria using the Walsh operators are not met in WT1 and WT2.
Figure 11: Results obtained when dealing with “Eye Blink” artifact – Note how the characteristics sought in WT1 and WT2 are not met, and that WT1 and WT2 have a reversed behavior with respect to a spike (with one peak in W1 instead of 2 and 2 peaks in W2 instead of 1).
Figure 12: Results obtained when dealing with EMG artifact – Note how the characteristics sought by the search criteria using the Walsh operators in WT1 and WT2 are not met.
Figure 13: Results showing multi-channel activity with detected spikes in channels F7, T3, F3 and C3.