

**École polytechnique de Louvain**

# **Ultra-low-power implementation of a parameters identification algorithm for interpretable detection of epileptic seizures**

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Academic year 2019–2020

Master [120] in Electrical Engineering



# Abstract

Epilepsy is a neurological disease affecting more than 60 million people in the world. It is characterized by the sudden onset of seizures, which can be dangerous to the patient, and even cause death. Until now, seizures appear in an uncontrollable and unpredictable manner, rendering care and prevention difficult to implement. Recently, intensive research has been led in order to identify, based on different indicators, the onset of a seizure. One of the most reliable indicators seems to be electroencephalogram (EEG) signals measured directly inside the cranial cavity. This master thesis is focused on one specific algorithm under investigation, that allows interpretable detection of a seizure onset by comparing features generated by the patient's EEG signals, with features generated by a neural mass model synthesizing EEG signals from three physiologically meaningful parameters. In this work, the move towards ultra-low-power implementation of this algorithm was started by transferring the code, previously implemented on Matlab, to C language, more adapted to a microcontroller such as ARM Cortex M4. Then, various ways to optimize memory and power usage of the algorithm were identified and investigated. It is shown that the resolution of the meaningful parameters fed to the neural mass model is of critical importance in these aspects. While the execution is still time-consuming, the algorithm has been brought a step closer to an implementation in a point-of-care device.

# Acknowledgements

This work and the completion of this master's thesis would not have been possible without the following people that helped me along the way. I would like to thank them here.

First, I would like to thank my supervisor, Prof. David Bol, for his support and encouragements during this very particular year. Despite his many tasks, he managed to make himself available to follow my work.

I also would give a special thank to Rémi Dekimpe, for his advices and expertise in the field of embedded programming. He spent time to offer me precious explanations.

Next, I would like to thank my readers Ludovic Moreau and Antoine Nonclercq to accept the reading of this work. A special thank to Antoine Nonclercq and his group for welcoming us to their offices and sharing their work with me.

Finally, I would like to thank my fellow students for the good times during the ELEC master and my family and loved ones for their unconditional support and encouragements in all situations.

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# List of Abbreviations

|             |                                       |
|-------------|---------------------------------------|
| <b>EEG</b>  | Electroencephalogram                  |
| <b>CNS</b>  | Central nervous system                |
| <b>PNS</b>  | Peripheral nervous system             |
| <b>ILAE</b> | International League Against Epilepsy |
| <b>NT</b>   | Neurotransmitter                      |
| <b>TLE</b>  | Temporal lobe epilepsy                |
| <b>iEEG</b> | Intracranial electroencephalogram     |
| <b>DFT</b>  | Discrete Fourier transform            |
| <b>FFT</b>  | Fast Fourier transform                |
| <b>EMD</b>  | Empirical mode decomposition          |
| <b>TP</b>   | True positive                         |
| <b>TN</b>   | True negative                         |
| <b>FN</b>   | False negative                        |
| <b>FP</b>   | False positive                        |
| <b>VNS</b>  | Vagal nerve stimulation               |
| <b>RNS</b>  | Responsive neurostimulation           |
| <b>RMS</b>  | Root mean square                      |
| <b>DL</b>   | Number of decomposition levels        |
| <b>MW</b>   | Mother wavelet                        |
| <b>db4</b>  | Daubechies of order 4                 |
| <b>db2</b>  | Daubechies of order 2                 |
| <b>IMF</b>  | Intrinsic mode function               |
| <b>IPSC</b> | Inhibitory postsynaptic current       |

**IPSP** Inhibitory postsynaptic potential  
**EPSP** Excitatory postsynaptic potential  
**IIR** Infinite impulse response  
**FIR** Finite impulse response  
**SD** Standard deviation  
**FPR** False positive rate  
**MFDD** Mean false detection duration  
**DSP** Digital signal processing  
**FPU** Floating-point unit  
**IDE** Integrated development environment

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# Introduction

Known since antiquity, epilepsy has been recognized as a brain disorder in the 18th or 19th century [1]. Epileptic patients suffer from epileptic seizures, which are characterized by an abnormal excessive neuronal activity in the brain [2], beginning at seizure *onset*. Epileptic seizures can manifest themselves as sudden and unforeseen repetitive twitching, stiffening of the body, shaking, biting of the tongue or loss of consciousness, deteriorating the patients' quality of life, or (rarely) can lead to death. The epilepsy is the most common brain disease in the world, affecting around 1% of the total population [3]. A wide variety of medications exist, but only 66% of those are really efficient and more than half of epileptic patients under medication are still having seizures [4]. Surgery is a possible treatment to epilepsy but not adapted to all types of epilepsies and is in certain cases risky. Furthermore, the neuronal and physiological mechanisms behind epilepsy are still poorly understood.

For all these reasons, it is still today essential to find solutions to detect seizures and avoid them by other treatments. A lot of ongoing research focusing on either the epileptic seizure detection, or the stimulation of affected brain areas or nerves is pursued, the ideal solution being to perform both. Detection is crucial, because aside from the pure seizure detection, it allows identification of the seizure mechanisms, improving the comprehension of the disease. Different types of detection procedures exist :

1. The prediction of the seizure aims to detect an incoming event before the onset.
2. The onset detection identifies a seizure at the onset to be able to react before the first symptoms appear.
3. The event detection identifies a seizure after the appearance of the first symptoms. This approach's main interest is medical research.

The technique investigated in this work belongs to the second category.

It is important that the developed treatments fulfil the patients needs. In particular, the detection should be highly accurate, avoiding any false positives or false negatives in order for the patient to regain confidence. Also, a detection device wearable by the patient and ideally even implanted inside their body would allow a continuous detection capability. Furthermore, it should not require too much maintenance (i.e. changing the battery, the components, the parameters, which requires a visit to the hospital). An ultra-low-power device would be able to match these criteria.

Different such devices are already being marketed today and many different onset detection algorithms are being developed. Most commonly, these algorithms are based

on electroencephalogram signals. Generally, the signals are treated and different features are identified, before a classification of the signal in seizure/non-seizure situation is done. These techniques present two main drawbacks :

- Their accuracy is limited, impacting the patients' quality of life.
- Their detection is based on mathematically defined features, which thus have no physiological meaning. This prevents communication with medical experts and does not contribute to comprehension enhancement.

In contrast, the algorithm investigated in this master thesis and developed at Université Libre de Bruxelles (group of Antoine Nonclercq) is based on the three physiologically meaningful parameters, namely average excitatory ( $A_e$ ), slow ( $B$ ) and fast ( $G$ ) inhibitory synaptic gains. This makes the algorithm interpretable by the medical community. Its general functioning is described in Fig. 1. A neural mass model, representing the functioning of four neuronal populations in the brain, is used to generate synthesized EEG signals based on different  $A_e$ ,  $B$ ,  $G$ , triplets. Features are then extracted from these EEG signals and are compared to features extracted from the recorded EEG time window. One representative triplet is then identified and the temporal evolution of the ratios  $\frac{A_e}{B}$ ,  $\frac{A_e}{G}$ ,  $\frac{A_e}{B+G}$ ,  $\frac{B}{G}$  is analyzed to determine the onset seizure.

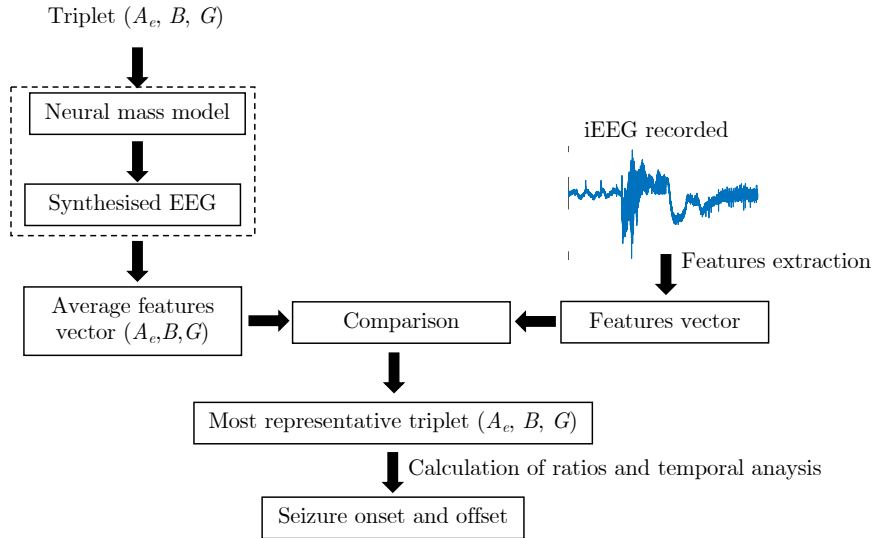


Fig. 1: Simplified representation of the algorithm studied in this thesis.

This algorithm is still, for now, far from a low-power and real-time implementation. The goal of this master thesis was to transform the code previously written in MATLAB to C language. Indeed, C language is the main language used for embedded programming, which is the programming method of small wearable devices. The focus was also put on the ultra-low-power and fast character of the program. Different aspects were considered, such as starting resolution of the neurological parameters, calculation methods, signal processing strategies.

In Chapter 1, a general description of epilepsy is given, allowing the reader to familiarize himself with the current understanding of this disease.

Then, in Chapter 2, an overview of the field of seizure detection is presented. The focus is mainly put on EEG-based detection algorithms, comparable to the one investigated in this work. Currently marketed devices are also mentioned.

Chapter 3 describes in detail the algorithm developed at ULB and its **MATLAB** implementation. The results of this implementation are discussed and the performances are analyzed.

In Chapter 4, the C code is described and the different choices of implementation and optimization are highlighted and justified. The final performances are then analyzed and several further optimization possibilities are mentioned.

Conclusions and further perspectives are drawn to complete this thesis.

# Chapter 1

## Epilepsy : fundamentals

This chapter introduces the field in which this master thesis falls. The context of epilepsy is first presented, through a summary of the functioning of the nervous system. The epilepsy disease and in particular epileptic seizures are then explained and the link with electroencephalogram (EEG) in the epileptic seizures' detection is highlighted. Finally, the treatments available to date for epilepsy are then mentioned.

### 1.1 Nervous system

As epilepsy is a neuronal disease, it is important to begin by a rapid explanation of the nervous system and its mechanisms.

#### 1.1.1 Structure

The nervous system is divided in two subsystems : the central nervous system (CNS) and peripheral nervous system (PNS) ([Fig. 1.1](#)). The CNS is composed of the brain, the spinal cord and the retinas of the eyes, it is the integration and command center of the body . The PNS consists of the sensory neurons, the ganglia, that are clusters of neurons, and nerves that connect all the members. All these nerves are carrying information between the CNS and all parts of the body. These informations lead to the initiation of movements and sensitivity (Somatic PNS), and digestion, respiration, hormone secretion among others (Autonomic PNS). The vagus nerve plays a crucial role in the performing of the autonomic PNS [5].

#### 1.1.2 Neuronal functioning

The brain is the most critical part of the human body. It controls all the actions of our body, including the movements and coordination of our muscles. The human brain is composed of thousands of neurons that hit each other to pass a flow of information. These collisions give rise to electricity, very small in amounts and transient in nature. The general structure of a neuron is represented in [Fig. 1.2](#).

The soma is the cell body of neuron. Its role is to maintain a constant potential between intra and extra-cellular fluids. The axon is a prolongation of the neuron; its

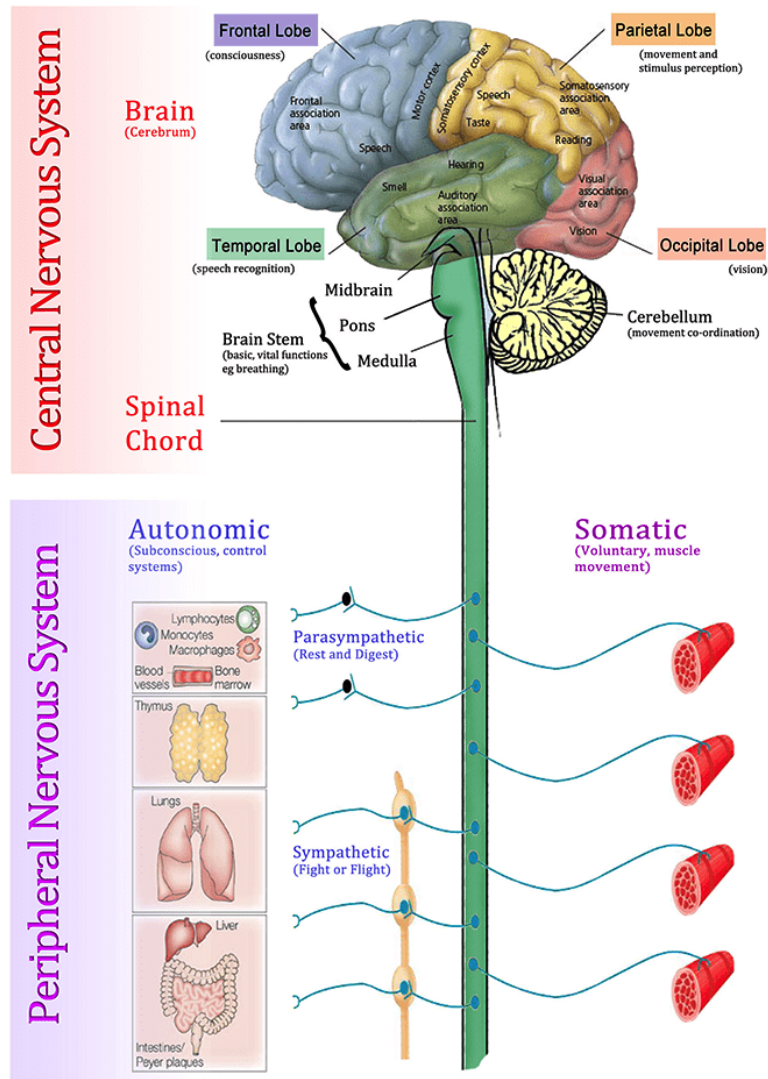


Fig. 1.1: Illustration of the nervous system [6].

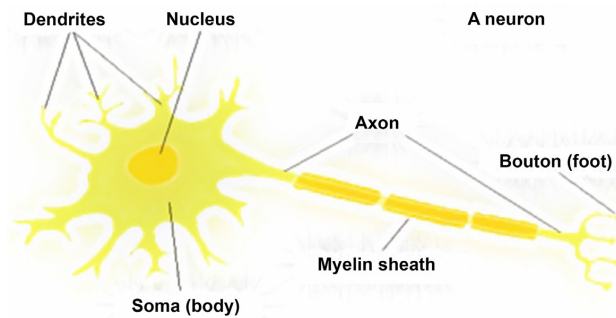


Fig. 1.2: General structure of a neuron [3].

role is to transmit the information in the form of an electrochemical signal to the bouton, that is responsible for converting the electrical signal to a chemical signal to be received by other neurons. The junction between two neurons is called the synapse and is responsible to transmit messages from to neuron through neurotransmitters (NT) that are chemical messengers. The dendrites' role is to receive this chemical message, by collecting the neurotransmitters through its receptors. The signal is then sent to the cell body, where the postsynaptic potentials, coming from the different dendrites, are summed up and modify the intra-cellular potential, consequently creating a variation in the membrane potential. If the total amount of charge is above a given threshold, an action potential, unit of activity of a neuron, is triggered. Postsynaptic potentials can be excitatory or inhibitory. The information transmitted from neuron to neuron is thus a flow of ions that are exchanged between neurons and can be modeled by currents that are represented by action potentials. Fig. 1.3 represents a schematic of an action potential triggered by an input current [3] [7].

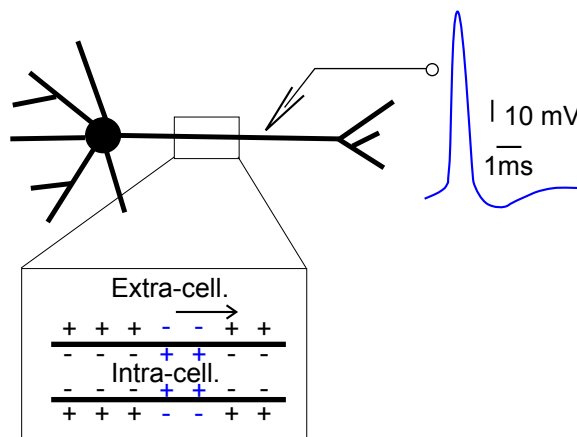


Fig. 1.3: Triggered action potential [7].

## 1.2 Epilepsy and electroencephalogram

An overview of epilepsy and the link with the electroencephalogram (EEG) will be presented in this section.

### 1.2.1 Epilepsy : definition

Epilepsy represents the situation of a person that has been affected by several, spontaneous epileptic seizures. These seizures are due to structural abnormalities in the brain. The International League Against Epilepsy (ILAE) describes an epileptic seizure as "a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain" [2]. The person is then defined as a "patient with epilepsy". It has variable clinical expressions, depending on the region of the brain, and the extent of neurons affected. Thus the symptoms are also very different from one type of epileptic manifestation to another. Various types of epilepsies exist, depending on where and how large is the epileptic source of the seizure. Two big classes are defined : the generalized seizures and the focal

seizures, according to the brain area touched by the seizure. Inside focal epilepsy, a classification could be further made, according to where the focal source is located. Temporal lobe epilepsy (TLE) is the most common form of the focal epilepsy, and the patients suffering from TLE are often drug resistant [8]. In this work, the focus is set on TLE.

Epilepsy represents a major health problem, as worldwide, about 50 million people are affected by epileptic seizures [9]. In Europe, the yearly incidence varies with age, with 3 different populations at risk : children and young adults < 20 years are linked to a 70/100 000 people/year, decreasing to 20/100 000 people/year in the 20-64 years then increasing to 100/100 000 people/year in the older ones (> 64 years) [9]. In Belgium, it is estimated that 70 000 patients suffer from epilepsy (0.8% of the population) and that 150 000 Belgians will suffer once in their life from a seizure [10]. It is considered a serious condition and a somewhat unmet need. A better health organization would be needed, and there is especially a need to create reference centres, as suggested by the Belgian chamber in 2017 [11].

### 1.2.2 Epileptic seizures : symptoms

A single epileptic seizure does not lead to an epilepsy diagnosis. Generally, it is considered that at least two unprovoked seizures are required to have an epilepsy diagnosis. The symptoms of an epileptic seizure are widely variable from patient to patient and through types of seizures. It goes from dizziness, staring blankly, unresponsiveness, repetitive twitching of limbs to stiffening of the body, shaking, loss of bladder and bowel control, biting of the tongue or loss of consciousness [12] [13]. The epileptic seizure is therefore dangerous for the patient himself but can also impact other people's life, on the road for example. The treatment of the epilepsy is thus essential.

### 1.2.3 Mechanism of ictogenesis and EEG

Ictogenesis describes the process of seizure genesis by an epileptogenic zone of the brain [14]. In a seizure signal, four states are identified, namely preictal, ictal, interictal and postictal. The portions of the signal before the first seizure and after the last are called pre-ictal and postictal. Ictal and interictal indicate intervals of seizures and between seizures. Ictal states can last for 10s to several minutes and are separated by long interictal states. The onset of the seizure characterizes the beginning of the epileptic seizure, while the offset is the end. The four states that characterize an epileptic seizure are illustrated in [Fig. 1.4](#), that represents an EEG signal.

The EEG signal is a valuable clinical tool in the detection of epileptic seizures. Indeed, the EEG signal describes the electrical activity of the brain. Its flow is impacted by the behaviour of the person [3]. Since epileptic seizures are characterized by abnormal activities in the brain, it can be seen through EEG signal flow. Therefore, EEG is useful in the detection of epileptic seizures. Moreover, the advantage of EEG with respect to other techniques of monitoring brain activity like PET or MRI is that its temporal resolution is high and its price is lower. Indeed, a very complex

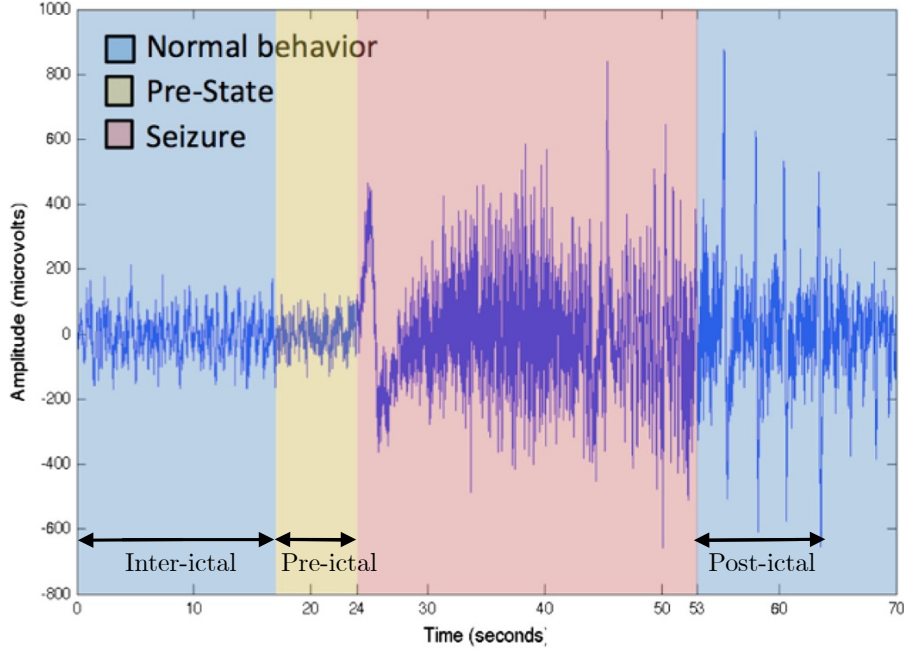


Fig. 1.4: Illustration of the four states of ictogenesis on a EEG recording [15]

neural activity can be read within a few minutes or seconds. However, the spatial resolution is low, it thus can be combined with other methods [3].

## Principle of EEG

In the brain, neurons communicate with each other by colliding among themselves and passing information by the collision. This collision generates a very low amount of electricity, that is measured by the EEG. To record these electrical signals, electrodes are placed on the human scalp during 20 to 40 minutes, or in other words 10 to 15 transactions. This duration is sufficient to understand the state of the human brain. Several systems of placement of electrodes on the scalp exist but the recommended system is 10/20 (recommended by the International Federation of Societies for Electroencephalography and Clinical Neurophysiology). This placement is represented in Fig. 1.5. The 10/20 notation refers to the distance between electrodes along the midline. They are placed at a distance of 10%, 20%, 20%, 20%, 20%, 10% of the nasion-inion distance between each other. All the other electrodes are placed in the same way. Each electrode has a letter to identify the lobe and a number to identify the hemisphere location. The letters F, T, C, P, and O stand for frontal, temporal, central, parietal, and occipital lobes, respectively. The  $z$  stands for zero and refers to electrodes placed on the midline, even numbers refer to electrodes on the right hemisphere and odd numbers to electrodes on the left hemisphere. A, G, and Fp identify the earlobes, nasopharyngeal, and frontal polar sites, respectively [3]. Thereupon, a large number of channels are recorded and the same number of EEG signals are recorded, coming from each electrode. An example of EEG recordings from the channels of electrodes placed on the scalp is available in Fig. 1.6. On this example, each signal is a bipolar signal as two channels have been subtracted to have a reference.

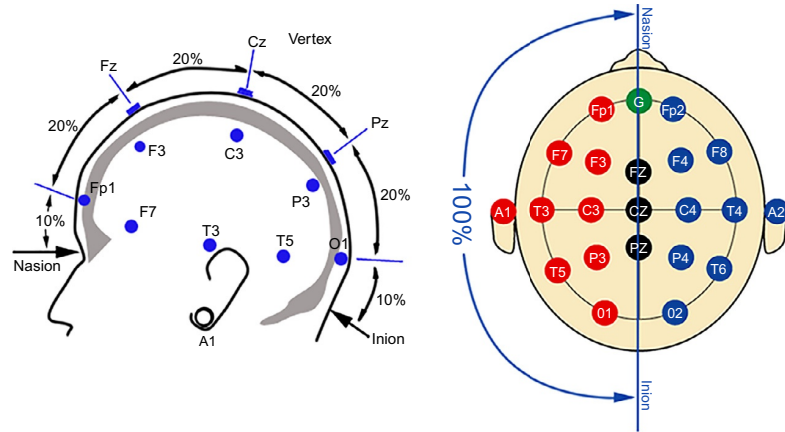


Fig. 1.5: The 10/20 system : standardized placement of electrodes on scalp for EEG measurements [3].

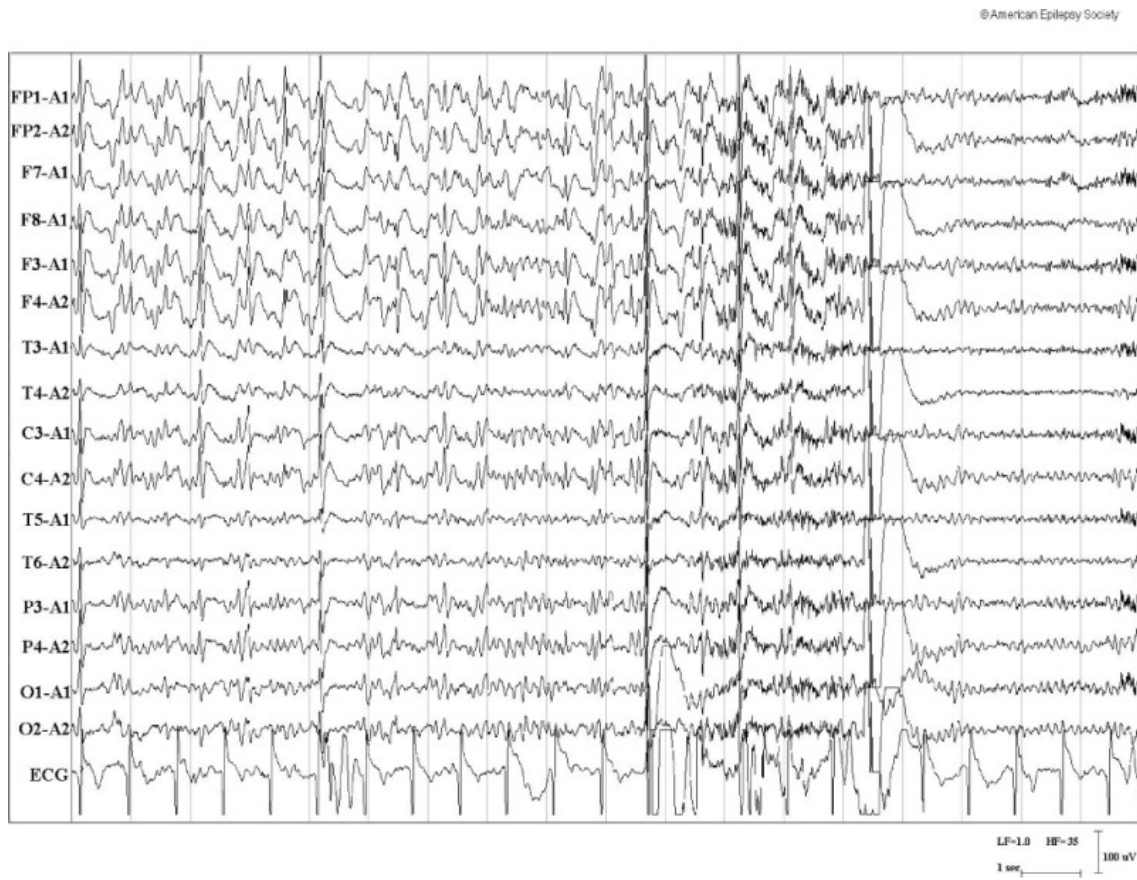


Fig. 1.6: EEG signals recordings from all the channels of the scalp electrodes [16].

During EEG recording, plenty of data is extracted and this data cannot be analysed by experts with the naked eye (Fig. 1.7a). Indeed, the scalp recorded electrical activity consists of a mix of genuine brain signals combined with lots of noise, named artifacts, that are generated by other parts of the body, such as heart activity, eye movements and blinks, other facial muscle movements, etc. (physiological artifacts), or by environmental sources or devices troubles (non-physiological artifacts), which produce electrical signals about 100 times greater than those produced by the brain. So an initial task of any EEG data analysis is signal processing, which consists of separating these other signals from the signal being emitted by the brain itself and in this way revealing the interesting signal [17]. This separation is mainly done using filters (high-pass for physiological artifacts and low-pass for non-physiological ones). After all unwanted signals are removed (Fig. 1.7b), the signal can therefore be analyzed by a specialist who may make observations on the status of the brain.

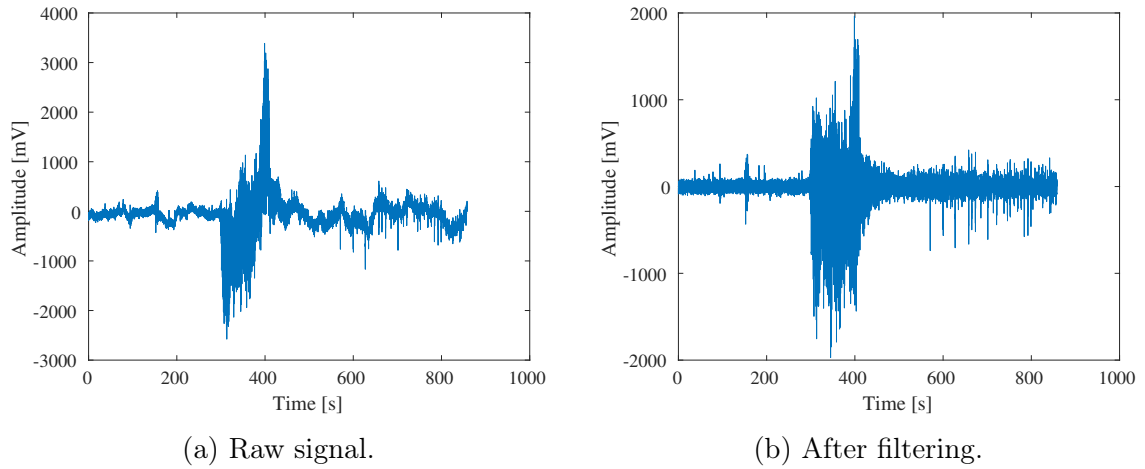


Fig. 1.7: EEG recording.

## Intracranial EEG

The algorithm studied in this work is focused on intracranial EEG. iEEG signals are captured by placing the electrodes directly on the surface of brain to record the brain activity from the cerebral cortex. The iEEG signal is therefore obtained from implanted subdural or deep electrodes (Fig. 1.8). The iEEG signal is widely used in the epilepsy field as it provides a good spatio-temporal resolution of the affected regions of the brain. It can be indeed placed at the closest possible area to the epileptogenic region, giving a good insight of what is happening in this zone [18].

The drawback is that it is an invasive method that requires a surgery, and can lead to bleeding, infection, brain oedema or neurological impairment in rare situations [20].

## 1.3 Existing treatments

The already existing treatments will here be presented. Generally, medical doctors begin by administrating medications to epileptic patients. However, a high proportion

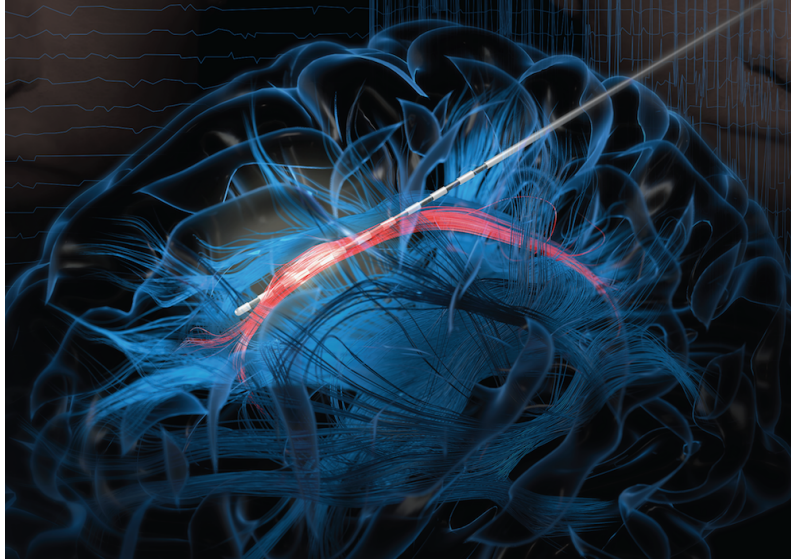


Fig. 1.8: iEEG method [19].

of epileptic patients under medication (more than one half) are still having seizures. Other methods such as the surgery and food regimes are then used [21] [22].

### 1.3.1 Medication

Fortunately, a good part of epileptic patients can become seizure free by taking anti-seizure medication, also called anti-epileptic medication. In other patients, the combinations of well chosen medications have an impact on the frequency and intensity of seizures. The use of medications may therefore be useful, but the choice of the adapted medication should be accurately made. There exist numerous different medications to control epilepsy, adequate for different types of epilepsy, types of seizure and patient's experiences [21] [23].

However, anti-epileptic medications could worsen the seizure or may have side effects if they are not carefully selected or administrated in too large quantities. The side effects could be fatigue, dizziness, weight gain, loss of bone density, skin rashes, loss of coordination, speech problems, memory and thinking problems or even depression, suicidal thoughts or behaviours, severe rash, inflammation of organs (e.g. liver) [21].

### 1.3.2 Surgery

In case the medications fail to control epileptic seizures, surgery is an option. The surgery is applied when the seizure source is a small, well-defined area of the brain, and the area to be operated is not interfering with vital functions such as language, hearing, motor function, vision. Before the surgery can be applied, an iEEG-base monitoring should be performed to identify the area to operate. This method is only used in 10-20% of uncontrolled epileptic seizures, but is efficient. Most operated people should continue to take medications, but the dosages are adapted [22] [19] [21].

### **1.3.3 Ketogenic regime**

The ketogenic regime is a very strict and carefully calculated regime that is generally used in epileptic children that have uncontrollable epileptic seizures. This diet is high in fat, low in protein and carbohydrates. It lasts generally 2 to 3 years and is efficient in 30% of children [22].

# Chapter 2

## State of the art : EEG and iEEG-based seizure detection

The epileptic seizure detection field is highly developed nowadays. As EEG recordings are usually tens or hundreds of hours long, manual detection of seizure periods is difficult and time-consuming. It is why lots of researches are made to be able to detect epileptic seizures with electronic devices and avoid these seizures to occur. The main goal of the research in which this master thesis is included is to detect or predict a seizure before it has impact on the patient and to stimulate the vagus nerve to avoid it. Indeed, the most promising therapy to treat epilepsy is to deliver an electrical stimulation to affected areas of the brain. The vagus nerve being a very important nerve in the body, having both sensory and motor functions, it can easily transmit the information to the corresponding brain area [24]. However, for this technique to be optimal, algorithms of detection should be robust [25]. Several algorithms are developed with different techniques and different goals. Also, some detection devices are already present on the market. This chapter will present a review of both algorithms and devices developed for epileptic seizure detection.

### 2.1 Seizure detection algorithms

The algorithms of seizure detection are classified in various ways depending on the articles. Some classifications are based on the linearity of the techniques, on the type of the detection (detection of the seizure event or of the seizure onset), on the method used to differentiate between ictal and interictal periods, etc. The classification chosen in this master thesis is the most frequent one, done in particular in [15] and [26] : a classification based on the transform domain of operations. The recent algorithms are therefore classified in five domains (Fig. 2.1) : time domain, frequency domain (with the Fast/Discrete Fourier transform : DFT/FFT), wavelet domain (time-frequency domain), empirical mode decomposition (EMD) and rational transform domain. Several existing algorithms are presented for each domain.

In most of the detection algorithms, four steps are performed : raw signal pre-processing, feature extraction, best feature selection and classification in two classes (seizure and non-seizure). The classification here developed focuses on the feature extraction step and the analysis of many different algorithms shows that the features

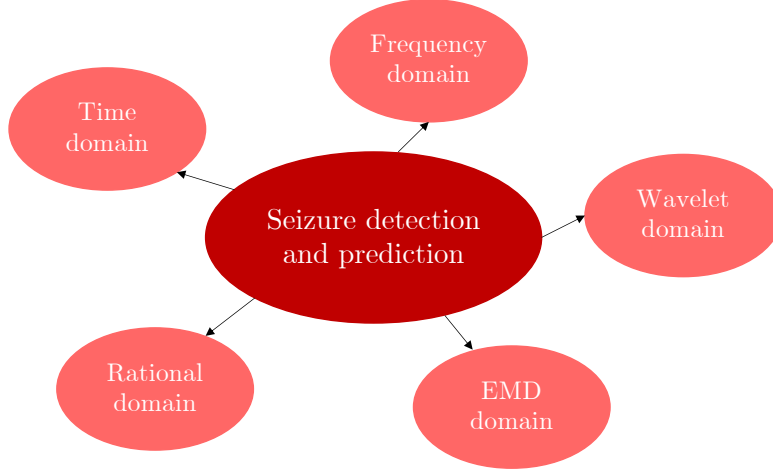


Fig. 2.1: Classification of the seizure detection algorithms.

are generally coming from different transform domains to get better results. These different transforms will be reviewed but it must be kept in mind that they are often used together.

To characterize the performances of each algorithm mentioned, some metrics are usually computed in each article : sensitivity, specificity, accuracy and false detection rate.

- Sensitivity : it refers to the percentage of epileptic seizures correctly detected by the algorithm [27]. A high sensitivity is thus better for automatic epileptic detection. It can be expressed as

$$\text{sensitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}} \cdot 100$$

where TP (true positive) is the number of seizures that are detected by both algorithm and expert and FN (false negative) is the number of seizures marked as seizure by the expert but not detected by the algorithm [26].

- Specificity : it is the percentage of non-seizure events correctly classed by the algorithm :

$$\text{specificity} = \frac{\text{TN}}{\text{TN} + \text{FP}} \cdot 100$$

where TN (true negative) refers to the number of non-seizure epochs, marked as well by the physician and algorithm, and FP (false positive) is the number of non-seizure events detected by the algorithm as epileptic seizures [26].

- Accuracy : it is defined by

$$\text{accuracy} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{FN} + \text{TN} + \text{FP}} \cdot 100$$

and corresponds to the accuracy of the detection algorithm, i.e. its capability to detect correctly seizure and non-seizure events.

- False detection rate : it is the percentage of non-seizure events that are identified as seizure ones [27].

### 2.1.1 Time domain based algorithms

The first domain in which features can be extracted is the time domain. This domain has the advantage that it does not require any transformation of the signal, as the information is directly extracted from the signal in time domain. It is therefore fast and is well adapted to real-time applications. Time domain methods are quite simple and are good choices for patient-specific algorithms, seizure detection devices and in networks. The features in time domain may be of different forms : seven different forms are presented in [Table 2.1](#). For each approach, an article in which this approach is applied is mentioned and performances are evaluated [26].

| Authors                          | Year | Features extraction approach                                                                                                                                                       | Performances                                                 |
|----------------------------------|------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|
| Shanir and Khan [28]             | 2015 | Mean and minimum value in each epoch.                                                                                                                                              | Accuracy : 99.81% ; sensitivity : 100%, specificity : 99.81% |
| Alotaiby <i>et al.</i> [29]      | 2016 | Five histograms of varying number of bins for each period                                                                                                                          | Sensitivity : 97.14% ; specificity : 98.58%                  |
| Runarsson and Sigurdsson [30]    | 2005 | Histograms on difference of amplitude and time between local maxima and minima in each segment.                                                                                    | Sensitivity : about 90%                                      |
| Mursalin <i>et al.</i> [31]      | 2017 | Mean, median, mode, minimum, maximum, skewness, SD, kurtosis, first and third quartile, interquartile range, mobility, complexity, Hurst exponent, detrended fluctuation analysis. | Accuracy : 98.45%                                            |
| Baldominos and Ramón-Lozano [32] | 2017 | Ratio of energy between foreground and background activity.                                                                                                                        | False detection rate : 0.39 for 24 h                         |
| Yoo <i>et al.</i> [33]           | 2012 | Energy in segments.                                                                                                                                                                | Accuracy : 84.4% and ultra-low-power.                        |
| Dalton <i>et al.</i> [34]        | 2012 | Mean, variance, zero-crossing rate, entropy, root means square (RMS) and autocorrelation.                                                                                          | Sensitivity : 91% ; specificity : 84%                        |

Table 2.1: Summary of various seizure algorithms, using time domain features, adapted from [26].

### 2.1.2 Frequency domain based algorithms

The signal is transformed to frequency domain by using the Fourier transform. The Fourier transform's magnitude and phase can therefore be exploited. The advantage to go in another domain is to provide new insight on the signal that can not be seen in time domain and frequency domain methods are more robust than time domain ones. When data is large, and long-time recordings are available, frequency domain methods are appropriate. As for time domain methods, frequency domain methods are presented in [Table 2.2](#).

| Authors                    | Year | Features extraction approach                                                                                                          | Performances                                      |
|----------------------------|------|---------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| Bhople [35]                | 2012 | Fast Fourier transform.                                                                                                               | Accuracy : 100%                                   |
| Rana <i>et al.</i> [36]    | 2012 | Phase slope index.                                                                                                                    | Sensitivity : 100% ; false detection rate < 2/h   |
| Khamis <i>et al.</i> [37]  | 2013 | Power spectral densities and frequency-moment signatures.                                                                             | Sensitivity : 91% ; false detection rate : 0.02/h |
| Acharya <i>et al.</i> [38] | 2012 | Four entropies, phase entropy 1, phase entropy 2, approximate entropy and sample entropy (time domain and frequency domain features). | Accuracy : 98.1%                                  |

Table 2.2: Summary of various seizure algorithms, using frequency domain features, adapted from [26].

### 2.1.3 Wavelet domain based algorithms

A wavelet is a waveform with limited duration and zero average value (some wavelet examples in Fig. 2.2), called mother wavelet. The wavelet transform is a time-frequency transform and is useful in extracting features from non-linear and non-stationary signals in selected sub-bands. The main challenge in wavelet transform domain is to select the correct number of decomposition levels and mother wavelet. It is why several papers using different mother wavelets and number of decomposition levels have been analyzed in Table 2.3.

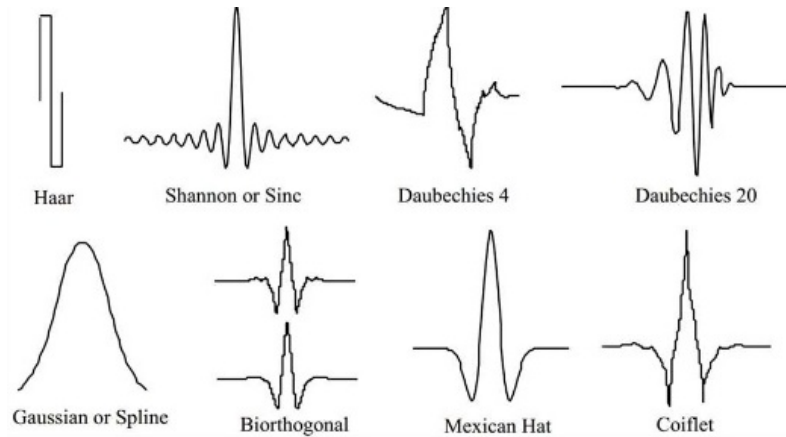


Fig. 2.2: Examples of mother wavelets.

The results of the detection are better with Daubechies of order 2 and 4 and Morlet as mother wavelets and a number of decomposition levels up to 5 is sufficient. Wavelet domain methods increase tremendously the accuracy of results.

### 2.1.4 EMD and Hilbert transform domain based algorithms

EMD is also a time-frequency technique, which is adaptive and does not require prior fixed basis. EMD is a signal decomposition technique, in which the signal is transformed into a group of functions or components called intrinsic mode functions (IMFs), which preserve the inherent properties of the original signal. In EMD based

| Authors                      | Year | Features extraction approach                                                                                                                                                                        | Performances                                                                                          |
|------------------------------|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| Polat <i>et al.</i> [39]     | 2016 | Mean, maximum, minimum, standard deviation and average power of absolute values of wavelet coefficients. Number of decomposition levels (DL) : 2. Mother wavelet (MW) : 4th order Daubechies (db4). | Accuracy : 100% and 96% for 2 datasets                                                                |
| Zainuddin <i>et al.</i> [40] | 2012 | Maximum, minimum, and SD of the absolute values of the wavelet coefficients. MW : Morlet and db4.                                                                                                   | Sensitivity and specificity : up to 98%                                                               |
| Niknazar <i>et al.</i> [41]  | 2013 | Alpha, beta, delta, theta, and gamma sub-bands. DL : 5. MW : db4.                                                                                                                                   | Accuracy : 98.67%                                                                                     |
| Zhou <i>et al.</i> [42]      | 2013 | Lacunarity (measure of heterogeneity) and fluctuation index. DL : 5.                                                                                                                                | Sensitivity : 96.25% ; false detection rate : 0.13/h                                                  |
| Chen <i>et al.</i> [43]      | 2017 | Magnitude of Fourier coefficients of 6 wavelet scales.                                                                                                                                              | Classification rate : 100%                                                                            |
| Liu <i>et al.</i> [44]       | 2012 | Relative amplitude, relative energy, coefficient of variation, and fluctuation index of three selected levels. DL : 5.                                                                              | Sensitivity : 94.46% ; specificity : 95.26% ; false detection rate : 0.58/h                           |
| Abbasi and Esmailpour [45]   | 2017 | Maximum, minimum, average and SD of four chosen levels. DL : 5. MW : db4.                                                                                                                           | Accuracy : 98.33% ; sensitivity : 100% ; specificity : 97.1%                                          |
| Panda <i>et al.</i> [46]     | 2010 | Energy, SD, and entropy. DL : 5. MW : db2.                                                                                                                                                          | Accuracy : 91.2%                                                                                      |
| Khan <i>et al.</i> [47]      | 2012 | Relative energy and a normalized coefficient of variation. DL : 5. MW : db4.                                                                                                                        | Accuracy : 83.6% ; sensitivity : 100% ; specificity : 91.8%                                           |
| Shoaib <i>et al.</i> [48]    | 2014 | Wavelet energy.                                                                                                                                                                                     | 4% decline in sensitivity, 0.15/h increase in false detection rate compared to baseline performances. |

Table 2.3: Summary of various seizure algorithms, using wavelet domain features, adapted from [26].

methods, IMFs could be features themselves or features can be extracted from IMFs. The Hilbert transform with EMD can provide information on the instantaneous frequency of the signal (frequency at instant  $t$ ). Hilbert spectral analysis of IMFs is a good information of time-frequency distribution of the signal. The EMD domain and Hilbert transform are usually combined to have better results than all other domains seen up to now. Researches is till largely ongoing in this domain, because it is not yet mastered but is very promising. Algorithms based on this method are mentioned in [Table 2.4](#).

| Authors                     | Year | Features extraction approach                                                                                               | Performances                                              |
|-----------------------------|------|----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| Tafreshi <i>et al.</i> [49] | 2008 | Means of the absolute values of 4 IMF's Hilbert transform.                                                                 | Accuracy : 90.69%                                         |
| Orosco <i>et al.</i> [50]   | 2009 | Energies of IMFs compared with thresholds.                                                                                 | Sensitivity : 56.41% ; specificity : 75.86%               |
| Guarnizo and Delgado [51]   | 2010 | Amplitude, average or instantaneous frequency, skewness, kurtosis and Shannon's entropy for all EMD components (4 IMFs).   | Accuracy : 98%                                            |
| Belhadj <i>et al.</i> [52]  | 2016 | Euclidian, Bhattacharya and kolomogorov distances between IMFs.                                                            | Accuracy : 98.84%                                         |
| Torse <i>et al.</i> [53]    | 2017 | Instantaneous frequencies from IMFs and instantaneous frequency details from Hilbert transform of IMFs.                    | Accuracy : 96%                                            |
| Alam and Bhuiyan [54]       | 2011 | Kurtosis, skewness, largest Lyapunov exponent, variance, approximate entropy, and correlation dimension from first 4 IMFs. | Sensitivity : 100% ; specificity : 100% ; accuracy : 100% |
| Bajaj and Pachori [55]      | 2013 | Instantaneous area estimated from the trace of analytic 2 IMFs and local mean of EMD.                                      | Sensitivity : 90% ; specificity : 89.31%                  |

Table 2.4: Summary of various seizure algorithms, using EMD domain and Hilbert transform based features, adapted from [26].

It can be concluded that up to four IMFs are sufficient to get a good detection.

### 2.1.5 Rational domain based algorithms

The rational domain is also a time-frequency domain that is based on rational functions. The basis rational function is as follows:

$$r_{a,k}(z) = \frac{1}{(1 - \bar{a}z)^k}, (a \in \mathbb{D}, z \in \overline{D}, k \in \mathbb{N}) \quad (2.1)$$

where  $a$  is the inverse pole and  $k$  is the order of the function. It is also adaptive in nature and its application in seizure detection started in 2018. The parameters basis of the rational domain is found by using optimization techniques. The disadvantage of this method is that it requires complex computations, but the advantages are numerous : flexible system to represent EEG signal, compact representation of the

signal with coefficients that can be used as features, basis functions can provide time and frequency information, the rational system gives a simple representation of the original signal, small number of arithmetic operations are required. This method is therefore well suited to real-time applications. Some algorithms that have been developed using rational functions are presented in [Table 2.5](#).

| Authors                   | Year | Features extraction approach                                                                                                 | Performances                                                              |
|---------------------------|------|------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
| Samiee <i>et al.</i> [56] | 2015 | Absolute mean value, absolute median value, absolute SD, absolute maximum value, absolute minimum value of the coefficients. | Accuracy : 99.8% and 99.3% for 2 datasets                                 |
| Samiee <i>et al.</i> [57] | 2017 | Feature extraction method based on sparse rational decomposition and local Gabor binary patterns (LGBP).                     | Sensitivity : 70.4% ; specificity : 99.1% ; false detection rate : 0.35/h |

Table 2.5: Summary of various seizure algorithms, using rational domain features, adapted from [26].

## 2.2 Existing devices for seizure detection

The benefits of developing devices for seizure detection are numerous. Indeed, a wearable therapeutic system that is capable to detect coming seizures could be efficient to alarm the patient or its family that a seizure is developing or to halt the seizure progression before symptoms appearance. It could limit the consequences of an epileptic seizure and thereby improve the quality of life of epileptic patients [27]. It has also the advantage that the patient has to undergo only short intermittent interventions in contrary with continuous pharmaceutical therapy [58]. These benefits and patients needs are illustrated in [Fig. 2.3](#).

The first test on humans of an implanted device for epileptic seizures detection was made between 2010 and 2011. The system is represented in [Fig. 2.4](#) and its objective is to inform the patient of the likelihood of a seizure development in the minutes or hours ahead. This seizure advisory system is a hand-held device that receives and analyses iEEG signals recorded by the intracranial electrodes array in brain, and provides a visual and audible signal to notify the patient. The leads array is connected to a telemetry unit that wirelessly sends information to the advisory device. The advisory device applied an algorithm of detection to the iEEG data and give the information to the patient by means of a colour code as well as an auditory or vibratory signal. The results of the study of efficacy and safety of the implantable device on humans can be found in [60].

Two main iEEG-based seizure detection and stimulation devices exist at this time : the vagal nerve stimulation (VNS) and the responsive (that applies detection and treatment in closed-loop) neurostimulation (RNS) [61]. The VNS is not responsive, it contains an implanted stimulator and a lead incorporating a bipolar electrode but an external pulse programming system, that applies the detection and triggers the stimuli generator. This system is shown in [Fig. 2.5a](#). The RNS consists in a

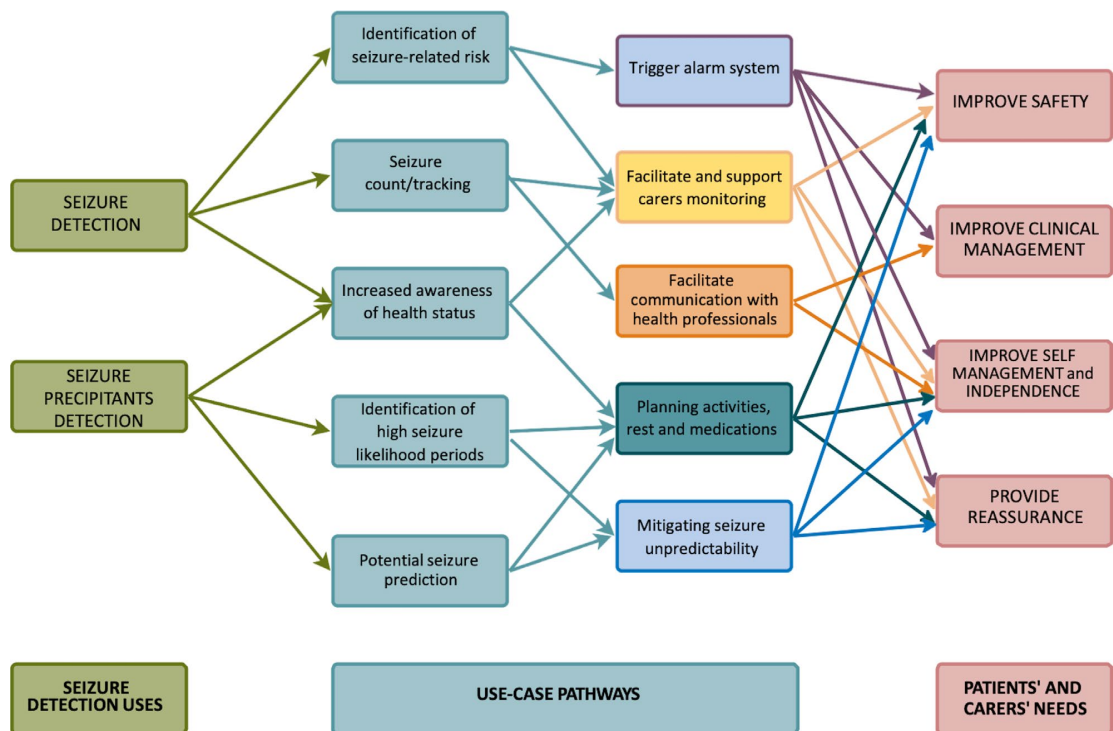


Fig. 2.3: Seizure benefits and patients' needs [59].

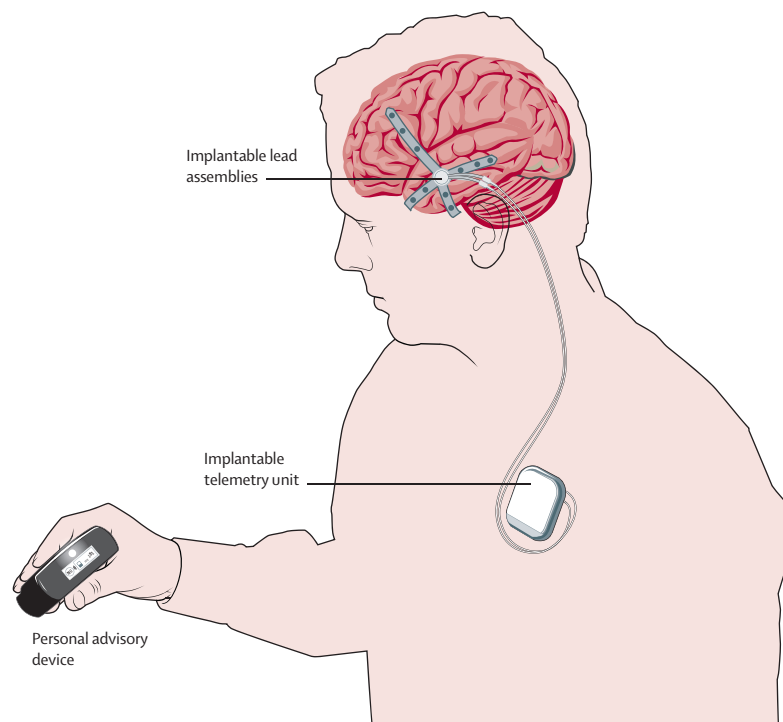
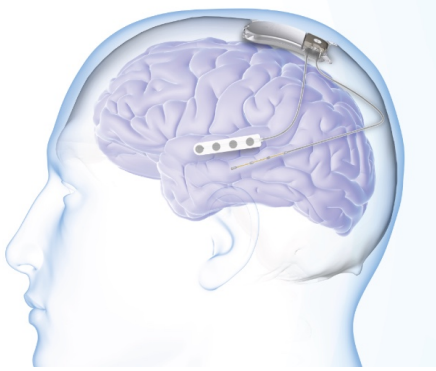
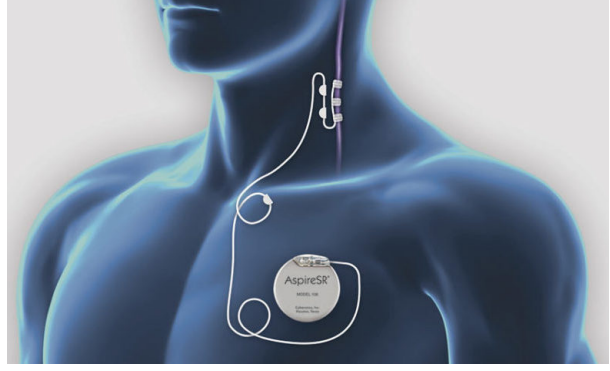


Fig. 2.4: Image of an alarming signal [60].

programmable, battery-powered microprocessor-controlled device implanted in the cranium, which delivers a short train of electrical pulses to the epileptogenic zone through intracranial electrodes when a seizure onset is detected. All is thus implanted in the brain. An external system is however available to allow a physician to do some adjustments. The RNS is illustrated in Fig. 2.5b.



(a) VNS system [62].



(b) RNS system [63].

Fig. 2.5: Representation of implantable medical devices for seizure detection and stimulation.

## 2.3 Interpretability of the seizure detection

In all the algorithms presented, it can be seen that the sensitivity and accuracy of the detection is generally high. However, false detections occur and not always all the seizures are detected (sensitivity  $\neq 100\%$ ). It could be a significant problem for patients, that can therefore not be totally confident in the detection device. There is therefore a large gap between algorithms and needs of patients. Moreover, all the algorithms are based on classification through features extraction from EEG signals. The features are of various forms and most of the methods are very promising but all the features are mathematical components and have no medical representation. The physicians and experts are therefore unable to verify if a seizure is well detected with regards to the features. A second need is not satisfied : the clinical management. For all these reasons, an algorithm that is based on the idea of interpretability of the seizures detection is very interesting.

# Chapter 3

## Parameters identification algorithm

This chapter will present the algorithm that has been implemented in this master thesis [64]. It has been developed by Xiaoya Fan and Antoine Nonclercq from Université Libre de Bruxelles (ULB), in collaboration with medical departments of Hôpital Erasme and Brugmann. The algorithm is based on the breakthrough discovery that the excitation/inhibition imbalance of neurons plays a key role in the mechanism of ictogenesis. Indeed, the contribution of the  $\gamma$ -aminobutyric acid (GABA)<sub>A</sub> receptors in epileptic seizures development is more recognized as proved in [65]. As said in [Chapter 1](#), there are several types of epilepsy. In this algorithm, the focus is on temporal lobe epileptic seizures characterized by a gradual change in the neuronal dynamics. Therefore, studying the temporal evolution of underlying neuronal parameters could provide information on the interictal to ictal transition. Indeed, 30 iEEGs were recorded from 10 patients who suffer from temporal lobe epilepsy (TLE).

The algorithm considered in this work is built on the estimation of three physiologically meaningful parameters in interictal to ictal transition, that are average excitatory ( $A_e$ ), slow ( $B$ ) and fast ( $G$ ) inhibitory synaptic gains. These three parameters are medical components, and can be therefore interpreted by experts. The detection can thus be verified at every moment and the patients could also verify each detection if he has some knowledges about the normal (non-seizure) values of these parameters. From these three parameters, four ratios were computed ( $\frac{A_e}{G}$ ,  $\frac{A_e}{B}$ ,  $\frac{A_e}{B+G}$ ,  $\frac{B}{G}$ ) and analyzed over time, that permits to predict the epileptic seizure [64]. The parameters  $A_e$ ,  $B$  and  $G$  are found for each period of 2 seconds of intracranial EEG (iEEG) through a comparison with synthesized EEG from a neural mass model. The algorithm is represented in [Fig. 3.1](#).

The left side represents the synthesized EEG signals generated by the neural mass model from a large range of possible parameters. The right side represents the recorded iEEG signals processing. The features are extracted from both synthesized (features vector  $\widehat{F}_s$ ) and recorded (features vector  $\widehat{F}_r$ ) EEG signals and compared through an Euclidean distance based error calculation. The best triplets are then selected and clustered to find the most representative triplet of parameters for each period of 2 seconds of recorded iEEG. The ratios are computed and their temporal evolution is compared to predefined thresholds to define seizure onset and offset. The rest of this chapter presents each step in detail, summarizing the work of Xiaoya Fan and Antoine Nonclercq, and ends with their validation of the algorithm. Performances

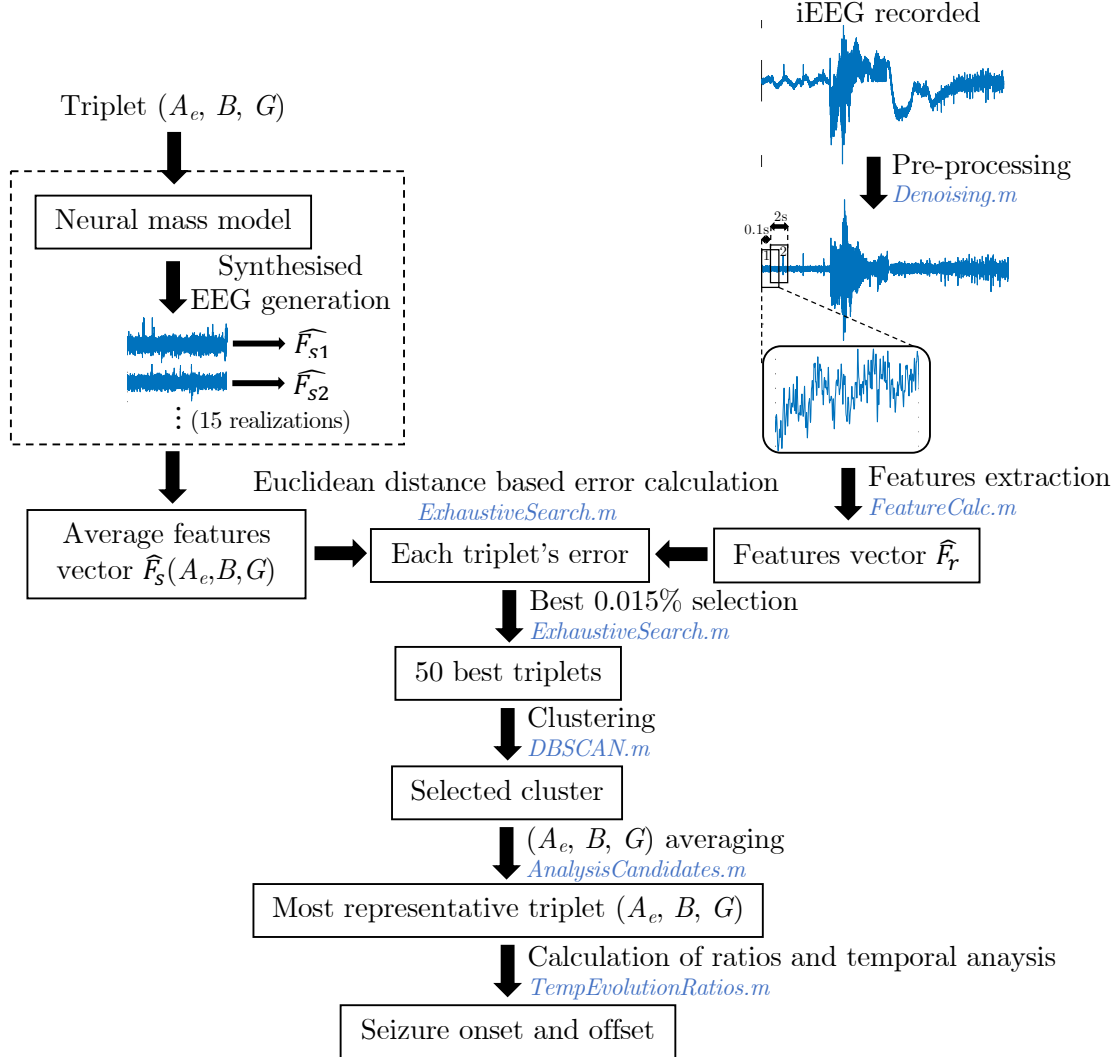


Fig. 3.1: Parameters identification algorithm, adapted from [64]. This algorithm has been implemented in MATLAB by Xiaoya Fan. The names of each MATLAB function is reused in this figure. The whole implemented algorithm could be found through this link : [MATLAB implementation](#).

are then evaluated in the purpose of this master thesis.

## 3.1 Neural mass model

The neural mass model implemented in this algorithm was developed in 2002 by Wendling *et al.* in [66]. This section will present first the context in which the model was developed and the mathematics behind it. Then, the focus will be set on the generation of EEG signals with respect to the parameters.

### 3.1.1 Model context and description

On one hand, studies of the 2000s showed that gamma oscillations, that appear as low-voltage rapid discharges, are often present during seizure onset and the regions they originate from are generally considered to be highly epileptogenic. Also, it has been shown that oscillations of gamma frequency are linked to the behaviour of inhibitory interneurons in hippocampus or neocortex. These oscillations in hippocampal pyramidal cells (main cells) may highly be induced by two types of (GABA)<sub>A</sub> inhibitory postsynaptic currents (IPSCs) : the first one is rapidly rising and decaying and is carried by somatic synapses and the second one is slowly rising and decaying and is mediated by dendritic synapses. Therefore, a link is established between the two types of inhibitors and epileptic seizures. On the other hand, Freeman proposed in 1978 a model based on the fact that EEG is the reflection of the dynamics between interconnected populations of neurons, precisely population of pyramidal cells and interneurons populations. The neural mass model described in [66] is based on this macroscopic organization of neurons and is represented in Fig. 3.2.

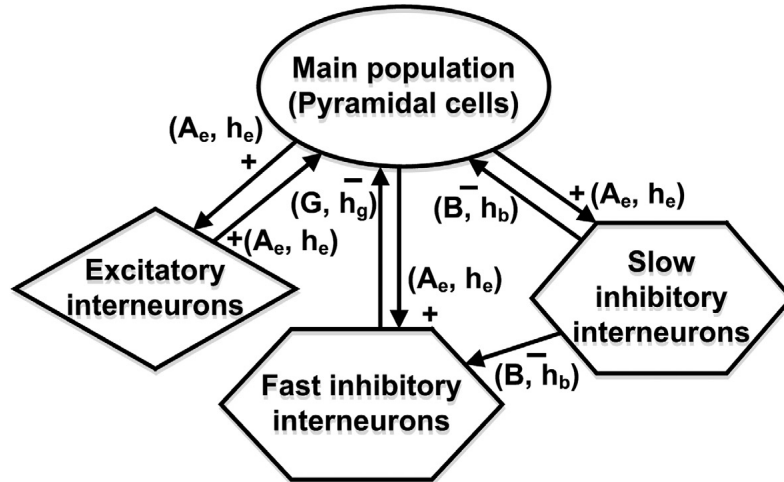


Fig. 3.2: Structure of the macroscopic neural mass model [64].

As can be seen, the model links four populations of neurons that interact with each other. The first subset is composed of the main cells (pyramidal cells in hippocampus or neocortex), which are very numerous in the cerebral cortex, making them very important in cognitive processes [67]. It receives feedback from three

other subsets composed of local interneurons, excitatory, slow dendritic-projecting ( $\text{GABA}_{A,slow}$ ) and fast somatic-projecting ( $\text{GABA}_{A,fast}$ ) inhibitory ones respectively. The pyramidal cells send excitatory currents to the other subsets and the slow inhibitory interneurons inhibit the fast inhibitory ones. All these interactions are symbolized by parameters that are described in Table 3.1.

The model can also be represented by a detailed scheme of interactions between populations (Fig. 3.3). Again, the four subsets are represented through their impulse response and parameters. The excitatory input  $p(t)$  represents the influence from all other neighbouring brain areas and is modelled by a white Gaussian noise ( $\mu = 90 \text{ pulses}\cdot\text{s}^{-1}$ ,  $\sigma = 30 \text{ pulses}\cdot\text{s}^{-1}$ ), that globally describes the average density of afferent action potentials. The model output is the sum of the postsynaptic potentials in activated pyramidal cells, it thus corresponds to the postsynaptic activity of the main population, that possesses the same characteristics as an EEG signal.

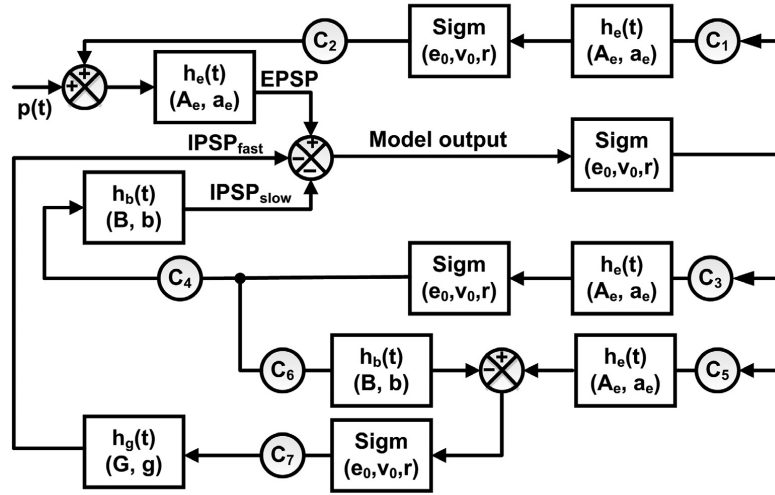


Fig. 3.3: Schematic detailed representation of the model [64].

Each population is characterized by a second order linear function ( $h_e(t)$ ,  $h_b(t)$ ,  $h_g(t)$ ) (Eq. 3.1) that transforms the average pulse density of afferent action potentials into an average postsynaptic membrane potential (IPSP : inhibitory postsynaptic potential ; EPSP : excitatory postsynaptic potential) and an asymmetric sigmoid function (Eq. 3.2) that relates the average postsynaptic potential of a given subset to an average pulse density of potentials fired by the neurons. Impulse responses are shown in Fig. 3.4. One can see that the impulse response  $h_g(t)$  is much faster than  $h_b(t)$ .  $C_1$  to  $C_7$  are the connectivity constants (average number of synaptic contacts) of the model and represent the weights of the interconnections between the populations. All the model parameters are described and their typical values are given in Table 3.1.

$$h_e(t) = A_e a_e t e^{-a_e t}, h_b(t) = B b t e^{-b t}, h_g(t) = G g t e^{-g t}, \text{ with } t \geq 0 \quad (3.1)$$

$$\text{Sigm}(\nu) = \frac{2e_0}{1 + e^{r(\nu_0 - \nu)}} \quad (3.2)$$

Thereupon, assuming each linear impulse response introduces a pair of first order differential equations where  $x(t)$  and  $z_1(t)$  are the input and output signals of each

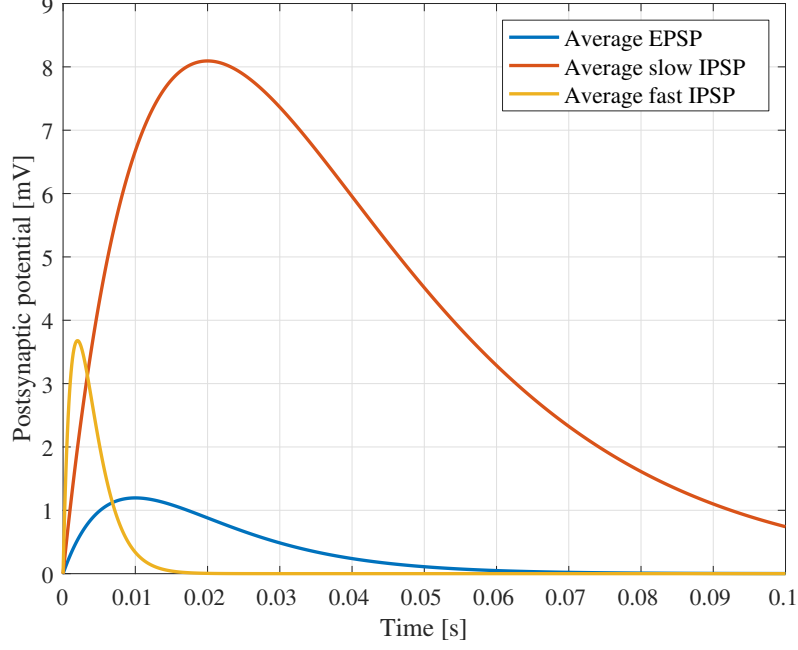


Fig. 3.4: Average postsynaptic membrane potentials along time, obtained from impulse responses  $h_e(t)$ ,  $h_b(t)$  and  $h_g(t)$ .

transfer function,  $W = A_e, B$  or  $G$  and  $w = a_e, b$  or  $g$  :

$$\begin{cases} \dot{z}_1(t) = z_2(t) \\ \dot{z}_2(t) = Wwx(t) - 2wz_2(t) - w^2z_1(t), \end{cases}$$

ten differential equations that govern the model are found. These ten equations are solved by numerical methods and give rise to a synthesized EEG signal, depending on the three parameters  $A_e$ ,  $B$  and  $G$  as inputs of the model.

### 3.1.2 Synthesized EEG signals and parameter space

As already said, the neural mass model generates a synthesized EEG signal whose appearance depends on the main parameters  $A_e$ ,  $B$  and  $G$ . Therefore, by varying these parameters, the model outputs different types of EEG activity, that can be related to different phases of an EEG signal, particularly normal background, sporadic spikes that appear during interictal periods, sustained spikes activity and slow rhythmic activity that may be encountered at seizure onset or during seizures, low-amplitude rapid discharges that are observed at the beginning of ictal periods and low quasi-sinusoidal activity that usually follows rapid discharges. The values of the three synaptic gains are thus linked to different phases of EEG signal in an epileptic patient. Identifying those parameters in a recorded EEG signal may therefore play a key role in epileptic seizure detection.

The technique developed in [64] is to generate EEG signals for each triplet of parameters varying around their standard value and extract relevant features from these EEG signals. As the excitation input  $p(t)$  is a white Gaussian noise, the EEG signal output from the model depends on each realization. To avoid this dependence, the model has been simulated 15 times for each triplet of parameters, as shown in

| Parameter  | Interpretation                                                                    | Value                  |
|------------|-----------------------------------------------------------------------------------|------------------------|
| $A_e$      | Average excitatory synaptic gain                                                  | 3.25 mV                |
| $B$        | Average slow inhibitory synaptic gain                                             | 22 mV                  |
| $G$        | Average fast inhibitory synaptic gain                                             | 10 mV                  |
| $a_e$      | Inverse of dendritic average time constant in the feedback excitatory loop        | $100 \text{ s}^{-1}$   |
| $b$        | Inverse of dendritic average time constant in the slow feedback inhibitory loop   | $50 \text{ s}^{-1}$    |
| $g$        | Inverse of somatic average time constant in the fast feedback inhibitory loop     | $500 \text{ s}^{-1}$   |
| $\nu_0$    | Postsynaptic potential when a 50% of firing rate is achieved                      | 6 mV                   |
| $e_0$      | Maximum firing rate of the population                                             | $2.5 \text{ s}^{-1}$   |
| $r$        | Steepness of the sigmoid function                                                 | $0.56 \text{ mV}^{-1}$ |
| $C_1, C_2$ | Average number of synaptic contacts in the excitatory feedback loop               | $C_1 = 135, C_2 = 108$ |
| $C_3, C_4$ | Average number of synaptic contacts in the slow feedback inhibitory loop          | $C_3 = C_4 = 33.75$    |
| $C_5, C_7$ | Average number of synaptic contacts in the fast feedback inhibitory loop          | $C_5 = C_7 = 13.5$     |
| $C_6$      | Average number of synaptic contacts between slow and fast inhibitory interneurons | $C_6 = 108$            |

Table 3.1: Model parameters, their interpretation and standard value, adapted from [66].

**Fig. 3.1.** For each simulation, features were extracted from the EEG signal and averaged features were obtained. However, if there is bimodality in feature values (existence of two peaks in probability density function), averaging the features is not relevant. The bimodality coefficient was calculated and 95.86% of the feature values are considered unimodal (bimodality coefficient below 0.555). Therefore, the features averaging is meaningful.

The three parameters varying around their standard value form a parameters space ([Table 3.2](#)) in which an exhaustive grid search is done to find the corresponding parameters set of the EEG period considered. The grid search has a resolution of 0.5 mV in slow and fast inhibition ( $B$  and  $G$ ) and of 0.125 mV in excitation ( $A_e$ ),  $A_e$  varying from 3 to 7 mV and  $B$  and  $G$  from 0.5 to 50 mV. In total, 4 950 000 synthesized EEG signals are generated to obtain 330 000 features vectors (15 simulations per triplet and then features vector), one for each triplet of parameters  $A_e$ ,  $B$  and  $G$ . These information are summarized in [Table 3.2](#).

| Parameter | Lowest limit [mV] | Highest limit [mV] | Resolution [mV] | Number of runs |
|-----------|-------------------|--------------------|-----------------|----------------|
| $A_e$     | 3                 | 7                  | 0.125           | 33             |
| $B$       | 0.5               | 50                 | 0.5             | 100            |
| $G$       | 0.5               | 50                 | 0.5             | 100            |

Table 3.2: Summary of resolution and extrema values of the grid search.

## 3.2 Pre-processing

As shown in the right branch of [Fig. 3.1](#), the recorded EEG signals should be pre-processed before we can extract some features from them. Indeed, as already said in [Chapter 1](#), EEG recordings suffer from parasitic artifacts that must be removed. The EEG signal is here passed through a high-pass filter with cut-off frequency of 0.16 Hz, a low-pass filter with cut-off frequency of 64 Hz and a notch filter that removes the 50 Hz frequency ([Fig. 3.5](#)).

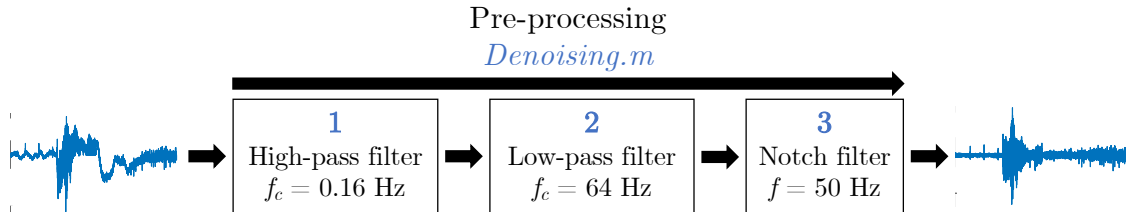


Fig. 3.5: Schematic of the pre-processing step.

### 3.2.1 High-pass filter

The high-pass filter removes the slow baseline drift of the signal, that comes from respiration, variations in electrode impedance, excessive body movements [68] and

in EEG particularly from eye movements and blinking [69]. The filter implemented in the algorithm is a second order Butterworth filter. The Butterworth filter is an infinite impulse response (IIR) filter. The advantages to use IIR filters and not finite impulse response (FIR) filters is that the order of an IIR filter compared to an equivalent FIR filter meeting the same specifications is much lower and thus the computational complexity is also lower. However, an IIR filter is less stable and introduces distortion in the signal. In this case, the algorithm deals with plenty of data and operations, so a low complexity is more interesting. An IIR filter is thus most relevant [70]. The choice for the Butterworth filter compared to other windows represented in Fig. 3.6 was encouraged by the fact that the Butterworth window is maximally flat, it does not add parasitic fluctuations in the signal, assuring a good quality of the output signal in all frequency bands, which is important to keep the frequency content unchanged. In contrary, the fall-off of the filter is not as sharp as for other filters but it does not have a strong influence here [71].

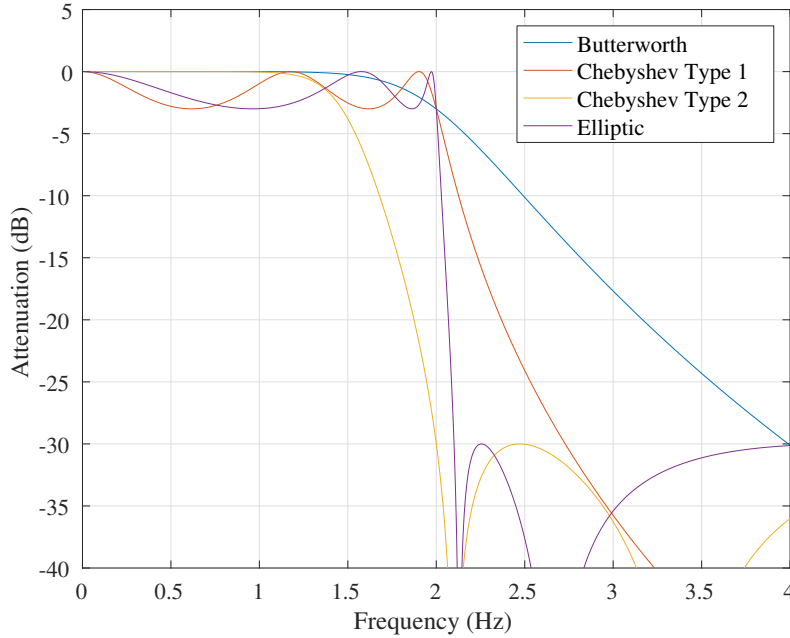


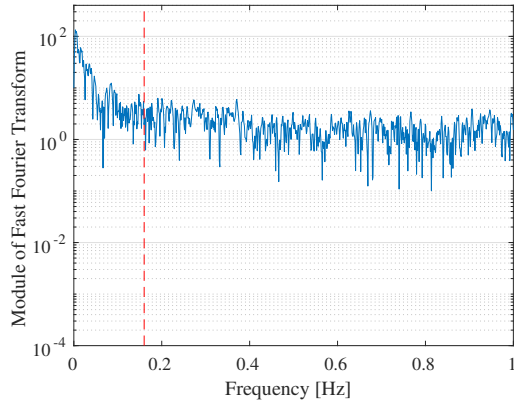
Fig. 3.6: Four types IIR filters [72].

The frequency content of input and output signals of the high-pass filter in the interesting range of frequencies (0 to 1 Hz) are represented in Fig. 3.7. One can see that the frequencies under 0.16 Hz are filtered.

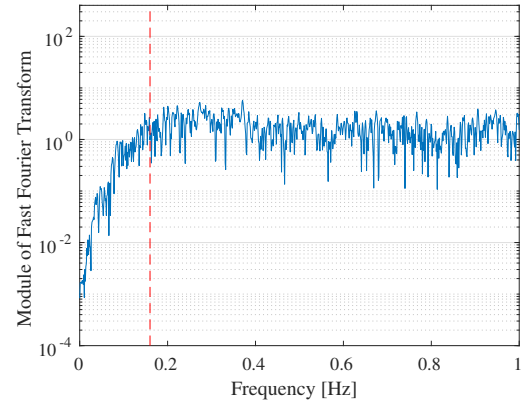
### 3.2.2 Low-pass filter

The low-pass filter, on the other hand, removes the electronic noise coming from data acquisition devices. Indeed, the devices used to acquire EEG signal (electrodes, operational amplifiers, etc.) introduce high-frequency noise that should be discarded. The low-pass filter is also a second order Butterworth IIR filter, for the same reasons as the high-pass filter.

The frequency content of the input and output signals of the low-pass filter may be observed in Fig. 3.8.

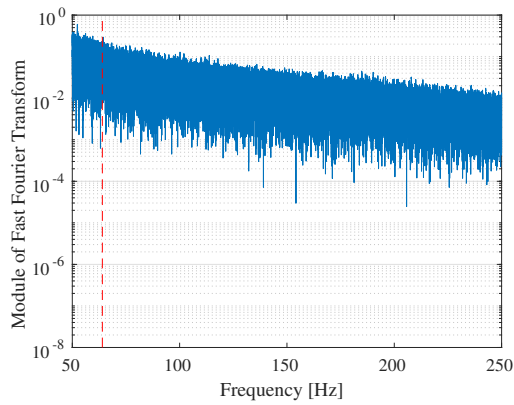


(a) Before high-pass filter.

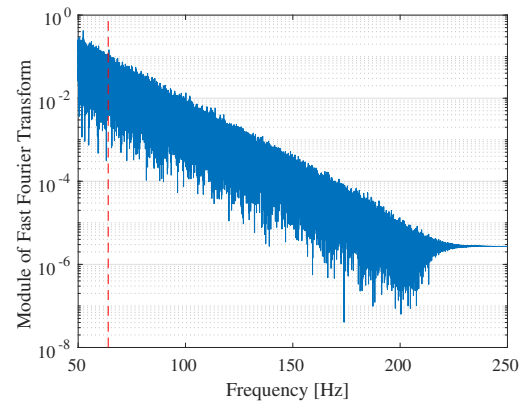


(b) After high-pass filter.

Fig. 3.7: Frequency content of EEG signal between 0 and 1 Hz. The cut-off frequency is highlighted by a red vertical line.



(a) Before low-pass filter.



(b) After low-pass filter.

Fig. 3.8: Frequency content of EEG signal between 50 and 250 Hz. The red line marks the cut-off frequency : 64 Hz.

### 3.2.3 Notch filter

The notch filter is, for its part, used to remove the power line noise. In our countries, the alternating currents in standard electric outlets oscillate at 50 Hz, so that the EEG is often contaminated by 50 Hz electric fields in the surrounding environment [73]. The notch filter is a second order IIR filter, that offers also a low complexity and delay.

The frequency content of the input and output signals of the notch filter is shown in Fig. 3.9. The power line at 50 Hz is well discarded in output signal. The output signal of the notch filter is also the output signal of the `denoising.m` function. This signal is therefore pre-processed.

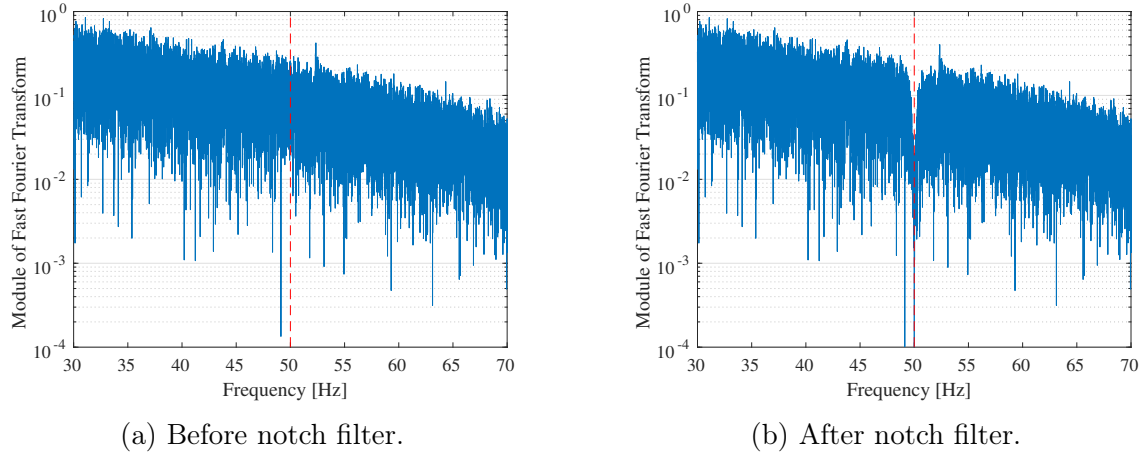


Fig. 3.9: Frequency content of EEG signal between 30 and 70 Hz. The red line marks the removed frequency (50 Hz).

## 3.3 Features extraction

Once the EEG signal is pre-processed and all the artefacts are removed, relevant features can be extracted from the signal. To make a pertinent extraction of features, the recorded EEG signal should be segmented into periods of 2 s with a step of 0.1 s. The segment size (2 s) is short enough to get quasi-stationary EEG signal and long enough to allow proper parameters identification. The step size (0.1 s) was chosen to track parameters with high temporal resolution. For each period, a feature vector ( $\widehat{F}_r$ ) is calculated, based on both spectral and temporal properties of the signal. Indeed, the feature vector of one segment contains seven spectral and seven temporal features. From this step till the epileptic seizure detection, all operations will apply over a period of 2 s at a time, being carried out on all segments until the end of the EEG recording. This step's description is illustrated by Fig. 3.10.

### 3.3.1 Spectral features

The spectral features are computed as the relative power within seven frequency bands. The frequency bands were chosen by looking at the spectral density in

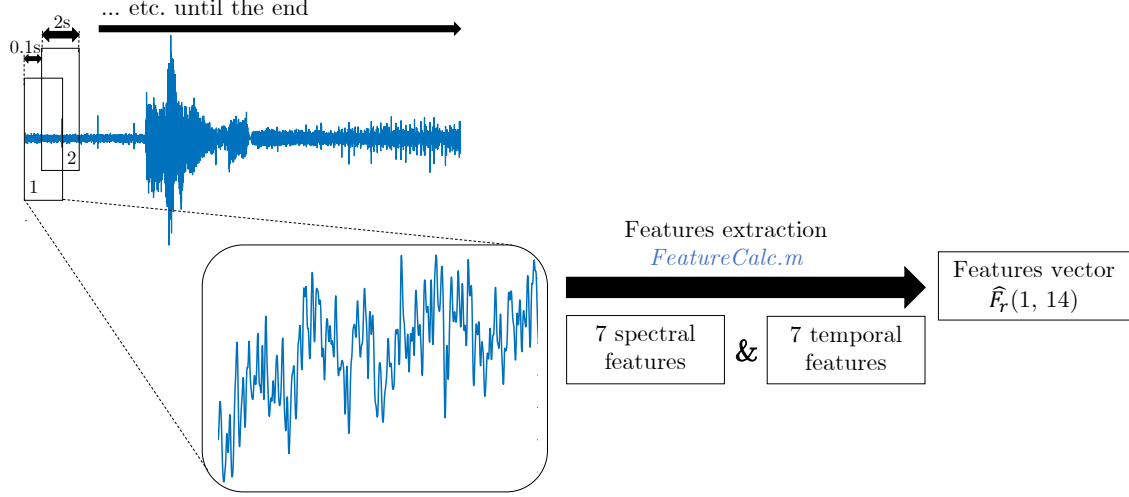


Fig. 3.10: Schematic of the features extraction step.

function of the frequency in EEG signal. Most of the frequencies in the human EEG signal are low (as observed in Fig. 3.7, Fig. 3.8 and Fig. 3.9) because the different waves in a human brain have low frequencies [74]. For that reason, the seven frequency bands are 0.5-1.5, 1.5-2.5, 2.5-4.5, 4.5-8.5, 8.5-16.5, 16.5-32.5 and 32.5-64.5 Hz.

The relative power in each frequency band was calculated from the Fast Fourier Transform (FFT) of the signal. Indeed, once the FFT was computed, the values of its module were selected for each band and the power in the band was calculated with Eq. 3.3. The relative power is then obtained by dividing the power of the band by the total power of the signal. An illustration of the relative powers in function of the frequency bands may be observed in Fig. 3.11.

$$\text{power} = \int_{\text{band}} |X(f)|^2 df \quad (3.3)$$

### 3.3.2 Temporal features

The temporal features are obtained by computing the absolute signal amplitude, dividing it in seven equally sized bins and calculating the ratio between the number of samples in each bin and the total number of samples. An illustration of seven temporal features is represented in Fig. 3.12.

## 3.4 Best parameters' triplets selection

As soon as the features are all extracted, the ones of the recorded signal ( $\widehat{F}_r$ ) should be compared to the ones of the synthesized signals ( $\widehat{F}_s$ ) generated from all possible combinations of the parameters  $A_e$ ,  $B$  and  $G$  to find the parameters associated to the considered period of the recorded signal. The comparison is done through an Euclidean distance based error function. The errors are then sorted and

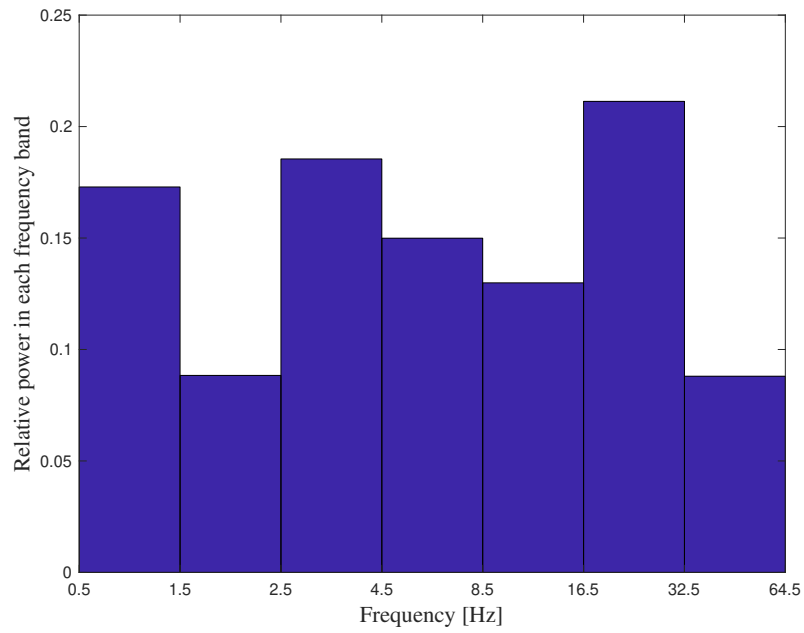


Fig. 3.11: Illustration of spectral features for the first period of 2 s.

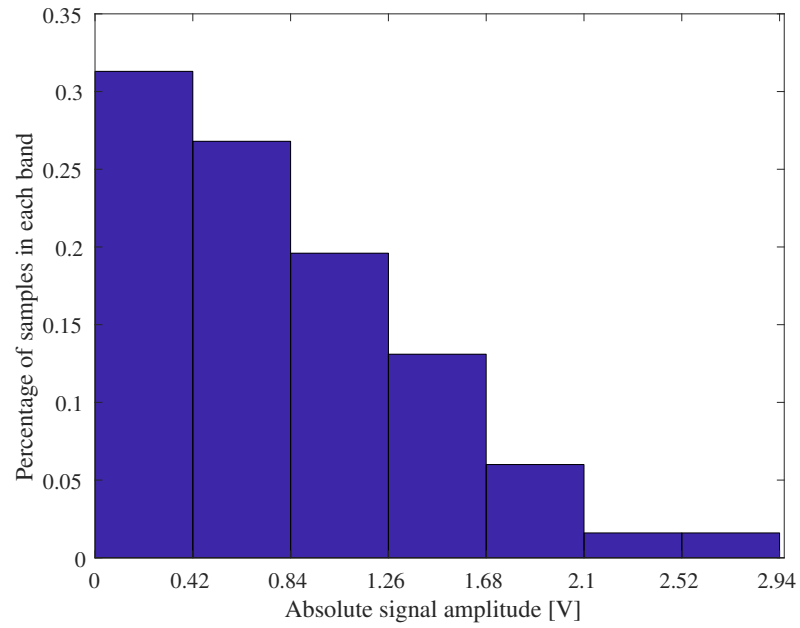


Fig. 3.12: Illustration of temporal features for the first period of 2 s.

the 50 best triplets of parameters associated with the 50 lowest errors are selected. These operations are summarized in Fig. 3.13.

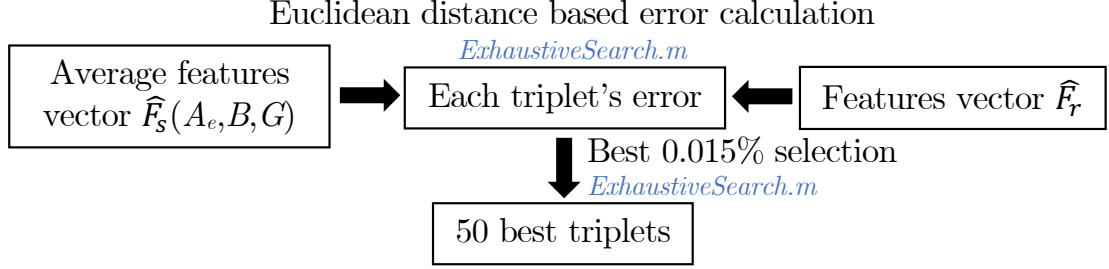


Fig. 3.13: Schematic of the parameters selection function.

### 3.4.1 Error calculation

For each 2 s period, an error is calculated between the features vector calculated by `featureCalc.m` and all the features vectors generated by the neural mass model  $\varepsilon(\widehat{F}_r, \widehat{F}_s(A_e, B, G))$ . This error evaluates the dissimilarity between the two signals by computing the Euclidean distance based error in the least squares between the two features vectors considered :

$$\varepsilon(\widehat{F}_r, \widehat{F}_s(A_e, B, G)) = \sum_{i=1}^{14} (\widehat{F}_{r,i} - \widehat{F}_{s,i}(A_e, B, G))^2 \quad (3.4)$$

A vector of 330 000 errors is thus generated for each period of 2 s.

### 3.4.2 Sort of errors and triplets selection

As it is assumed that parameters with similar values (close in parameter space) enable the model to generate similar signals, the errors are then sorted in ascending order by the *quicksort* algorithm and the 0.015% of triplets of parameters with smallest errors are selected to be potential solutions. Quicksort algorithm is chosen because it has a computational complexity of  $\mathcal{O}(n \log_2 n)$  on average. It can be in worst case  $\mathcal{O}(n^2)$  but this behaviour is very rare.

The *quicksort* algorithm is a divide-and-conquer algorithm, meaning that it works by recursively dividing a problem into two or more sub-problems until it could be solved simply [75]. It selects a pivot, generally the last element of the dataset and classifies the elements into two sub-arrays according to whether they are larger or smaller than the pivot. After that, the pivot is in its final position. The two sub-arrays are partitioned using the same technique, and it goes on until all the elements are in good position [76]. The algorithm is illustrated in Fig. 3.14 and is available at this link : [Quicksort algorithm](#).

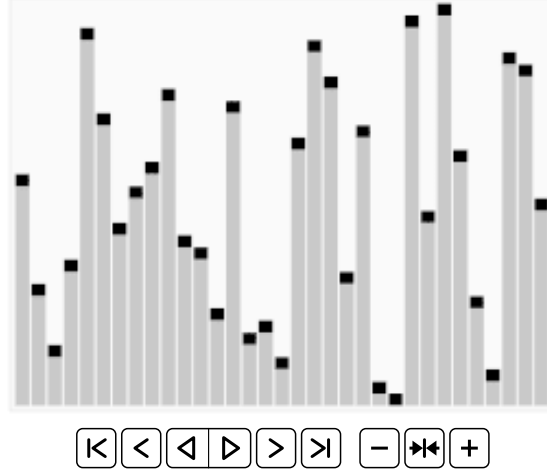


Fig. 3.14: Dynamic illustration of the *quicksort* algorithm[76].

### 3.5 Clustering and parameters averaging

Among the 50 potential solutions of the parameters triplets, one triplet of parameters should be computed to be able to interpret the epileptic character of the considered segment of signal. To have the most representative triplet of the model, it is not the "best" triplet that is selected, i.e. the one that has the smaller error, but all these 50 solutions are grouped into clusters in order to discard the potential outliers. In order to do this, a density-based spatial clustering of applications with noise (DBSCAN) is used and the best cluster, that is the one that minimizes the error function is further selected. Then, each parameter  $A_e$ ,  $B$  and  $G$  is the average of all the parameters of the cluster selected. The set of parameters calculated in this way is therefore the most representative of the model behaviour. A reminder of this step is in Fig. 3.15.

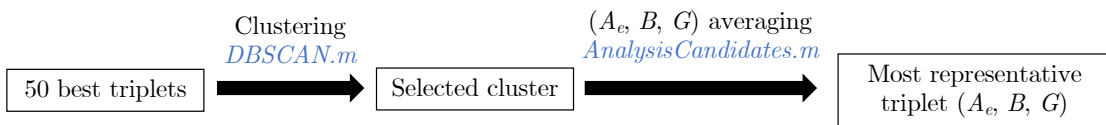


Fig. 3.15: Schematic of the operations done.

#### 3.5.1 DBSCAN clustering

DBSCAN is an unsupervised clustering machine learning algorithm. A clustering algorithm aims to group similar data points into clusters (artificial defined groups). An unsupervised clustering algorithm does it without pre-labeled targets. The particularity of the DBSCAN versus other clustering techniques is that the number of clusters should not be pre-specified and it works with arbitrary shaped clusters [77]. This can be observed in Fig. 3.16.

The DBSCAN works by linking neighbour points together. Two parameters are defined :  $\epsilon$ , the maximum distance of the neighbourhood, and *minPoints*, the

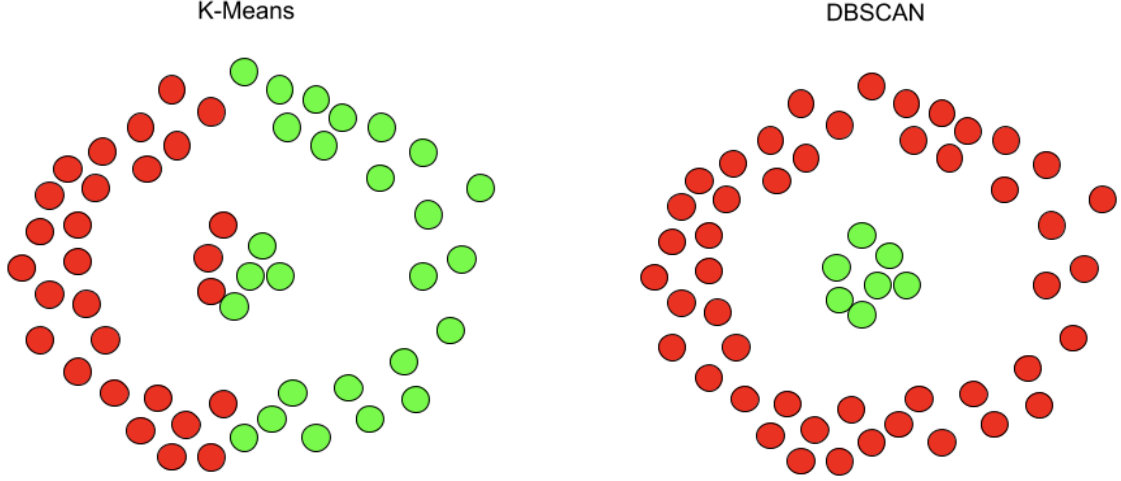


Fig. 3.16: The same dataset clustered by KMeans (partition-based clustering) and DBSCAN [77].

minimum number of data points within  $\varepsilon$  for the neighbourhood to be considered in the cluster. Three additional terms should also be defined :

1. Core point : a core point have at least *minPoints* within an  $\varepsilon$  distance around it.
2. Border point : a border point is in the neighbourhood of a point but has less than *minPoints* points in its surrounding.
3. Outlier : an outlier is not part of a neighbourhood. It is located in a low-density area.

Thereupon, the DBSCAN operation is as follows : a first random point is selected as a core point. Then, each point in its neighbourhood is evaluated to determine if it is a core point, a border point or an outlier. Each core point is added to the cluster and the neighbourhood is also evaluated. The cluster is complete when there are no more points within the  $\varepsilon$  distance of from any point in the cluster. A new random point is therefore selected and a new cluster is formed. The DBSCAN is illustrated in Fig. 3.17 with  $\varepsilon = 1$  unit and *minPoints* = 4.

In the algorithm implemented in [64],  $\varepsilon$  is chosen to be 4.2071 and *minPoints* is set to 5.

### 3.5.2 Averaging parameters

The different clusters are defined among the 50 triplets of parameters. The cluster with the smaller average error is taken as the optimal cluster. A varying number of triplets are then retained. For each parameter, the mean of this parameter in each triplet is computed :

$$\begin{cases} A_e = \text{mean}(\forall A_e \text{ in cluster}) \\ B = \text{mean}(\forall B \text{ in cluster}) \\ G = \text{mean}(\forall G \text{ in cluster}) \end{cases}$$

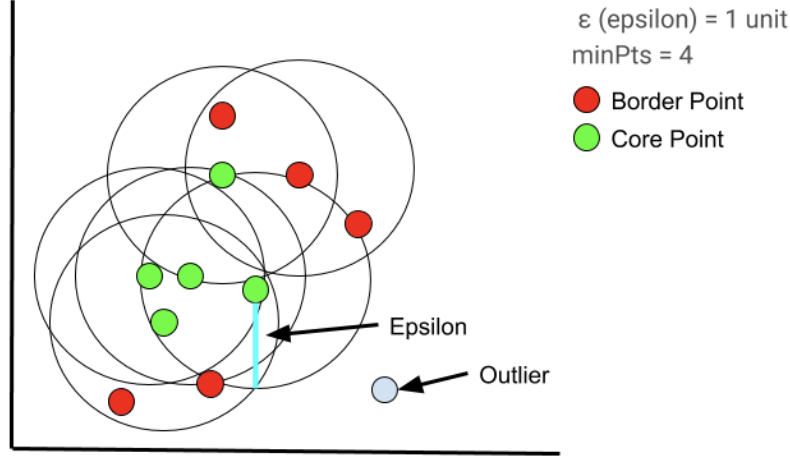


Fig. 3.17: Illustration of the density-based spatial clustering of applications with noise [77].

The triplet with these parameters  $A_e$ ,  $B$  and  $G$  is the center of the selected cluster and therefore assumed to be the most representative one.

### 3.6 Temporal analysis of ratios

As said in the beginning of this chapter, the epileptic seizure reflects an imbalance between neuronal excitation and inhibition, this is why the ratios between the parameters  $A_e$  (average excitatory synaptic gain),  $B$  (average slow inhibitory synaptic gain) and  $G$  (average fast inhibitory synaptic gain) are computed and analyzed over time to detect seizure occurrence. This step is represented in Fig. 3.18.

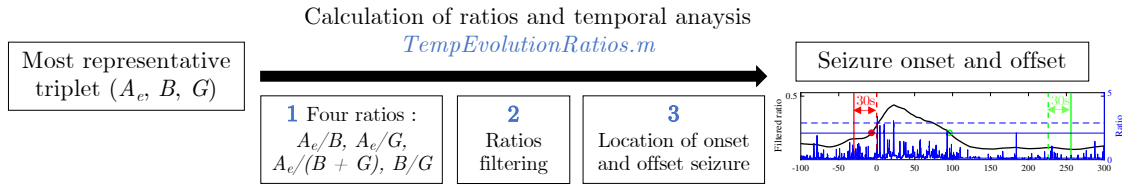


Fig. 3.18: Illustration of the ratios computation and temporal analysis of those ones.

Four ratios are therefore computed from the representative triplet of parameters :

1.  $\frac{A_e}{G}$  : the ratio between excitation and fast inhibition ;
2.  $\frac{A_e}{B}$  : the ratio between excitation and slow inhibition ;
3.  $\frac{A_e}{(B+G)}$  : the ratio between excitation and the sum of slow and fast inhibition ;
4.  $\frac{B}{G}$  : the ratio between fast and slow inhibition.

These ratios are expected to increase around seizure onset and to decrease around seizure offset. To be able to observe correctly the trend of each ratio, a low-pass moving average filter is applied, using a 30s window to smooth the signal. This is

why two points of interest were defined :  $I_{\text{rise}}$  (red dot in Fig. 3.19), that is related to seizure onset and is the first point when the ratio crosses one standard deviation (SD) above the mean (blue dashed horizontal line in Fig. 3.19) and continues to increase to at least two SD above the mean ; and  $I_{\text{fall}}$  (green dot in Fig. 3.19), that is related to seizure offset and is the point when the ratio falls below one SD above the mean after  $I_{\text{rise}}$ . The red and green dashed vertical lines refer to medically defined seizure onset and offset, respectively.

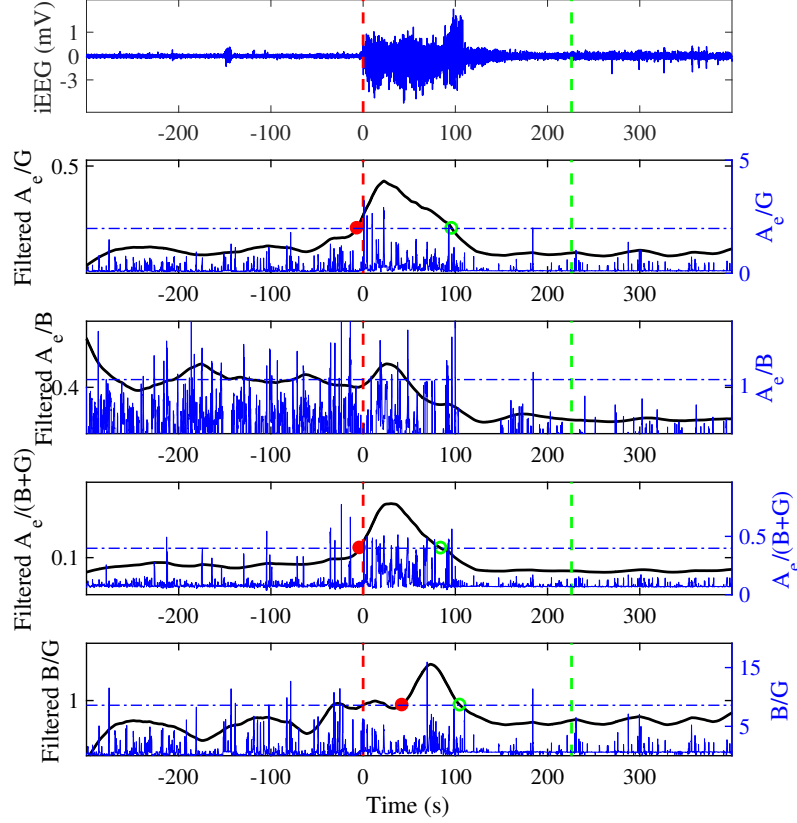


Fig. 3.19: Illustration of the iEEG recording and the temporal evolution of the four ratios, as well as the filtered four ratios.

$I_{\text{rise}}$  is considered to be seizure onset if it locates between 30s before onset and offset and similarly,  $I_{\text{fall}}$  is related to offset if it locates within the period from onset to 30s after offset. The seizure is detected in three ratios out of four and  $I_{\text{rise}}$  occurs around seizure onset for two ratios ( $\frac{A_e}{G}$  and  $\frac{A_e}{(B+G)}$ ).

### 3.7 Results and validation

To validate the algorithm, analyses of each ratio in each patient and for all the 30 iEEG recordings were performed in [64]. Some results are highlighted from these analyses. First, Fig. 3.20 shows how  $I_{\text{rise}}$  is positioned related to the onset of the seizure. For each seizure and each ratio, it illustrates the delay between  $I_{\text{rise}}$  and the onset. When  $I_{\text{rise}}$  precedes the onset, the delay is negative and in contrary positive when  $I_{\text{rise}}$  follows the onset. The red horizontal line marks 30s before onset and the green dashed line corresponds to offset. Similarly, Fig. 3.21 gives an insight on the

delay between  $I_{\text{fall}}$  and the offset of the seizure. The red line corresponds therefore to the onset and the green dashed line to 30 s after the offset. All the  $I_{\text{rise}}$  and  $I_{\text{fall}}$  of the different ratios that lie between the two lines are related to seizure onset and offset, respectively.

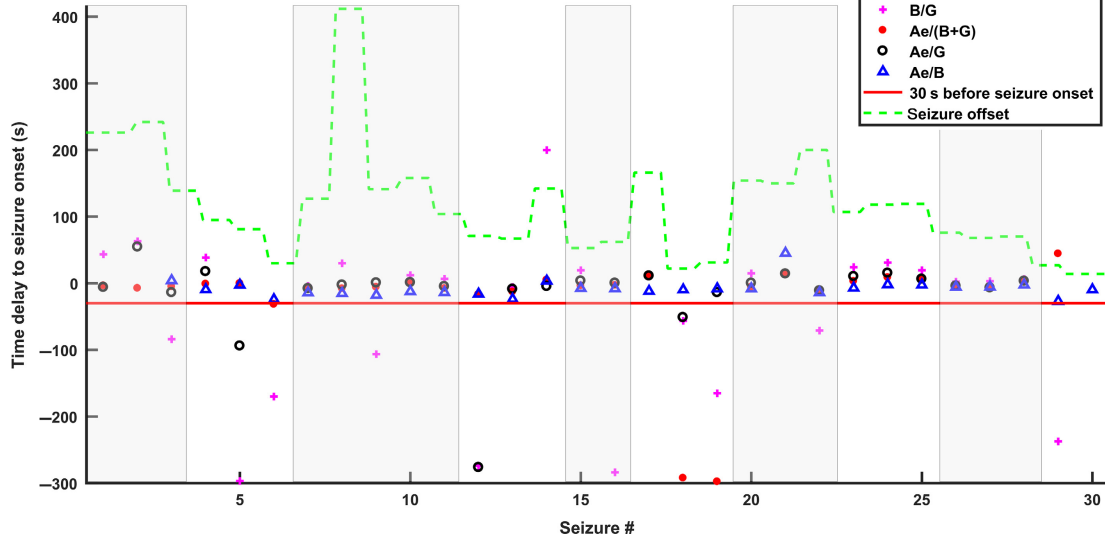


Fig. 3.20: Illustration of the delays between  $I_{\text{rise}}$  and onset for 30 seizures and all ratios [64].

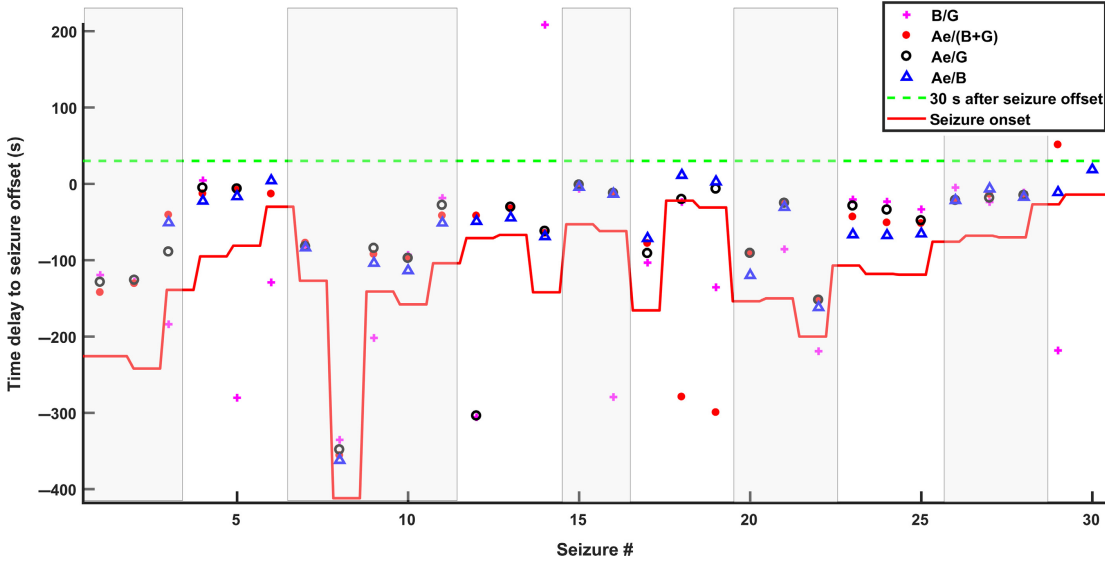


Fig. 3.21: Illustration of the delays between  $I_{\text{fall}}$  and offset for 30 seizures and all ratios [64].

Among 30 seizures, 83.3% of the  $I_{\text{rise}}$  for  $\frac{A_e}{(B+G)}$  (excitation over slow and fast inhibition), 93.3% for  $\frac{A_e}{B}$  (excitation over slow inhibition), 30% for  $\frac{A_e}{G}$  (excitation over fast inhibition) and 60% for  $\frac{B}{G}$  (slow inhibition over fast inhibition) may be related to seizure onset. Further analysis shows that the ratios restored before seizure offset in most cases : 25/25 for  $\frac{A_e}{(B+G)}$ , 24/28 for  $\frac{A_e}{B}$ , 24/24 for  $\frac{A_e}{G}$  and 17/18 for  $\frac{B}{G}$ .

Other analysis could be concluded by the fact that excitation over slow inhibition rises and restores earlier than excitation over fast inhibition for most seizures.

The sensitivity of the chosen parameters (period size, period step, number of best triplets, low-pass moving average filter length) was also conducted. The delay between  $I_{\text{rise}}$  and onset and  $I_{\text{fall}}$  and offset were calculated while varying the parameters. In conclusion, they vary less than 5% for all parameters, excepted for the  $\frac{B}{G}$  ratio where the rise and fall are more sensitive to the period step. Indeed, they vary by more than 10% with the step changing. This could be due to the complexity of interactions between fast and slow inhibitory neurons.

The algorithm can also be validated by the usual metrics presented in chapter [Chapter 2](#). Four metrics was computed in [78] to demonstrate the validation of their algorithm : the sensitivity ([Chapter 2](#)), the false positive rate (FPR) that is the number of FP, i.e. seizures detected by algorithm but not marked this way by the physician, occured on the total recording time ( $\frac{\text{FP}}{\text{Total time}}$ ), the mean false detection duration (MFDD) that corresponds to the average of the durations of all FP and the detection delay that is the between the seizure onset marked by the expert and the one detected by the algorithm. In [78], the algorithm was tested on more iEEG recordings and also more patients than in [64]. The metrics are therefore computed for 12 TLE (temporal lobe epilepsy) patients, 8 FLE (frontal lobe epilepsy) patients and 3 patients that suffer from fronto-temporal lobe epilepsy (FTLE), parieto-temporal-occipital lobe epilepsy (PTOLE) and occipital lobe epilepsy (OLE). Table [Table 3.3](#) summarizes these metrics for each type of epilepsy tested with this algorithm of detection.

| Patient group | Sensitivity (%) | FPR (/h) | MFDD (s) | Detection delay (s) |
|---------------|-----------------|----------|----------|---------------------|
| TLE           | 93.33           | 0.28     | 19.1     | 14.4                |
| FLE           | 60.87           | 0.17     | 9.3      | -3.25               |
| FTLE          | 100.00          | 0.06     | 3.0      | 31.3                |
| PTOLE         | 50.00           | 2.85     | 40.0     | 28.0                |
| OLE           | 0.00            | 0.17     | 34.5     | N/A                 |

Table 3.3: Summary of the four metrics values for each type of epilepsy, inspired from [78].

As, for FTLE, PTOLE and OLE, the dataset is not representative (only one patient of each), conclusions for these types may not be made. However, it can clearly be concluded that the algorithm is more adapted to TLE patients than FLE patients. The sensitivity is indeed much higher. However, the FPR is higher too, that can be explained by the fact that one patient of the TLE group has probably a pathological network between the temporal lobe and fronto-orbital regions, which makes him an unclassifiable patient. The negative delay for FLE patients means that the algorithm detected the seizure onset before the expert.

### 3.8 Performances

To conclude this chapter on the parameters identification algorithm and to introduce the work realized in the master thesis, performances in terms of execution time were analyzed. As the focus of this work is the real-time aspect, and the different segments done in the EEG signal last 2 s with a 0.1 s step, the three parameters selection and the detection should ideally be performed in less than 0.1 s for each period of 2 s. It is why analyzing the execution time profile is interesting. To track the execution time of the all algorithm, the MATLAB profiler was used. The profiler informs about time-consuming functions and helps the user to focus on these functions' optimization. The profiler of the main function that runs the entire algorithm with all the functions detailed in Fig. 3.1 is in Fig. 3.22. This time profile does not include the neural mass model and therefore the generation of the 330 000 features vectors. The features vectors were then just loaded in this run of the algorithm.

| Line Number         | Code                              | Calls | Total Time | % Time | Time Plot                                                                            |
|---------------------|-----------------------------------|-------|------------|--------|--------------------------------------------------------------------------------------|
| <a href="#">121</a> | [RESULT, FVAL] = ExhaustedSear... | 1     | 359.503 s  | 94.2%  |   |
| <a href="#">124</a> | [RESULT_DBSCAN] = AnalysisCand... | 1     | 10.230 s   | 2.7%   |   |
| <a href="#">132</a> | TempEvolutionRatios(result,win... | 1     | 5.967 s    | 1.6%   |   |
| <a href="#">67</a>  | Dat = load([PathEEG filename '... | 1     | 3.256 s    | 0.9%   |  |
| <a href="#">27</a>  | load('FeatureVectorsModel.mat'... | 1     | 0.634 s    | 0.2%   |                                                                                      |
| All other lines     |                                   |       | 1.876 s    | 0.5%   |                                                                                      |
| Totals              |                                   |       | 381.465 s  | 100%   |                                                                                      |

Fig. 3.22: MATLAB profiler of the main function running the algorithm.

As it can be observed, the total time of execution of the algorithm for a recorded EEG signal of 14 min and 18 s is of 381.465 s. Most of this time is spent to do the exhaustive search in which the error calculation takes 52.7% and the sorting 45.6% of the execution time of `ExhaustiveSearch.m`. It can be seen in Fig. 3.23. The error calculation being a least squares error and being applied 330 000 times for each feature out of 14, the computational complexity is high. A squared operation is indeed applied 4 620 000 times. The sorting operation, even if the chosen algorithm is a low complexity algorithm, has a complexity of  $\mathcal{O}(n \log_2 n)$  with  $n = 330\,000$ .

The error calculation and the sorting operation therefore require special attention in the ultra-low-power implementation.

| Line Number        | Code                              | Calls | Total Time | % Time | Time Plot                                                                             |
|--------------------|-----------------------------------|-------|------------|--------|---------------------------------------------------------------------------------------|
| <a href="#">29</a> | CostAll = sum((FeatureVectorsM... | 8561  | 189.543 s  | 52.7%  |    |
| <a href="#">31</a> | [CostAscend, IndexAscend] = so... | 8561  | 164.013 s  | 45.6%  |  |
| <a href="#">28</a> | [FeatureVector]= FeatureCalc(d... | 8561  | 5.174 s    | 1.4%   |  |
| <a href="#">32</a> | Candidates = Params(1:3,IndexA... | 8561  | 0.282 s    | 0.1%   |                                                                                       |
| <a href="#">34</a> | RESULT{CurWin} = Candidates';     | 8561  | 0.207 s    | 0.1%   |                                                                                       |
| All other lines    |                                   |       | 0.279 s    | 0.1%   |                                                                                       |
| Totals             |                                   |       | 359.499 s  | 100%   |                                                                                       |

Fig. 3.23: MATLAB profiler of the ExhaustiveSearch.m function.

# Chapter 4

## Ultra-low-power implementation

In this chapter, the implementation of the parameters identification algorithm will be explained, highlighting the choices made in each function to limit the computational complexity, the usage of memory and the power envelope. The final performances of the implementation will then be presented. The complete C implementation is available online, the reader can message the author at [alice.borbath@student.uclouvain.be](mailto:alice.borbath@student.uclouvain.be) or the supervisor at [david.bol@uclouvain.be](mailto:david.bol@uclouvain.be).

As the main purpose of this master thesis is to develop the embedded programming for a microcontroller, the implementation of the algorithm has been made in C language. Indeed, Embedded C is a very frequently used programming language to do embedded programming, because it is more portable than low-level assembly languages. It can run on a lot of different architectures processors without modifications. And it is less complex and much more efficient (20% with regard to a modern language like C++, estimated by experts) than traditional high-level languages [79]. The [Fig. 4.2](#) illustrates the implementation that has been made, with the size of inputs and outputs of the different functions. The microprocessor targeted is a Cortex-M processor, as Cortex-M processors are specifically designed for microcontrollers, thanks to their optimized cost and energy-efficient characteristics [80]. The Cortex-M4 in particular has been chosen for this implementation because of its signal processing and high efficiency capabilities. The Cortex-M4 has many various specifications (shown in [Fig. 4.1](#)) but the two of interest in this work are the digital signal processing (DSP) extension and the Floating-Point Unit (FPU), the first being able to manage and process signals and the second being useful to handle `floating-point` numbers. These two features are used in the implementation. Finally, the integrated development environment (IDE) used to run the C code and simulate the Cortex-M4 behaviour is the Keil  $\mu$ Vision IDE.

As it can be seen, the main difference with the MATLAB implementation is the application of the filters on a period of 1000 samples only (2s). The other big specificity is that the algorithm generates a triplet of parameters  $A_e$ ,  $B$  and  $G$  but does not give the information of seizure or non-seizure. As in the algorithm implemented by [64], the detection results from an analysis of the behaviour of the ratios along all the recording time and is based on two pre-determined thresholds, it is impossible to determine if a seizure is detected or not following the same reasoning in a real-time application. The detection could be made on the only information of the three parameters and the values of their ratios, but would be less accurate.

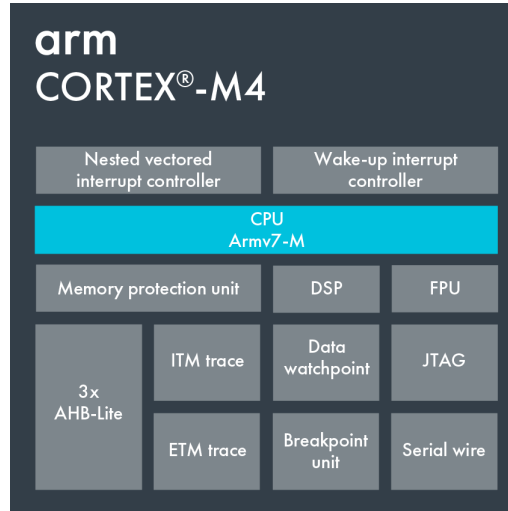


Fig. 4.1: Cortex-M4 scheme [81].

As the three parameters are physiologically meaningful, an expert could therefore assume there is a seizure or not and a discussion with experts and physicians could be made to find a solution to get a final detection in real-time.

## 4.1 Choices of implementation

In this section, the choices of implementation and optimization of the algorithm that have been made will be explained and justified.

### 4.1.1 Sorting operation

First, the sorting function was analyzed. It is indeed one of the two functions that has the biggest execution time in **MATLAB**. To overcome this high computational complexity, an adaptation of the *Quicksort* algorithm has been chosen : the *Quickselect* algorithm, also known as "Hoares's selection algorithm". This algorithm is similar to *Quicksort* one but, while *Quicksort* is doing a complete sorting of the input, *Quickselect* only finds the  $k^{th}$  lowest or largest element of the input, called *pivot* and partitions the input data into values smaller or larger than the pivot (Fig. 4.3, available at [Quickselect algorithm](#)). The difference with *Quicksort* is that, instead of recurring for both sides after finding the final place of the pivot, it recurs only on the side in which lies the  $k^{th}$  element. The complexity is then reduced from  $\mathcal{O}(n \log_2(n))$  to  $\mathcal{O}(n)$ , with a worst-case being still  $\mathcal{O}(n^2)$ . To lower the probability of having the worst-case, the pivot has not been chosen as last element (as it is generally done), but random element. Indeed, the worst-case occurs when the pivot is continuously the minimum or maximum of the dataset. Therefore, in an already sorted input, taking the last element leads to worst-case. By taking a random element at each iteration however, the probability of having the worst-case is very low.

As, in the case of this algorithm, the goal is to only select the 50 best triplets, not to sort all the 330 000 parameters triplets according to their error, the *Quickselect* algorithm is more appropriate and the resulting complexity is  $\mathcal{O}(n)$  where  $n =$

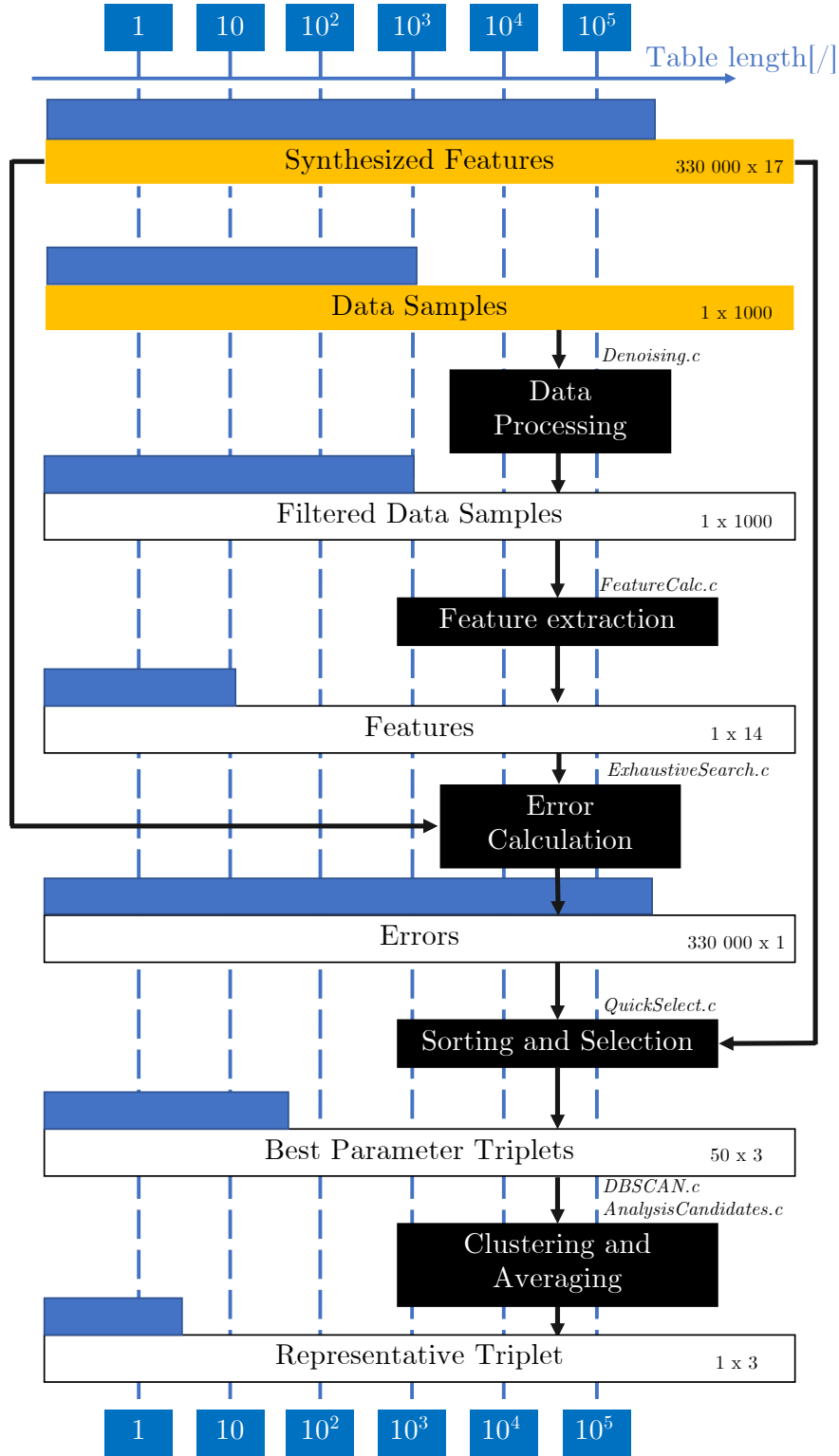


Fig. 4.2: Complete view of the C implementation of the algorithm, as well as the sizes of inputs and outputs. The two yellow datasets (data samples and synthesized features) are loaded in the algorithm, the data samples being recorded by the iEEG and the synthesized features and the corresponding parameters being generated by the neural mass model.

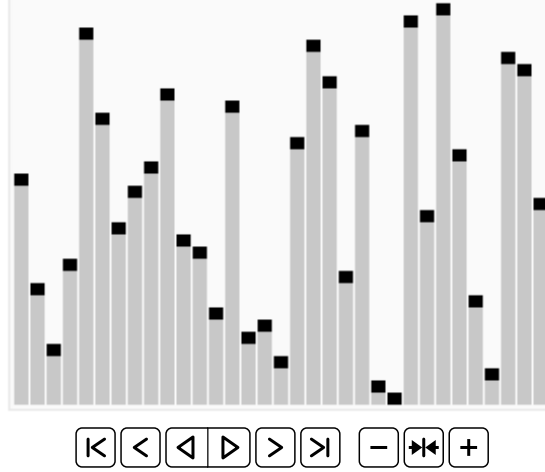


Fig. 4.3: Dynamic illustration of the *quickselect* algorithm[82], in comparison with the *quicksort* algorithm.

330 000.

#### 4.1.2 FFT operation

The FFT operation being a divide and conquer algorithm applied on recursive dataset divided by 2, it has been chosen to have a size of FFT equal to a power of 2. The closest power of 2 of 1000 is 1024 that was selected as FFT size in order to have a slightly increased resolution but a still reasonable computational complexity. 24 zeros were then padded to the data signal. The computational complexity of the FFT operation is  $\mathcal{O}(n \log_2 n)$ ,  $n$  being here chosen to 1024.

#### 4.1.3 Grid search resolution

In order to reduce the execution time and the memory requirements, the grid search resolution has been decreased. The results of the C implementation were compared to the ones of the MATLAB implementation to evaluate the performances with a resolution decrease. The results of several simulations are presented in Table 4.1. Three segments were tested for each modification of resolution : the first segment of 2s recorded, the 17<sup>th</sup> because  $B$  and  $G$  are changing, and the 3500<sup>th</sup> because it is during the seizure.

As seen in Table 4.1, the 3500<sup>th</sup> segment, located during the seizure is not well performed. As the seizure is the point of interest, the third resolution has been selected, i.e.  $A_e$  varying from 3 to 7 mV with a step of 0.125 mV,  $B$  going from 0.5 to 50 mV in increments of 0.5 mV and  $G$  being reduced from 0.5 to 49.5 mV, with a resolution of 1 mV. It could be deduced that the algorithm during seizure is not very sensitive to  $G$  parameter resolution decrease. However, a too large decrease leads also to higher errors, as it is shown in the last line of Table 4.1. Another conclusion which can be drawn from this Table is that the  $A_e$  parameter is less sensitive to resolution reduction than other parameters. Indeed, the error of the  $A_e$  parameter is under 6% in every case.

| Parameter |            |            | Results                                   |                           |                                            |                            |                                              |                                            |
|-----------|------------|------------|-------------------------------------------|---------------------------|--------------------------------------------|----------------------------|----------------------------------------------|--------------------------------------------|
| $A_e$     | $B$        | $G$        | Segment 1<br>MATLAB = (3.56, 5.02, 44.32) |                           | Segment 17<br>MATLAB = (3.4, 10.675, 28.2) |                            | Segment 3500<br>MATLAB = (3.95, 8.11, 18.85) |                                            |
|           |            |            | C                                         | Error [%]                 | C                                          | Error [%]                  | C                                            | Error [%]                                  |
| 3:0.25:7  | 0.5:0.5:50 | 0.5:0.5:50 | 3.62, 6.93, 44.95                         | 1.81, <b>27.5</b> , 1.41  | 3.52, 9.66, 34.2                           | 3.37, 9.48, <b>18.79</b>   | 5.1, 39.31, 42                               | <b>22.52</b> , <b>79.36</b> , <b>55.11</b> |
| 3:0.125:7 | 0.5:1:49.5 | 0.5:0.5:50 | 3.59, 6.43, 44.4                          | 0.96, <b>22</b> , 0.2     | 3.43, 9.67, 31.61                          | 1.02, 9.45, 10.8           | 5.45, 44.54, 40.13                           | <b>27.4</b> , <b>81.78</b> , <b>53.02</b>  |
| 3:0.125:7 | 0.5:0.5:50 | 0.5:1:49.5 | 3.52, 5.31, 43.2                          | 1.1, 5.4, 2.51            | 3.49, 9.89, 33.5                           | 2.64, 7.35, <b>15.8</b>    | 3.06, 8.25, 18.17                            | <b>22.5</b> , 1.64, 3.78                   |
| 3:0.25:7  | 0.5:1:49.5 | 0.5:0.5:50 | 3.6, 6.6, 45                              | 1.25, <b>23.88</b> , 1.52 | 3.57, 10.79, 34.82                         | 4.68, 1.09, <b>19.01</b>   | 5.05, 43.3, 48.6                             | <b>21.72</b> , <b>81.26</b> , <b>61.2</b>  |
| 3:0.25:7  | 0.5:0.5:50 | 0.5:1:49.5 | 3.52, 6.63, 42.83                         | 0.92, <b>24.25</b> , 3.36 | 3.57, 10.79, 34.86                         | 4.64, 1.03, <b>19.1</b>    | 4.92, 40.91, 37.87                           | <b>19.68</b> , <b>80.17</b> , <b>50.22</b> |
| 3:0.125:7 | 0.5:1:49.5 | 0.5:1:49.5 | 3.5, 5.9, 42.45                           | 1.66, 14.84, 4.2          | 3.49, 10.5, 32.48                          | 2.72, 1.64, 13.18          | 4.89, 43.92, 36.19                           | <b>19.15</b> , <b>81.53</b> , <b>47.91</b> |
| 3:0.25:7  | 0.5:1:49.5 | 0.5:1:49.5 | 3.53, 7.52, 42.07                         | 0.68, <b>33.25</b> , 5.06 | 3.21, 5.79, 29.79                          | 5.46, <b>45.8</b> , 5.32   | 5, 48.9, 37.7                                | <b>20.94</b> , <b>83.41</b> , <b>50</b>    |
| 3:0.125:7 | 0.5:0.5:50 | 0.5:1.5:49 | 3.58, 6.69, 44.06                         | 0.79, <b>24.93</b> , 0.57 | 3.41, 8.86, 31.59                          | 0.18, <b>16.97</b> , 10.73 | 5.11, 42.47, 31.5                            | <b>22.57</b> , <b>80.9</b> , <b>40.15</b>  |

Table 4.1: Comparison of results between C and MATLAB implementations for several modifications of grid search resolution. The original resolutions are  $A_e = (3:0.125:7)$ ,  $B = (0.5:0.5:50)$ ,  $G = (0.5:0.5:50)$  and the percentage error is calculated between MATLAB and C results for each parameter separately. The errors larger than 15% are highlighted in red.

However, even with a lowest resolution of the grid search and a number of parameters triplets reduced to 165 000, the execution time stays high : 37.328 s. This execution time is estimated using the Performance Analyzer tool provided by Keil  $\mu$ Vision, shown in Fig. 4.4. The Keil  $\mu$ Vision IDE simulates the program in complete Arm system, including the processor, the memory and the peripherals [83]. The execution time estimated by Keil is therefore a good approximation of what is going to happen in a real Cortex-M4 processor. The frequency of the ARM Cortex-M4 is set to 24 MHz, the optimization level, that indicates how much the IDE optimizes the program code and discards not used functions at compilation time, is set to image size (program size optimization).

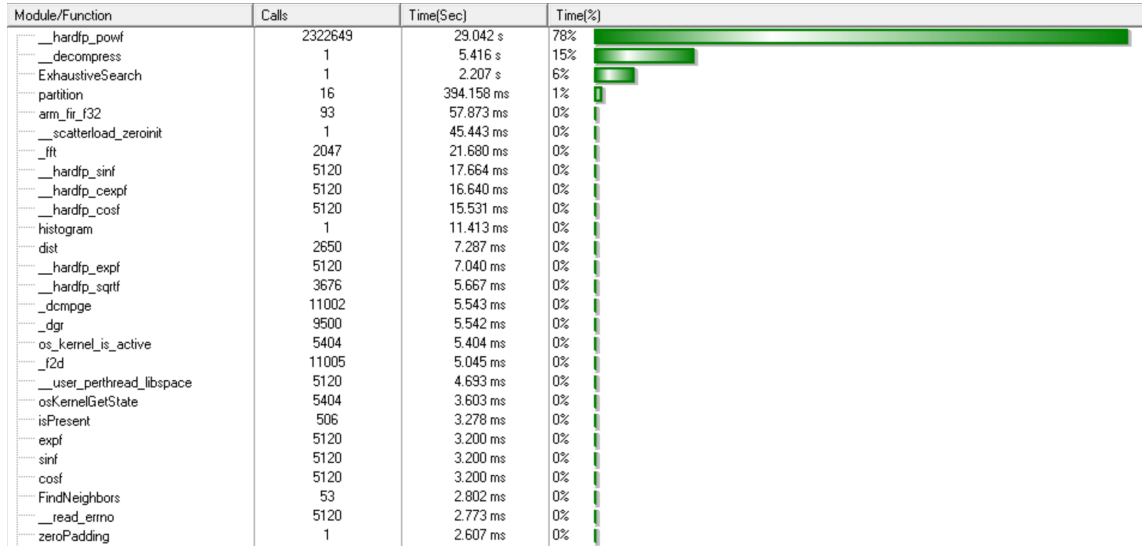


Fig. 4.4: Performance Analyzer for the implementation of the algorithm with modifications already mentioned : 1000 samples filter, FFT size of 2024, reduced grid resolution, *Quickselect* selection.

The *decompress* function is executed at the system initialization step, before the algorithm has began. Therefore, it should only be executed one time at the beginning, which is not too problematic for the target application studied in this work.

#### 4.1.4 Error calculation

As the execution time is quite high even with a grid resolution reduction, other optimizations should be done to be able to have information in real-time. As the least squares error calculation was the other time-consuming function in MATLAB and is also time-consuming in C implementation, as shown in Fig. 4.4 (*powf* being the squared value of the difference), it has been tested to evaluate the error only by the absolute value of the difference. It can be seen that the difference is non negligible, as the execution is reduced by 77.69% (8.327 s). Moreover, the performances are not too much affected, keeping an error percentage of (0.95, 39.86, 5.98)% for the three parameters. The *B* parameter is worse, but as mentioned in Chapter 3, the *B* parameter is very sensitive. These results are only based on the first segment of 2 s.

### 4.1.5 Cortex-M4 frequency increase

The frequency of the core was increased to 64 MHz, reasonable value for a Cortex-M4. The increase of frequency further reduces the time execution, leading to a total execution time of 3.123 s with the initialization step. Therefore, the algorithm execution is one step closer to the real-time operation. However, increasing the core frequency increases also the power usage, as it is directly proportional to the frequency [81].

## 4.2 Performances

In this section, the final performances of the algorithm will be presented and illustrated.

### 4.2.1 Memory requirement

The algorithm implemented includes several big arrays that contain a lot of data, as seen in Fig. 4.2. The Table 4.2 summaries these arrays, the size of each one and the memory it needs. It takes in consideration that the resolution has been decreased. The 4<sup>th</sup> big array is the windowing function used to apply the FFT. It is a Hamming window of size 1000.

| Array               | Size         | Memory  |
|---------------------|--------------|---------|
| Input data          | 1 x 1000     | 4 kB    |
| Parameters triplets | 3 x 165 000  | 1.98 MB |
| Features vectores   | 14 x 165 000 | 9.24 MB |
| Hamming window      | 1 x 1000     | 4 kB    |

Table 4.2: Size and memory requirement of the four main loaded arrays.

Therefore, the memory requirement is significant as these four arrays add up to 11.228 MB. The program code, for its part, has a size of 19 kB with optimization level set to reduce especially its size. Zero-initialization data that include the array of errors take up 1.745 MB.

### 4.2.2 Time execution

The final time execution and the principal time-consuming functions are shown in Fig. 4.5. The *decompress* function presents therefore the largest execution time. Without the initialization step, the time would be reduced to 1.092 s approaching the timing goal.

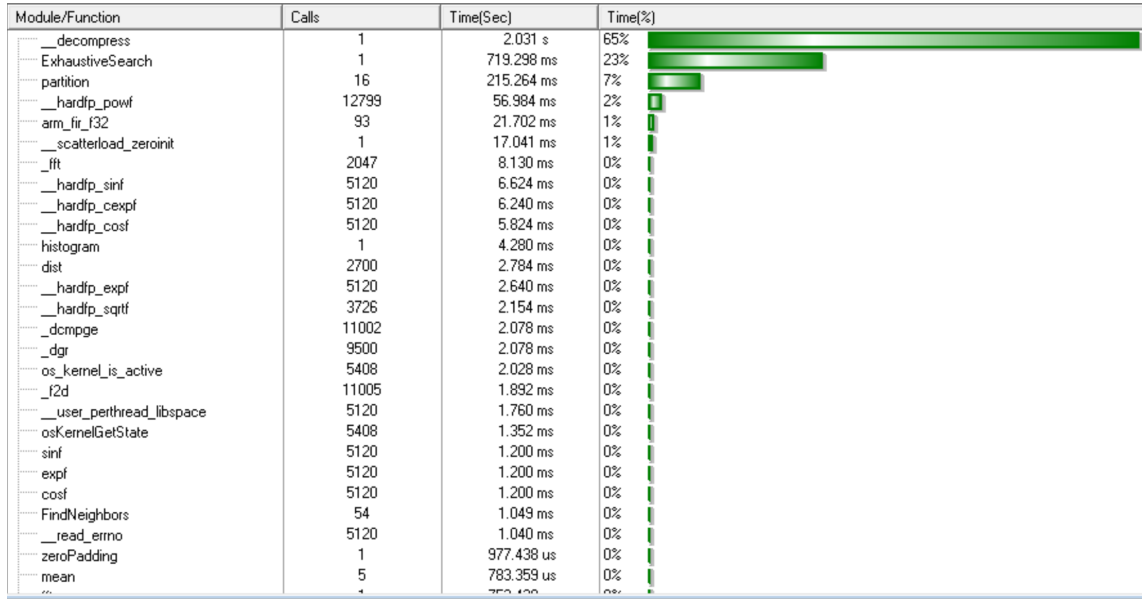


Fig. 4.5: Performance Analyzer for the implementation of the algorithm with following modifications : 1000 samples filter, reduced grid resolution, *Quickselect* selection, absolute value of difference as error.

## 4.3 Further optimizations

Further optimizations are required to further reduce the execution time, as well as lower the memory requirements. Several ideas are described in this section.

### 4.3.1 Type and size of variables

First, the types of variables could be modified. Indeed, the algorithm uses a very large amount of numerical data that all have decimal numbers. The **MATLAB** code treats all these values as **double** (real floating-point number with double precision [84]) but this is not optimal in terms of time and memory. Indeed, the microcontrollers may not support floating-point numbers and need to manage these numbers by doing a lot of additional operations. Even if the Cortex-M4 has an FPU that optimizes the time spent to manage floating-point numbers, this has a consequence on the execution time but also on the memory requirement for program code. The variables should therefore be transferred to **fixed-point** type. Part of this task has already been addressed during this master thesis, but could not be completed (work in progress will be made available, along with the full code).

### 4.3.2 Transversal analysis

In this work, each parameter and function were analyzed in terms of time execution and memory requirements separately. To have a global idea of all the mutual dependences and interactions on the execution time and performances between all those parameters, a transversal analysis could be made.

### 4.3.3 Filters type

The filters in the C code have been implemented using FIR type filters of order 29. To decrease the complexity of the filters, IIR filters with an order of 2 or 3 would be more appropriate.

### 4.3.4 Optimized FFT

In this master thesis, the FFT function has been fully reimplemented as the FFT available in the DSP library of ARM is code size consuming. To increase the resolution of the algorithm and the precision of the parameters generation, a 2048-size FFT would be better suited. In order to have an efficient, more precise and smaller program, the 2048-size FFT could be computed through several FFT from the ARM library of smaller sizes (512, or even 256), with a conquer and divide method, as illustrated in Fig. 4.6.

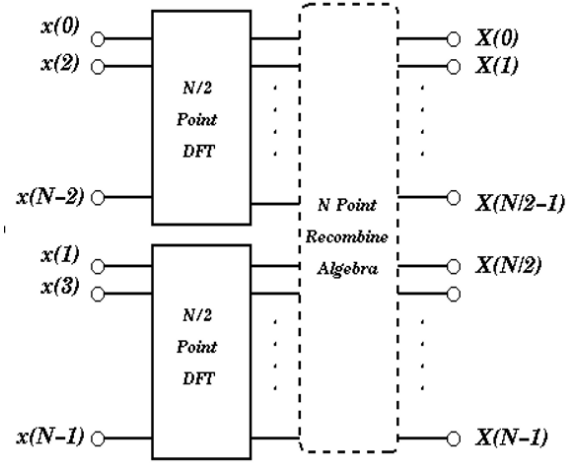


Fig. 4.6: Illustration of a method to compute high size FFT with smaller ones [85].

# Conclusion

The seizure detection algorithm was successfully transferred from its original MATLAB implementation to a C implementation compatible with a microcontroller environment.

Based on this code, several aspects were optimized to limit the time and memory usage, in particular :

- The sorting operation was performed with a *Quickselect* algorithm to reduce its computational complexity ;
- The grid search resolution was decreased to improve the time execution and the memory requirement ;
- The error calculation was simplified to reduce the execution time ;
- The size of FFT operation was reduced to decrease the computational complexity, as well as the execution time.

The Keil  $\mu$ Vision IDE allowed to simulate execution on a Cortex-M4 microcontroller, with regard to the execution time, the memory requirement and the peripherals use.

After all these steps, the algorithm runs in 1.092 s, which is still too slow for a real-time usage. Further optimizations should therefore be done. Conversion from **floating-point** to **fixed-point** numbers, from FIR to IIR filters, further reduction of FFT size and transversal analysis should be carried out in future works.

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