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Automated detection of epileptic seizures in pediatric patients based on accelerometry and surface electromyography

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Dissertation presented in partial fulfillment of the requirements for the degree of Doctor in Engineering

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Preface

None of us got to where we are alone. Here I would like to thank all those who have directly or indirectly been present in my life in last five years.

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In Leuven, 16.04.2015.

Milica Milošević

Abstract

Epilepsy is one of the most common neurological diseases that manifests in repetitive epileptic seizures as a result of an abnormal, synchronous activity of a large group of neurons. Depending on the affected brain regions, seizures produce various severe clinical symptoms. There is no cure for epilepsy and sometimes even medication and other therapies, like surgery, vagus nerve stimulation or ketogenic diet, do not control the number of seizures. In that case, long-term (home) monitoring and automatic seizure detection would enable the tracking of the evolution of the disease and improve objective insight in any responses to medical interventions or changes in medical treatment. Especially during the night, supervision is reduced; hence a large number of seizures is missed. In addition, an alarm should be integrated into the automated seizure detection algorithm for severe seizures in order to help the patient during and after the seizure. Frontal lobe and tonic-clonic seizures are accompanied with violent movements which could lead to injuries; also there is the danger of suffocation caused by vomiting or the breathing can be obstructed. These situations require intervention during the seizures, however, in case of pediatric patients comforting is sometimes needed after the seizures, since a child gets scared and upset. Combined video/electroencephalography (EEG) monitoring remains the gold standard for epilepsy monitoring, whereas solely EEG is traditionally used for automated seizure detection in specialized hospitals. However, EEG electrodes have to be attached to the scalp by the trained nurse, and long-term wearing EEG can become uncomfortable, which makes EEG-based home monitoring not feasible.

In this thesis, we investigate the application of less intrusive sensors, namely accelerometers (ACM) attached to the wrists and ankles within wrist-bands, and surface electromyography (sEMG) registering the muscle activity of the biceps at both arms, for the detection of epileptic seizures. This thesis aims at developing automated seizure detection algorithms using aforementioned modalities in pediatric patients.

First, two feature selection methods are applied to identify the most relevant features for the distinction between each epileptic seizure class and all other nocturnal movements using ACM signals. For this purpose, a large number of features was collected from the literature. Feature selection methods were tested using least squares support vector machine classifiers. It is shown that a fast filter method, although significantly reducing the number of features, did not degrade the classification performance compared with the complete feature set. Next, this method is applied as part of an ACM-based automated seizure detection algorithm for the detection of (tonic-)clonic seizures. Patient-independent detectors were tested both on the data recorded with a wired system and data recorded in a home environment using a wireless system. In the last part of this thesis, ACM and sEMG-based automated tonic-clonic seizure detectors were compared. In addition, we examined whether an integrated approach could yield a better result. The ACM and sEMG classification outputs were combined using a late integration approach. The results showed that there was a need for a patient-specific measurement system for the detection of epileptic seizures based on prior knowledge on patient's seizure characteristic and his/her typical non-epileptic behavior. The techniques proposed in this thesis pave the way to the development of home monitoring algorithms for pediatric patients.

Beknopte samenvatting

Epilepsie is een van de meest voorkomende neurologische ziekten die zich manifesteert in herhaaldelijke epileptische aanvallen als gevolg van een abnormale, synchrone activiteit van een grote groep neuronen. Afhankelijk van de getroffen hersengebieden, veroorzaken convulsies diverse ernstige klinische symptomen. Er is geen remedie voor epilepsie en soms kunnen zelfs medicatie en andere therapieën, zoals chirurgie, vagus nervus stimulatie of een ketogeen dieet, het aantal aanvallen niet onder controle houden. In dat geval zouden lange termijn (thuis)monitoring en automatische aanvalsdetectie het mogelijk maken om de evolutie van de ziekte op te volgen. Bovendien vergroot het een objectief inzicht in de reactie op een verandering van medicatie. Vooral tijdens de nacht, is er een verminderd toezicht waardoor een groot aantal aanvallen wordt gemist. Bovendien moet een alarm worden toegevoegd bij de automatische aanvalsdetectie voor ernstige aanvallen, zodat de patiënt tijdens en na de aanval kan worden geholpen. Frontale kwab en tonisch-clonische aanvallen gaan gepaard met hevige bewegingen die kunnen leiden tot letsels; ook is er een gevaar voor verstikking als gevolg van braken of kan de ademhaling worden belemmerd. Deze situaties vergen een tussenkomst tijdens de aanvallen, maar in het geval van pediatrische patiënten is het soms nodig om hen na de aanvallen gerust te stellen, omdat een kind sneller van streek raakt. De combinatie van video- en elektro-encefalografie (EEG) blijft de gouden standaard voor epilepsiemonitoring, terwijl normaliter uitsluitend EEG wordt gebruikt voor automatische aanvalsdetectie in gespecialiseerde ziekenhuizen. EEG-elektroden moeten echter door een ervaren verpleegkundige op de hoofdhuid worden aangebracht, en het op lange termijn dragen ervan kan oncomfortabel worden, waardoor EEG-gebaseerde thuismonitoring niet haalbaar is.

In dit proefschrift onderzoeken we de toepassing van minder hinderlijke sensoren, namelijk accelerometers (ACM) bevestigd aan de polsen en enkels, geïntegreerd in een armband, en oppervlakte-elektromyografie (EMG) voor het registreren van de spieractiviteit van de biceps in beide armen, voor de detectie van epileptische annvallen. Dit proefschrift legt zich toe op het ontwikkelen van geautomatiseerde aanvalsdetectiealgoritmen met behulp van voornoemde modaliteiten bij pediatrische patiënten.

Eerst worden kenmerkselectiemethoden toegepast om de meest relevante kenmerken te bepalen die het onderscheid kunnen maken tussen elk type van epileptische annval en andere nachtelijke bewegingen op basis van ACM-signalen. Daartoe werd een groot aantal kenmerken verzameld uit de literatuur. Kenmerkselectiemethoden werden getest met behulp van classificatoren op basis van kleinste kwadraten support vector machines. Er wordt aangetoond dat de snelle filter methode, hoewel dit het aantal kenmerken significant vermindert, de performantie van de classificatie niet verslechtert in vergelijking met de volledige kenmerken set. In de volgende studie wordt deze werkwijze toegepast als onderdeel van een geautomatiseerd aanvalsdetectiealgoritme op basis van ACM voor (tonisch)-clonische aanvallen. Patiënt-onafhankelijke detectoren zijn zowel getest op data afkomstig van een bedraad systeem als data die zijn opgenomen in een thuisomgeving met behulp van een draadloos systeem. In het laatste deel van dit proefschrift, worden ACM en sEMG-gebaseerde geautomatiseerde tonisch-clonische aanvalsdetectoren vergeleken. Daarnaast bekijken we of een geïntegreerde aanpak een beter resultaat kan opleveren. De ACM en sEMG classificatieresultaten zijn samengevoegd door middel van een late-integratie-aanpak. De resultaten tonen dat er behoefte is aan een patiënt-specifiek meetsysteem voor de detectie van epileptische annvallen op basis van voorkennis over aanvalskarakteristieken van de patiënt en zijn/haar gebruikelijk niet-epileptisch gedrag. De in dit proefschrift voorgestelde technieken banen de weg naar de ontwikkeling van thuismonitoringalgoritmen voor pediatrische patiënten.

Nomenclature

Symbols

a, b, ...	scalars
$\mathbf{A}$, $\mathbf{B}$, ...	matrices
$\mathbf{a}$, $\mathbf{b}$, ...	vectors

Metrics

μm	micrometer
μV	microvolt
g	unit of Earth's acceleration
h	hour
Hz	Hertz
mAh	milliampere-hour
mV	milivolt
nm	nanometer
s	second

Abbreviations

ACM	Accelerometry
AED	Antiepileptic Drugs
AR	Auto-Regressive
AUC	Area Under the receiver operating characteristic Curve
BASFI	Bath Ankylosing Spondylitis Functional Index
CSA	Coupled Simulated Annealing
CWT	Continuous Wavelet Transform
DBS	Deep Brain Stimulation
ECG	Electrocardiography
ECoG	Electrocorticogram
EDA	Electrodermal Activity
EEG	Electroencephalography
EOG	Electrooculography
FDR	False Detection Rate
FL	Frontal Lobe seizure
FN	False Negative
FP	False Positive
GTC	Generalized Tonic-Clonic seizure
GUI	Graphical User Interface
HMM	Hidden Markov model
HP	High-Pass filter
HR	Heart Rate
HRV	Heart Rate Variability
HSD	Honestly Significant Difference
ICD	International Classification of Diseases

ILAE	International League Against Epilepsy
iMEMS	Integrated microelectromechanical system
IR	Infrared
LASSO	Least Absolute Shrinkage and Selection Operator
LB	Left Biceps
LDA	Linear Discriminant Analysis
LOPO	Leave-One-Patient-Out
LP	Low-Pass filter
LS-SVM	Least-Squares Support Support Machines
LW	Left Wrist
M	Myoclonic seizure
MAS	Movement Acquisition System
MLP	Multi-Layer Perceptron
mRMR	minimum-redundancy maximal-relevance feature selection method
NICU	Neonatal Intensive Care Unit
NP	No-Pass (or notch) filter
PDF	Probability Density Function
PPV	Positive Predictive Value
PSD	Power Spectral Density
PWT	Packet Wavelet Transform
RA	Right Ankle
RB	Right Biceps
RBF	Radial Basis Functions
RFE	Recursive Feature Elimination
RIP	Respiratory Inductance Plethysmography
RNS	Responsive Neuro-Stimulation

ROC	Receiver Operating Characteristic
RP	Recurrence Plot
RW	Right Wrist
S	epileptic Spasm
sEMG	Surface electromyography
SMA	Signal Magnitude Area
STIP	Spatio-Temporal Interest Points
SUDEP	Sudden Unexpected Death in Epilepsy
SVM	Support Support Machines
T	Tonic seizure
TC	Left Ankle
TC	Tonic-Clonic seizure
TLS	Temporal Lobe Seizure
TN	True Negative
TP	True Positive
U	Unclassified seizure
V	Versive seizure
VNS	Vagus Nerve Stimulation
ZCR	Zero Crossing Rate

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Chapter 1

Introduction

This chapter aims at introducing epilepsy and the different ways of monitoring and detecting this brain disease. Section 1.1 starts with the main general facts and figures about epilepsy, fully describes the seizure classification in Subsection 1.1.1 and possible therapeutic methods applied in clinical practice in Subsection 1.1.2. Next, Section 1.2 briefly explains the epilepsy diagnostics where video/EEG monitoring has a predominant role. EEG-based seizure detection is explained in Subsection 1.2.1, whereas Subsection 1.2.2 reviews alternative modalities. The latter enable the monitoring of patients at home and assist the clinicians in the nearby future in decision making concerning the diagnosis of epilepsy. Attention was focused to accelerometry and surface electromyography, as these modalities are further investigated in this thesis. The goals and challenges of the thesis are described in Section 1.3. Section 1.4 gives a chapter-by-chapter overview of this thesis. Finally, Section 1.5 lists the collaborations realized through this doctoral project, whereas Section 1.6 gives a summary of the personal contributions.

1.1 Epilepsy

Epilepsy is the disease of the brain which occurs in 1% of the world population [225]. According to the operational clinical definition of epilepsy, it is defined by any of the following conditions [73]:

1. At least two unprovoked seizures occurring over 24 hours apart

2. One unprovoked seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years

3. Diagnosis of an epilepsy syndrome

Epilepsy is considered to be *resolved* for a patient who have remained seizure-free for the last 10 years, with no seizure medication for the last 5 years [73].

A seizure is the result of the transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain [74]. Seizures originate and are sustained in a large neuronal population due to a temporary loss of control over the balance between inhibition and excitation. Since inhibitory mechanisms fail, neurons fire simultaneously at a rate much higher than normal. The abnormal activity might spread to other regions in the brain through pathways which otherwise exist to facilitate normal function. There are different explanations on how a seizure terminates, including the depletion of oxygen supply to the neurons involved in the seizure, and chemical changes which restore the initial imbalance or lack of inhibition [220].

Depending on the brain regions involved in the seizure, the patient may have diverse clinical symptoms. Seizures can affect at least one of the following functions: sensory, motor and autonomic functions; consciousness; emotional state; memory; cognition and behavior [74]. In addition, some patients can develop some degree of retardation [183]. Accordingly, epilepsy has direct influence on the quality of the life of the epileptic patients. In addition, there are social and economic implications related to the epilepsy [53, 176].

Epilepsy is a disease with onset at the extremes of life. Age-specific incidence (or rate of occurrence) is consistently high in the youngest age groups, with highest incidence occurring during the first few months of life. Incidence falls dramatically after the first year of life, seems relatively stable through the first decade of life, and falls again during adolescence [25, 67, 85, 158]. It is believed that immature brain is more susceptible to seizures, since it exhibits increased neuronal excitation and diminished inhibition [178].

There is no cure for epilepsy, but existing treatments focus on suppression of symptoms, i.e. seizures. Anti-epileptic drugs try to control seizures, however 30% of patients do not adequately respond and still continue to experience the seizures [111]. In the latter case, other therapies, like surgery, diet, vagus nerve stimulation or responsive neurostimulation, can be explored. Nevertheless, the success of these therapies depends on many factors.

The occurrence of the seizure is unpredictable and it can result in a lapse of attention or a whole-body convulsion. Therefore, frequent seizures increase a patient's risk of sustaining physical injuries and may even result in death. A device capable of quickly detecting and notifying a caregiver or delivering therapy in a closed-loop system could ease the burden of seizures and decrease their negative impact on quality of life of a patient [212]. A long-term home monitoring system would facilitate a better supervision of the patient, improve insights in the effects of the prescribed medication or therapy, and enable an objective measure of seizure frequency. Within this thesis, alternative modalities to gold standard electroencephalography (EEG), namely accelerometry and surface electromyography, are proposed and explored for epileptic seizure detection.

1.1.1 Epileptic seizure classification

While for a neurologist understanding the classification of epileptic seizures is the first step towards the correct diagnosis, treatment and prognostics of the condition, for an engineer knowing the characteristics of these seizures can help in the design of the detection algorithm.

The classification of epileptic seizures is still largely based on clinical observation and expert opinions. The International League Against Epilepsy (ILAE) first published a classification system in 1960. The last official update for seizures was published in 1981 [9], and the last official update for the epilepsies was in 1989 [70]. Even though the 1981 and 1989 updates from the officially accepted classification system, occasionally conceptualization, terminology, and definitions of seizures and epilepsy are updated, modified and improved with the use of the newer multidisciplinary approaches to study epilepsy [15]. The utilization of the same terminology and underlying definitions facilitates the communications and knowledge exchange.

In this thesis, epileptic seizure classification and related terminology are deduced from the recently published report on International Classification of Diseases (ICD) by ILAE [98]. According to this special report, seizures are classified into three classes: primary generalized, focal seizures and so called "unknown". In the latter case, there is no sufficient evidence to classify these seizures as focal, generalized or both. The difference between the other two classes is in how they begin. Primary generalized seizures begin with a widespread electrical discharge that involves both sides of the brain at once, whereas focal seizures begin in one limited area of the brain. Figure 1.1 schematically represents the division of epileptic seizures into the focal, generalized and unknown seizures and corresponding subclasses.

Here, we describe the main seizure subclasses and their characteristics, which can be found in the databases used in this thesis (see Chapter 2).

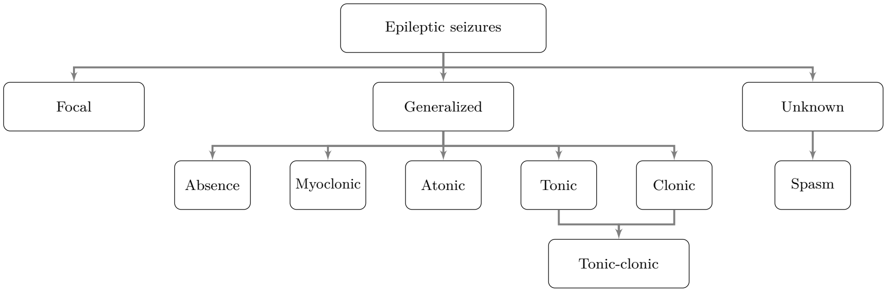

Figure 1.1: The division of epileptic seizures into focal, generalized and unknown seizure classes. From [98].

- *Myoclonic seizures* are sudden short (< 0.5 sec) jerk-like movements [83]. The myoclonus is a twitch-like contraction which mostly includes shoulders and one of the proximal limbs. Consciousness is not impaired and there is no post-ictal confusion with single myoclonic jerk. Myoclonic seizures can also occur in clusters. They tend to occur close to sleep onset and upon awakening from sleep. Even people without epilepsy can experience myoclonus in hiccups or in a sudden jerk that may wake you up as you are just falling asleep.

- *Clonic seizure* is a series of myoclonic contractions of agonist and antagonist muscles that regularly occur from 0.2 to 5 times in second with impairment of consciousness and a short post-ictal phase. They can lead into a clonic-tonic-clonic seizure. Usually the whole body is involved. The movements can not be stopped by restraining or repositioning the arms or legs.

- *Tonic seizure* is tension resulting in a change of posture. Consciousness is usually preserved. It mostly involves all proximal limbs and it lasts ≥ 2 seconds.

- *Atonic seizure* is opposite of tonic seizure and it is characterized by a weakening of the muscles, which can lead to a head drop, a limb drop, or a drop of the whole body. These seizures are also called "drop attacks" or "drop seizures." These attacks are really short. Atonic seizures last less than 5 seconds, and there is minimal post-ictal confusion. They may be preceded by a brief myoclonic jerk or tonic component.

- *Tonic-clonic seizure*, also known as grand mal seizure, is a combination of tonic and clonic seizure. First there is a stiffening of the body and then jerking starts; the same limbs are involved and the frequency of the jerks decreases with time. When muscles stiffen, air is forced past the vocal cords causing a cry or groan. The person loses consciousness and falls down. Gasping respirations occur as the respiratory muscles are involved in the clonic activity. The patient may also become cyanotic. Urinary incontinence may occur. At the end of the seizure, the patient is unconscious for a brief period of time and then gradually recovers. However, the person may feel drowsy, confused, agitated, or depressed for a long time. Tonic-clonic seizures may lead to injuries such as burns, head injuries, vertebral compression fractures, shoulder dislocations, tongue and cheek lacerations.

- *Epileptic spasm* is a seizure which mainly involves axial muscles, leading to flexion or extension of the neck (and legs) and abduction of both arms. Epileptic spasms can also occur in clusters.
- *Versive seizure* is characterized by turning of the head to an almost uncomfortable angle. Sometimes the trunk is also involved.
- *Frontal lobe seizure with hyperkinetic movements (previously called hypermotor seizure)* manifests itself through (normal) movements in abnormal circumstances (such as pedaling in bed). Movements are quite rapid, violent and repetitive, involving trunk and proximal limbs. Similar as during tonic-clonic seizures, there is a high risk of injuries. Patients may be confused after a seizure, and they often recall the seizure as a "strange feeling" and need comforting [209].
- *Subtle clinical seizures* can only be seen on EEG and very subtely on video, not on sEMG and ACM, e.g. smacking, eye blinking.
- *Subclinical seizures* can only be seen on EEG.
- *Unclassifiable seizures* represent all the seizures which we could not clearly classify. In addition, seizures for which video are missing or corrupted, are added to this group.
- *Other seizures* are the seizures that could be classified but are not part of the previously mentioned ones, e.g. atypical frontal lobe seizures, focal temporal seizures, automatisms, ...

As mentioned previously, myoclonic seizures and epileptic spasms can occur in clusters. In those cases, instead of annotating each seizure individually, a *series of myoclonic seizures or epileptic spasms* is annotated when minimum 10 contractions occur on a regular basis with no more than 60 seconds in between.

This thesis mainly focuses on automated detection of tonic-clonic and clonic seizures, which predominately are generalized seizures, but there are some exceptions (secondarily generalized seizure or atypical clinical manifestations). Described seizure classes are the classes which appear in the database recorded in Pulderbos Rehabilitation Center (see Chapter 2). However, it has to be stressed that this list was compiled to accommodate the epileptic seizures classes while there are other classes, like absent seizure which are characterized by a sudden onset behavioral arrest, a blank stare, unresponsiveness, and sometimes a brief upward rotation of the eyes and as a result can not be reliably detected with the sensors used in this thesis. Accordingly, the symptoms related to the certain seizure classes which could not be detected with the system used here are not described here. The reader is refer to the ILAE reports [9, 15].

1.1.2 Epilepsy treatments

The management of a patient with seizures begins with an identification of the patient's seizure class and epilepsy syndrome. Specific seizure classes or syndromes often respond better to specific medications or surgical approaches. Some seizure classes or syndromes carry a benign prognosis or high likelihood of seizure remission by a certain age. Other seizure syndromes may carry a far poorer prognosis, and early knowledge of this allows focused treatment and lifestyle modifications for patients and families.

In around 70% of epileptic patients the seizures can be completely controlled with medication, i.e. antiepileptic drugs (AED). Even if the first AED does not work, other AEDs can be tested, sometimes even in a combination. However, the probability of an AED to be effective decreases with the number of different AEDs tested. Therefore, if after a while, medication does not work, the neurologist may have to use alternative strategies. In the case the patient is not responding to the AEDs, we say he/she has refractory epilepsy.

One alternative to AEDs for controlling epileptic seizures is a surgery. However, there are some requirements to be fulfilled before the surgery is scheduled. Since the goal of the surgery is to remove the part of brain responsible for seizure occurrence, the so-called epileptogenic zone or seizure onset zone, this zone has to be clearly identified, it has to be small and not interfering with the other brain functions.

Next alternative method is the ketogenic diet. In this special diet, the consumption of fat is high and that of carbohydrates is low. As a result, when the body uses fat as an energy source, ketones are produced; hence the name. A higher level of ketones in the body often leads to an improved seizure control, although the mechanism behind it is not completely clear.

Another alternative is the vagus nerve stimulation (VNS). The vagus nerve is the tenth cranial nerve, and interfaces with parasympathetic control of the heart and digestive tract. VNS therapy consists of a pacemaker-like device with the size of a small watch. The device, or generator, is usually implanted in the left chest area. A thin thread-like wire, or lead, connected to the generator, runs under the skin and is attached to the left vagus nerve in the neck. The device delivers mild, intermittently-pulsed signals to the vagus nerve, which then activates various areas of the brain. Using an external dose adjustment system, the neurologist adjusts the stimulation duration, frequency and intensity. Treatment is automatically delivered at regular intervals during the day, so treatment is automatic and continuous. A meta-analysis of VNS efficacy was evaluated on 74 clinical studies with 3321 patients suffering from refractory epilepsy, implanted with a VNS device. Results showed that, on average, approximately 50% of the patients attained a clinically significant reduction in seizure frequency greater than 50%, with about 12% experiencing a 90% decrease in seizures [68]. Another study showed at least 50% reduction in seizures for more than 60% of patients [65]. Additionally, studies have shown that the efficacy of VNS typically improves over time [66, 189].

With the success of deep brain stimulation for treatment of movement disorders, deep brain stimulation (DBS) has received renewed attention as a potential treatment option for epilepsy. Responsive neuro-stimulation (RNS) aims to suppress epileptiform activity by delivering stimulation directly in response to electrographic activity. The first implantable responsive closed-loop neurostimulator for epilepsy, the NeuroPace RNS system (NeuroPace, Inc., Mountain View, CA, USA), has been evaluated for safety and efficacy in clinical trails for the treatment of intractable focal onset epilepsy in adults. The device continuously analyzes the patient's electrocorticogram (ECoG) and triggers electrical stimulation, when specific ECoG characteristics, programmed by clinician as indicative of seizure, are detected. Fountas and Smith [75] followed up eight patients who were implemented the described NeuroPace RNS system between 6 and 26 months (mean 11.3 months). Seven (87.5%) of these patients had more than 45% reduction in seizure frequency (with two patients having more than 75% decrease) while one patient had slight increase (around 2%) in seizure frequency, but a significant decrease in seizure intensity was observed. Another study of 24 subjects with complete data using the NeuroPace RNS system demonstrated excellent safety and tolerability, with more than 50% in seizure reduction [200]. Morrell [148] succeeded to perform larger scale study involving 191 adults. One month after implantation of NeuroPace RNS system, subjects were randomized 1:1 to receive stimulation in response to detections (treatment) or to receive no stimulation (sham). Efficacy and safety were assessed over a 12-week blinded period and a subsequent 84-week open-label period during which all subjects received responsive stimulation. Seizures were significantly reduced in the treatment (-37.9%, n=97) compared to the sham group (-17.3%, n=94; p=0.012) during the blinded period and there was no difference between the treatment and sham groups in adverse events. During the open-label period, the seizure reduction was sustained in the treatment group and seizures were significantly reduced in the sham group when stimulation began. There were significant improvements in overall quality of life (p=0.02) and no deterioration in mood or neuropsychological function. Even though NeuroPace RNS system shows promising results in reduction of seizure frequency, it is only used for adults and for localized (focal) seizures.

In addition, recently a new technique was proposed for neuronal inhibition, so-called optogenetics [72]. Optogenetics relies on optical control of opsins targeted to living cell membranes by gene transfer. The first studies in animal models show promising results of the arrest of spontaneous seizures using a real-time, closed-loop system, but more research is needed before these findings can be applied as a therapeutic approach in humans [109].

1.2 Epilepsy monitoring and seizure detection

If there is a suspicion that a patient has epilepsy, the patient has to be monitored typically during 24 hours with video/electroencephalography (EEG). An EEG specialist visually inspects the data in order to properly diagnose the patient (Subsection 1.1.1), so that the neurologist can prescribe the therapy (Subsection 1.1.2). Apart from the video/EEG monitoring, the exact diagnosis is also based on other information of the patients, such as medical history, blood tests or brain imaging.

In case of refractory epilepsy, long-term monitoring can be requested to follow the evolution of the disease, track the response on medication alternation and set an alarm for dangerous seizures. Even though the gold standard for epilepsy monitoring is video/EEG, in the last decade new systems based on other modalities are emerging. In the next subsections these systems are described.

1.2.1 EEG-based seizure detection

The oldest records show that the epilepsy has been affecting people since the beginning of the recording history. However, at that time it was perceived as spiritual possession (the word *epilepsy* originates from the Greek verb *epilambanein* which means *to seize, possess, or afflict*) and persons suffering from epilepsy were sometimes treated as criminals [174]. In the 20th century, the development of electroencephalography (EEG) enabled the visualization of the brain waves and presence of abnormal hypersynchronous discharges of population of cortical neurons during epileptic seizures. Moreover, EEG revealed the different patterns during different epileptic seizures, enabling their distinction, classification and localization.

Automated methods of EEG-based seizure detection emerged from the concept that normal brain dynamics, which involve limited, transient synchronization of disorganized neural activity, evolve into a persistent, highly synchronized state that incorporates specific regions of the brain during epileptic seizures [89]. The first automatic seizure detection systems date back to the 1980s [77]. Since then, a large variety of seizure detection algorithms were proposed. The majority of the proposed algorithms are based on machine learning techniques incorporating the feature extraction and selection, training and application of the chosen classifier [57, 80, 161, 172, 199, 216]. For an extensive literature overview, we refer to [211]. Apart from seizure detection, intracranial EEG can be used for seizure prediction and therapy/stimulation can be delivered in the closed-loop system [147, 198, 206] as explained in Subsection 1.1.2. An extensive review on intracranial EEG-based seizure prediction can be found in [146]. Figure 1.2 illustrates the difference between the prediction and detection.

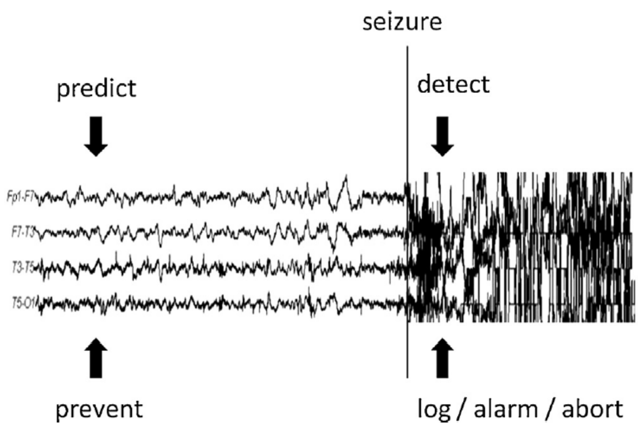

Figure 1.2: EEG recording before a seizure onset: prediction vs. early EEG-based seizure detection. From [212].

While EEG provides a great amount of data that can be interpreted visually or via automated methods, it can be difficult for patients to wear the EEG electrodes for prolonged periods of time. It is labor-intensive for the technical staff as it takes 20 to 40 minutes to glue all the electrodes on the scalp. Moreover, prolonged surface electrode recordings may become difficult to read because of increasing impedance. Additionally, some patients may develop skin abrasions due to prolonged exposure to surface electrodes. Hence, other modalities have been proposed and investigated for long-term (home) epilepsy monitoring.

1.2.2 Alternative modalities

As described in Section 1.1.1, apart from the changes in EEG there are other clinical signs which could be used to detect epileptic seizures. This subsection gives an overview of the research done using other body signals to detect the epileptic seizures by reporting the main information and obtained results within those studies. Since this thesis is focused on ACM and sEMG, these two modalities will be described first and then the list will be extended with the rest. Metrics used to describe and compare algorithms proposed in the literature are defined in Section 3.4, whereas Figure 1.3 illustrates the changes in ACM, sEMG and ECG signals during a tonic-clonic seizure.

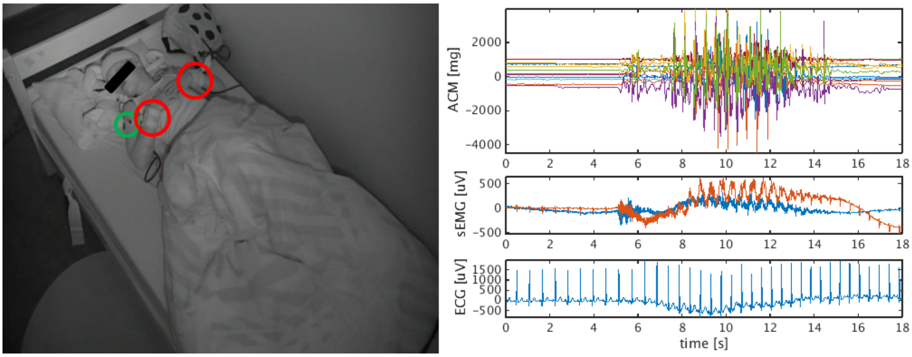

Figure 1.3: A tonic-clonic seizure registered with camera, four ACM sensors attached on wrists and ankles (wrist ACM sensors are indicated with red circles), two sEMG sensors on biceps muscles (right sEMG sensor is indicated with green circle) and one-lead ECG measurement setup

- **ACM (accelerometry):** Accelerometers are devices that measure applied acceleration acting along a sensitive axis which can be used to measure the rate and intensity of body movement in up to three planes (anterior-posterior, mediolateral and vertical) [193]. As they respond to both the frequency and intensity of movement they are superior to actometers or pedometers, which are attenuated by impact or tilt [134]. ACMs can also be used to measure tilt (body posture) making them superior to those devices that have no ability to measure static characteristics [126, 134]. With these characteristics, ACM is capable of providing sufficient information for measuring movements and a range of human activities. Therefore, ACMs have been widely accepted as useful and practical sensors for continuous, unobtrusive and reliable human movement detection and monitoring in either clinical (laboratory) settings or free-living environments [134].

ACMs were first investigated in the 1950s to measure gait velocity and acceleration, however they were found to be unsuitable for this purpose since they were expensive and large [90]. ACM measurement of human motion was studied in more detail during the 1970s due to technological advances [149]. It was also shown that accelerometers had advantages over other techniques in quantitatively measuring human movement. Advances in integrated microelectromechanical systems (iMEMSs) have enabled the size and cost of the ACM device to be greatly reduced while ensuring the fabrication of these devices is maintained at a high quality and reliability as required by industrial standards [44]. In the meantime, ACM sensor performance had been enhanced while the power consumption was greatly reduced. The first batch-fabricated MEMS accelerometers were reported in 1979 [188]. Since then various research and commercial applications have used iMEMS accelerometers in wearable systems for gait analysis and physical activity monitoring [34,91,100,102,112,129,132,133,135,181,221]. Advantages of ACM devices include their small size, ability to record data continuously for periods of days, weeks and even months. Compared with the video, ACMs can measure body movement more easily under blankets and can better separate the movements of the individual limbs, but the sensors still have to be attached to the body parts.

ACM sensors are frequently combined with gyroscopes and magnetometers into motion sensors for the real-time tracking of body segments. Sensor fusion is performed using dynamic algorithms whose output should allow for a detailed movement analysis [19,125,187,190]. Nevertheless, these modalities are rarely combined and as such used for detection of epileptic seizures. Magnetometers are highly sensitive on the presence of outside magnetic fields, whereas gyroscopes consume lot of energy preventing wireless long-term monitoring. However, as it can be seen from the following literature review these modalities are not fully investigated, and we should determine the trade-off between their limitations and their added value in seizure detection set-up.

Since Nijsen et al. showed that the three-dimensional ACMs are a valuable sensing method for seizure detection [155], accelerometry is one of the most frequently used modalities for detection of epileptic seizures with motor component. In the same study, a seven times higher number of seizures were registered using the measuring system with five 3D ACM sensors compared with the number of seizures observed by the nurses. The same group focused on detection of myoclonic seizures using time-frequency and wavelet analysis [151, 154], since short myoclonic seizures preceded 81% of tonic and 37% of tonic-clonic seizures [155]. 80% of myoclonic seizures were correctly identified with only 15% of false positive predictive values. The same models were tested for detection of tonic seizures [153]. Overall sensitivity was 83% and positive predictive value of 35%. Both studies were performed on the segments containing the seizures and non-seizures.

Jallon et al. [93] also investigated the detection of epileptic seizures using ACMs. The patient moves were modeled with hidden Markov models (HMM) [177] and Bayesian analysis of the signal was performed. The model parameters are not set by hand but computed with an automatic learning algorithm presented within the paper. This methodology resulted in a sensitivity of 88% and 89% in two patients. The corresponding positive predictive values were 75% and 55%, respectively. This group recently published the work on (tonic-)clonic seizure detection using one simple feature (acceleration norm entropy) and thresholding resulting in 80% sensitivity with a 95% specificity on segment-based (predefined events) data using three ACMs located on upper arms and head.

Conradsen et al. [39] used a multimodal approach for detection of simulated myoclonic, versive and tonic-clonic seizures. Sixteen motion sensors (ACM, gyroscopes and magnetometers) and 14 sEMG electrodes were employed. Different modalities were combined and tested, however the best performances were obtained when using all sensors: 100% sensitivity, 0 false detection rate (FRD) per hour and 0.75 seconds median latency. The main drawback of the study is the large number of sensors and the use of simulated instead of real-life data.

In the study of Schulc et al. [192], Wii Remote (ACM sensor) placed on upper arm was used to detect generalized tonic-clonic seizures using a threshold-based algorithm. The algorithm was developed on the recordings of 20 adult patients and it resulted in 100% sensitivity (four TC seizures) and positive predictive value higher than 75%. However, the reported results were obtained on training data; no test data were available. Dalton et al. [51] used a dynamic warping algorithm to distinguish simple motor seizures from a predefined set of instrumental activates of daily living. The algorithm was transferred to a commercially available internet tablet. The body sensor network on the Mercury platform was developed. From a dataset of 21 seizures (five patients), the sensitivity was found to be 91% and specificity of 84%. A battery reached a lifetime of 10.5 hours on the Mercury platform.

Within our group, previous PhD students focused on the detection of frontal lobe seizures with hyperkinetic movements [47–49, 58, 123, 213].

Decaigny et al. [58] used the data of four ACM sensors attached to the wrists and ankles of four pediatric patients to detect frontal lobe seizures. Movement epochs were detected by comparing the calculated standard deviation of a sliding window to a threshold. Afterwards a moving average filter was applied and thresholds were set to the signals of the four accelerometers in order to classify an event as an epileptic seizure or as normal movement. This resulted for three patients in a sensitivity and a positive predictive value (PPV) of 100%, for the last patient the sensitivity was 100% and the PPV was 30.2%. Cuppens et al. [48] tested more complex methods based on novelty detection or outlier detection. Using (abundance of) normal movements probability density function (PDF) was estimated using non-parametric Parzen windows [17], and all events below a certain threshold level were considered abnormal movements, i.e. seizures. For seven patients with 51 frontal lobe seizures, a mean sensitivity of 95.2% and a positive predictive value of 60% were obtained. However, a noticeable inter-patient difference was observed.

Apart from the research studies describing seizure detectors in development phase, the first commercially available detectors that were built in wireless, wrist-worn sensors were presented by BioLert (the EpiLert watch), Smart Monitor Company (the SmartWatch) and Danish Care Technology ApS (Epi-Care Free). All systems have been validated in clinical validation studies [14, 108, 118], mainly for detection of generalized tonic-clonic seizures. In the study of Lockman et al. [118], the SmartWatch was worn by 40 patients (6 with tonic-clonic seizures). Seven of the eight seizures were detected. Non-seizure movements were detected 204 times, with opportunity for false alarm canceling by the patient (only one false detection was registered during sleep). Detection latency from the clonic phase of tonic-clonic seizures ranged from 4 to 15 seconds. Kramer et al. [108] validated the EpiLert watch in a study on 31 patients with tonic-clonic, clonic and tonic seizures. 20 of the 22 seizures were detected (91%) with a total of 8 false alarms during the 1692 hours of monitoring (0.11/24h) and median latency of 17 seconds. Finally, Beniczky et al. [14] validated the Epi-Care Free wireless watch for the detection of generalized tonic-clonic seizures on 20 patients with 39 seizures, and additional of on 53 patients without seizures for estimating the false detection rate. Thirty-five of 39 (89.7%) generalized tonic-clonic seizures generated the alarm, whereas 40 false alarms were registered within 4878 hours of recordings (0.2/24h).

- **sEMG (surface electromyography):** sEMG measures the muscle tension which is most pronounced during tonic seizures and the tonic phase of tonic-clonic seizures. Andriaas et al. [3] performed a small study with four tonic seizures using sEMG on both biceps muscles. Applying the threshold to the cross-correlation coefficient outperformed the linear discriminant analysis (LDA) classifier by correctly identifying all tonic seizures without false positives, whereas the LDA classifier gave two false alarms. Conradsen et al. have recently turned to sEMG-based GTC seizure detection instead of ACM modality [37, 38]. Employing the zero-crossing rate as the only feature calculated from the deltoid muscle and using a rule-based algorithm, a sensitivity of 100%, false detection rate of 0.04/24h and a median latency of 13.7 seconds were obtained in the first study. The same algorithm was further evaluated on the data of four patients. The data was recorded with the same device but on the tibias muscle. Even though the false detection rate was preserved at low rate at 0.07/24h, the sensitivity degraded significantly to 57%, which could be the consequence of sensor location.

- **Mattress sensors:** Mattress sensors register movements or sound. In the former case, the best known is the EmFit quasipiezoelectric sensor (Emfit Ltd.) placed under the mattress which was used for periodic limb movement screening [180], evaluation of sleep stages [105] and as a sensor for cardiac measurements [106]. This sensor was tested in a clinical study with 22 patients and the system was able to detect 16 of 18 GTC (80%) seizures with PPV of 43% [150]. Apart from this study, the Emfit mattress was compared with with the Epi-Care device and Epi-Care Free bracelet [214]. These devices were tested on one patient for 36, 17 and 19 nights, respectively. Even though, the Emfit mattress exhibited the highest seizure detection sensitivity (78% vs. 40% vs. 41%), the false detection rate per night was much higher especially compared to the Epi-Care Free bracelet (0.55 vs. 0.41 vs. 0.05). Van de Vel et al. [214] also compared the systems for their user-friendliness. The Emfit was preferred, with the least discomfort for the patient; however, it was not always kept well in place under the mattress (this was resolved using an extra attachment). The Epi-Care was judged comfortable and easy to use as well but detached easily. The Epi-Care Free was said to be equally comfortable and user friendly, but disadvantages were the fact that asymmetric clonic jerks mainly involving the opposite arm were not detected and the fact that the alarm reverberated not only on the beeper carried by the staff but also on the receiver in the patient's room which can be burdensome when many false alarms occur.

  The MP5 mattress monitor (Medpage Ltd.) is designed to detect seizures occurring during sleep. Placed between the mattress and box spring, the microphone of adjustable sensitivity in the monitor detects tapping and spring noise. In the clinical study of Carlson et al. [26], during 1528 hours, 64 patients experienced eight tonic-clonic seizures. The MP5 monitor was able to correctly detect five seizures (62.5%), but it generated 269 false positives (during 146 hours). Thus, the device suffered from a poor positive predictive value of 3.3%.

- **Video:** Camera systems were studied in multiple applications from gesture or activity recognition to surveillance [20,87,113,173,210]. The automatic vision-based monitoring can also be a solution for monitoring of epileptic patients.

  Apart from being part of the gold standard for epilepsy monitoring, video is the most common way (and most of the time the only way) for clinicians to retroactively evaluate the detected events by means of other modalities, like ACM. Apart from the diagnostic purposes, this modality can also be used for detection. It has the advantage of being non-invasive and contactless, that is, in the case that no (reflective) markers attached to the patient are used [182]. A downside is that most video-based detection approaches make use of markers [30,117,182] or other ways to track limbs, like using colored pyjamas [121].

  A variety of models have been developed to quantify rather than detect seizures using video monitoring [30, 45, 164, 182]. For instance, Rémi et al. [182] investigated the behavior and motion pattern of the frontal lobe seizures with hyperkinetic movements. They proposed features extracted from the video which resulted in an identification probability of hyperkinetic seizures of 80.8%. Karayiannis et al. [101] did not use any markers, but the moving limbs of the 54 patients were clearly visible as they were monitored in the Neonatal Intensive Care Unit (NICU). Predefined video segments were classified using neural network classifier. The best obtained result had a sensitivity above 90% and a specificity above 85%, in patients with myoclonic and focal seizures. Cuppens et al. [50] applied an optical flow algorithm on 73 video segments (11 seizures). The best result was achieved when using a variable threshold, which resulted in a sensitivity of one in all the test sets and a PPV of 100, 82.1, and 100, respectively, for the three test sets. The same group also tested a spatio-temporal interest points (STIP) method for detection of myoclonic seizures in pediatric patients with resulted in a sensitivity of over 75% and a PPV of over 85%. Current video detection systems are limited by the area that is covered by the video camera (this is less problematic at night) and by the inability of detectors to capture events which occur when patients are obscured from view, such as under covers.

- **Thermal cameras:** A thermographic camera (also called an infrared camera or thermal imaging camera) is a device that forms an image using infrared radiation, similar to a common camera that forms an image using visible light. Instead of the 450-750 nm range of the visible light camera, infrared cameras operate in wavelengths as long as 14 μm. Analogous to regular cameras, thermal cameras are often used in the recognition of human motions and surveillance [84, 226]. They could potentially be used for epileptic seizure detection, especially during the night since the sheets and clothing of the patients would not be an issue anymore. Nevertheless, the resolution of these cameras is still lower than of conventional cameras, and the cost is much higher which make them less attractive.

- **Radar systems:** Radar (RAdio Detection And Ranging) uses radio waves to determine the range, altitude, direction, or speed of objects in the space. In biomedical applications, they are mostly used for telemonitoring [122]. Suzuki et al. [203] used this modality for detection of vital signs (electrocardiography and respiration) in an ambulance. Since high frequency waves can pass though the sheets and clothing radar system can be used to detect epileptic seizures. Bonroy et al. [21] developed a movement acquisition system (MAS) consisting of four wireless accelerometers, camera and radar for motioning of epileptic children in a home replacement environment. Apart from measurement system, a screening tool was used to quickly review the most intensive and longest events. The screening tool was evaluated on 57 nights in total, which resulted in a mean sensitivity of 67.30% compared with the reports of the caregivers, including 44% seizures that were was not recorded by the caregivers.

- **Audio systems:** To date, baby-phones are the most frequently used devices to monitor the epileptic children sleeping in a separate room. These devices transmit and alarm the parents when the child is screaming, singing, humming, laughing, weeping, lip smacking or bed noises which are the result of movements. The previous sounds can be normal sound or a consequence of epileptic seizures [54]. In addition, other sounds are recorded, like snoring or speech. As a result, baby-phone and similarly audio-based seizure detection devices generally perform poorly. Nevertheless, due to the low cost and user-friendliness they are still the most frequently used devices for long-term home monitoring of epileptic children.

  De Bruijne et al. [54] investigated the detection of epileptic seizures through audio classification. Sounds were observed in 61 of 95 seizures (64.2%). Seventy-eight real and 175 simulated sounds were studied. Average sensitivity 95-98%, specificity 72-97% and PPV 2-40% were obtained and they were highly dependent on the sound type.

- **ECG (electrocardiography):** Electrocardiogram is the recording of electrical activity of the heart. It allows detecting heart rate (HR), heart rate variability (HRV, changes in beat-to-beat interval which reflect the autonomic nervous system [128]) and ECG morphology. Lack or large changes in these parameters can be predictors for a broad number of disorders. For instance, persistent HR elevations after exercise, decreased HRV and cardiac repolarisation abnormalities are established predictors of sudden cardiac death in other medical conditions or in healthy populations [201].

The most pronounced HR changes are observed during GTC, frontal lobe seizures with hyperkinetic movements and temporal lobe seizures (TLS) [212]. Hence, these events subsequently increase the risk of Sudden Unexpected Death in Epilepsy (SUDEP). Many research groups studied the HR and HRV changes before, during and after different seizure classes. It is observed that HR increases or even resulted in tachycardia related to TLS [59, 94, 115, 159, 197, 229]. Time-frequency analysis of the tachogram (RR intervals) illustrated that the energy in the low frequency component (0.04-0.15 Hz) increases, whereas the high frequencies (0.15-0.4 Hz) content decreases by a decreased parasympathetic activity during the seizure activity [97, 137, 157, 191]. Surges et al. [201] found a change in ECG morphology characterized by a shortening of the QT interval during GTC seizures. The main challenge is to transfer these findings to the detection algorithm able to perform well on continuous ECG data. In general these ECG rescordigns contain complex changes that occur in both physiological and pathological conditions, such as exercise, emotional states, disease states, and in response to the 24 hour circadian rhythm.

The utilization of cardiac changes in seizure detectors has been most commonly applied to newborns, in whom signs of seizures are subtle [63, 79, 127]. Because EEG use in newborns is difficult and requires specialist interpretation, adjunct systems based on changes in heart rate might be particularly useful in neonatal intensive care units. Malarvili et al. [127] computed heart rate using an automated R-peak detector from which various spectral features were calculated. A two-phase wrapper-based feature selection technique was then applied to rapidly reduce the feature set. The proposed methodology outperformed the other methods [63, 79] achieving a high sensitivity of 85.7% and specificity of 84% but the test dataset was limited.

Van Elmpt et al. [215] developed a new model for the automatic detection and quantitative analysis of the HR patterns during the seizures. Using curve-fitting algorithm, in two out of three patients with more than 10 seizures a PPV of at least 50% yielded a sensitivity above 90%. Massé et al. [131] modified the HR model during epileptic seizures and the new algorithm was transferred onto the miniaturized wireless ECG monitor which yielded an overall sensitivity of 75% and specificity of 70.4% (one patient deteriorated the overall performances). De Cooman et al. [55]

compared these two methods with their own algorithm. For a fixed sensitivity (80%), they obtained a 5-9 times lower FDR/h compared with the other methods.

- **Respiration monitoring:** There are numerous methods to monitor respiration, including the sensing of airflow temperature, pressure or velocity; chest movement or volume changes; transcutaneous blood-oxygen concentration or partial pressure; oxygen or carbon dioxide concentration; and transcutaneous audio or vibration signals resulting from breathing turbulence in the larynx.

  A thermocouple or thermistor placed below the nose senses airflow temperature, a mask covering the nose and mouth senses airflow pressure and a pneumotachography mask senses airflow pressure or velocity. Although these devices are in common use, they are associated with several disadvantages, including their discomfort and influence on breathing [16]. Sensing chest and abdominal wall movement in order to measure respiratory rate/depth/effort is often performed by measuring volume differences between the upper and lower chest using two straps (respiratory inductance plethysmography, or RIP) [16], two electrodes (impedance pneumography) [160] or magnetometers [16], although it can also be performed using a single EMG (electromyography, on diaphragm or intercostal muscles) or ACM sensor (on chest or bed), and through remote measurement using video or microwaves. One disadvantage is that respiratory movements can continue when there is already apnoea.

  The commercially available bed-mounted seizure-detection systems Ep-It P139 (Alert-It) and Emfit (Emfit Ltd) can detect respiration changes by monitoring movement but the clinical validation of these systems was not performed (at least not published). A pulse oximeter is a clamp attached to ear lobe or fingertip (which could be integrated into a ring). For babies, it can be integrated into a foot strap or body sticker. It consists of a saturometer (which uses infrared waves to sense blood-oxygen concentration) and a plethysmograph (which measures changes in volume within an organ, resulting from fluctuations in the amount of blood, or of air. Oximetry is important, as it can identify rises in blood pressure due to airway blockage (e.g. because of prone position), despite continuing respiratory movements. The complex interaction between brain, heart and respiration makes recording of data on oxygenation crucial in addition to information on respiration and ECG [169, 184]. Electrodes that sense the transcutaneous partial pressure of oxygen can detect respiration abnormalities faster and with fewer false positives than saturometers produce. Poets and et al. [169] have searched for possible mechanisms of Sudden Infant Death Syndrome by measuring different respiration parameters. In this study, electrodes were combined with pulse oximetry and chest movement detection, with the following findings: decreased pressure without decreased saturation indicates changes in skin perfusion, but not arterial hypoxaemia; decreases in both pressure and saturation accompanied by tachycardia and slower, irregular or absent respiration indicates an epileptic seizure; and decreases in both pressure and saturation, preceded by increased amplitude and irregular breathing movement (often combined with tachycardia and massive body movements) indicates suffocation [169]. Oxygraphy and capnography monitor the concentration (using infrared waves, as in pulse oximetry) or partial pressure (using electrodes, as above) of oxygen and carbon dioxide in respiratory gases [186].

Finally, a miniature device attached to the skin of the suprasternal notch on the neck can measure airflow by detecting sound created by turbulence occurring in the human respiratory system. Such a device is manufactured by the UK company Ervitech. Although it is assumed to detect apnoea during seizures, the only article published to date does not focus on epilepsy [42].

Respiration is frequently altered during seizures, and monitoring is also important in preventing SUDEP, not only for monitoring breathing and apnoea, but for detecting sighs, yawns and arousal. Low arousability is a possible sign of near-SUDEP, and two important mechanisms involved in auto-resuscitation are arousal and gasping [86, 169].

- **EDA (electrodermal activity):** During a seizure, a patient might start sweating, which results in changes in conductivity of the skin. Modulation in skin conductance, referred to as electrodermal activity, is a parameter which reflects purely sympathetic activity of the brain [23], [43]. Poh et al. [171] found that epileptic seizures induce a surge in EDA. These changes were greater in generalized tonic-clonic (GTC) than in focal seizures, reflecting a massive sympathetic discharge. They used the obtained results to develop a biosensor based on ACM and EDA measurement to detect GTC seizures. Two modalities were fused in an early integration approach applying an SVM classifier to a patient-independent data division, resulting in 94% sensitivity, 0.74/24h false detection rate (130 false alarms in 4213 hours) and 31.4 seconds median latency. To our knowledge, there were no other publications using EDA measurement for detection of epileptic seizures, either individually or in combination with other sensing methods.

- **Skin temperature:** Temperature changes can be measured by thermometers that exist in the form of adhesive stickers, or by thermal cameras that additionally could detect movement. It still remains to be investigated whether temperature can be used to detect epileptic seizures. Van de Vel et al. [212] suggested the use of changes in temperature for detection of febrile seizures, however the relationship of these seizures to epilepsy is not known.

- **EOG (electrooculography):** An electrooculogram records both eyelid and ocular movements. To measure eye movement, pairs of EEG electrodes are typically placed either above and below the eye or to the left and right of the eye. EOG is capable of differentiating epileptic seizures from syncope, psychogenic or other non-epileptic seizures [36]. Epicall system (Epicall Ltd) uses a sticker placed on the side of the face to measure eye movements, HR and pulse as early seizure markers. A clinical trial is expected.

1.3 Research motivation and objectives

Having epilepsy has a major impact on the quality of life of the patients, especially children, but also on their closest family. There is a need from the parents whose children suffer from epilepsy to monitor their children and offer their children the best outcome through therapy and long-term monitoring. Monitoring is especially important during the night when the child is alone and hence not continuously supervised. In addition, continuous supervision is burdensome and can affect the relations within the family.

The goal of this thesis is to explore the potential of automatic epileptic seizure detection in pediatric patients. In this thesis, two modalities less intrusive and more suitable for long-term monitoring compared with gold standard, namely ACM and sEMG, are employed for automatic detection of epileptic seizures. In order to accomplish the aim of this thesis, multiple objectives are define:

1. Investigate the use of two automated feature selection methods for the detection of epileptic seizures within a machine learning framework. Identification of the most informative features for this application is defined as a secondary objective.

2. Develop and explore the potential of automated ACM-based algorithms for detection of epileptic seizures with rhythmic component. In order to get reliable detection performance the algorithms should be tested on long-term continuous data.

3. Compare and integrate ACM and sEMG modalities for the detection of tonic-clonic seizures. In case of a large number of sensors, the number of sensors should be reduced while retaining the detection performance.

1.4 Chapter-by-chapter overview

The outline of this thesis is depicted in Figure 1.4. Each chapter is briefly described here.

Chapter 1 provides an overview of the background of epilepsy from a neurological and etiological point of view. In particular treatment, monitoring and monitoring methodologies are discussed. Finally, the motivation and objectives of the presented research are presented, followed by a short overview of the chapters of the thesis. In addition, collaboration and personal contributions are added at the end of this chapter.

Chapter 2 presents the measurement systems and describes the collected data which were used for this research. Data were acquired at different locations and under different circumstances (with and without gold standard). In addition, preprocessing phases of ACM and sEMG signals are explained, preparing the data for further analysis.

Chapter 3 describes the methodological aspects of this thesis. We introduce feature selection and classification methods applied in the following chapters.

Chapter 4 investigates the use of feature selection methods for detection of epileptic seizures within a machine learning framework. On the one hand, filter feature selection methods are fast algorithms which rank the features based on the predefined criterion. On the other hand, wrapper methods use classification algorithms as a black box and the chosen classification metric is used as a ranking criterion. As a result, a wrapper feature selection algorithm is as fast as the employed classification algorithm. In this study, the discriminating potential of a large number of features found in the literature was studied using a filter method based on mutual information and a hybrid method which combined previously described filter method and wrapper methods using a least-squares support vector machine classifier in a two stage process.

Chapter 5 studies the development of automated detection of (tonic-)clonic seizures based on 3D accelerometry signals. A database annotated using gold standard video/EEG were both used for building and testing in the leave-one-patient-out approach. In addition, built classification models were tested on data recorded in similar to home environment were nurses monitored the children on semi-based approach. For the latter datasets, patient-specific and semi-patient-specific algorithms were compared with patient-independent algorithms.

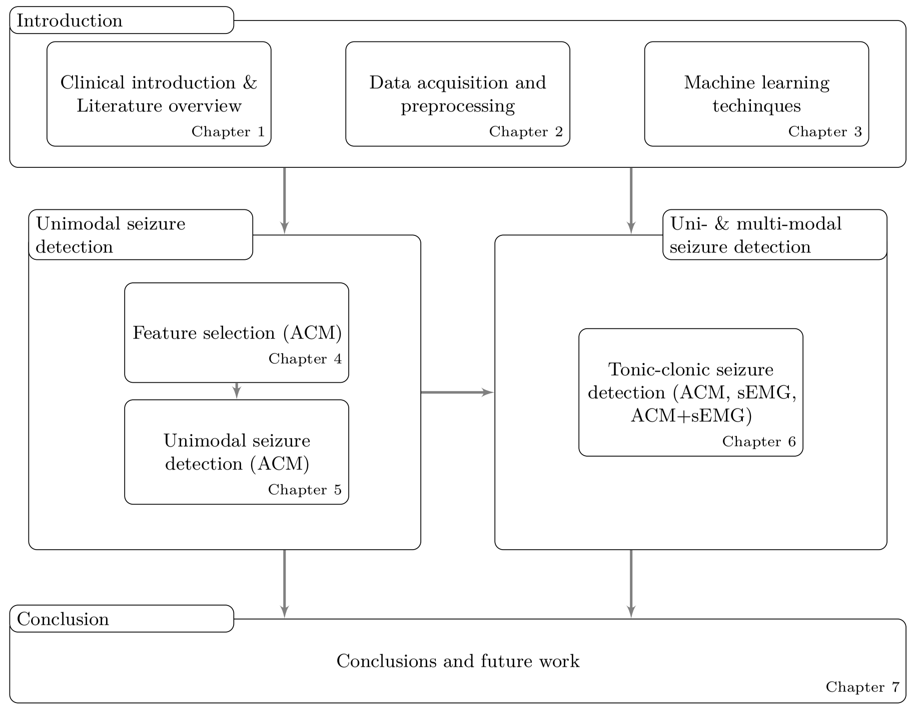

Figure 1.4: Outline of the thesis. Abbreviations used in figure: accelerometry (ACM), surface electromyography (sEMG)

Chapter 6 compares and combines ACM and sEMG-based tonic-clonic seizure detection in pediatric patients. The idea was to improve seizure detection performance by exploiting the complementary information found in the aforementioned modalities using a late integration approach (combining the classification outputs).

Chapter 7 summarizes the main findings of this thesis and suggests possible directions for the future work.

1.5 Collaborations

My Ph.D. research was conducted within the Biomedical Data Processing research group (BioMed), STADIUS, Department of Electrical Engineering (ESAT), KU Leuven, under the supervision of Prof. Sabine Van Huffel and co-supervision of Prof. Bart Vanrumste.

The work presented in this thesis was carried out in close collaboration with Prof. Berten Ceulemans (UZ Antwerp) and Prof. Lieven Lagae (UZ Leuven). Long-term video/EEG, ACM, sEMG and ECG monitoring of pediatric patients diagnosed with epilepsy was conducted in the Rehabilitation Center for Children and Youth, Pulderbos, Belgium. The data was collected within the context of the IWT TBM 070713-Accelero project. Pediatric EEG specialist, Anouk Van de Vel annotated all the data and her explanation on how to interpret various ACM patterns was very valuable. Automated epileptic seizures detection methodology was developed in close collaboration with Anouk Van de Vel. Dr. Ir. Kris Cuppens and Ir. Bert Bonroy synchronized the ACM wired sensors with the already existing recording system (EEG, ECG and video) which was used to monitor the epileptic children in the Pulderbos Rehabilitation Center. They also built the recording system for long-term home monitoring which included wireless ACM, radar and video modalities. Together with Anouk Van de Vel, they succeed to monitor four epileptic patients for one month each. Those data were used to further test the developed algorithms.

1.6 Personal contributions

My own contribution to this thesis was limited to the development of epileptic seizures detection algorithms, whereas other engineers and clinicians supported the data acquisition and annotation (see Section 1.5).

I started working on the detection of epileptic seizures (myoclonic, (tonic-)clonic, clonic and spasms) using ACM signals. A small scale study was performed on motion segments and the results were presented at the 5th International Conference of Advances in Medical Signal and Information Processing (MEDSIP) [138]. When new data were added, a large number of features was tested for epileptic seizure detection through the use of feature selection methods. The results are submitted to the Journal Medical & Biological Engineering & Computing [142]. Chapter 4 addresses this topic. Obtained results were used to investigate automated detection of (tonic-)clonic seizures within a machine learning framework. The results from this research were published as a conference paper in the Proceedings of the IEEE International Workshop on Machine Learning for Signal Processing (MLSP) [139]. Furthermore, the developed models were tested on two patients who were monitored in a home-like environment for one month. The results will be submitted to Epilepsia [141]. Chapter 5 summarizes both studies. Finally, since I observed large inter-patient and -seizure detection variability, I focused in my last study only on the detection of tonic-clonic seizures. For this purpose, I compared ACM and sEMG modalities, and investigated the integration of these two modalities. This study is described in Chapter 6 and submitted to IEEE Journal of Biomedical and Health Informatics [140].

In addition, I was involved in several other studies which were not included in this thesis in order to preserve its coherence. First, I was involved in a study of the influence of VNS therapy on HR and the derived linear and nonlinear HRV parameters in epileptic children. The study design, measurements, data selection and most of the interpretation were the work of Prof. Dr. Katrien Jansen from the neurology division of Prof. Dr. Lagae from the Department of Paediatrics at the University Hospitals Gasthuisberg (Leuven, Belgium), whereas Dr. Ir. Steven Vandeput supervised and continued the work. This research resulted in multiple publications [95, 143, 218].

I also supervised a master thesis of Ir. Griet Goovaerts focusing on the detection of drowsiness in drivers. The experiments were designed and performed by Prof. Dr. Geert Boxtel (Department for Psychology, Tilburg University, Netherlands) and Ir. Ad Denissen (Brain, Body and Behavior Group, Philips Research, Eindhoven, Netherlands). The results were published in the Proceedings of the International Conference on Bio-inspired Systems and Signal Processing (BIOSIGNALS) [76].

Finally, the last research project in which I was involved was performed in collaboration with Dr. Thijs Swinnen, Dr. Kurt De Vlam and Prof. Dr. René Westhovens (Department of Rheumatology, University Hospitals Gasthuisberg). The goal of the study was to develop reliable and robust algorithms to automatically detect movement duration during performance-based tests using a body-worn sensor. The results were compared to the established self-reported Bath Ankylosing Spondylitis Functional Index (BASFI), which is the established method to assess the physical function in patients with axial spondyloarthritis. While Dr. Thijs Swinnen designed and performed the experiments in the laboratory, I contributed by developing an automated segmentation algorithm. The obtained results are submitted to the Journal of Arthritis Research & Therapy [204]. The collaboration also resulted in the approval of interdisciplinary project (IDO/3M140203), entitled "Sensor-based Platform for the Accurate and Remote monitoring of Kinematics Linked to E-health" involving four research groups and started on October 1, 2014.

Chapter 2

Data collection and preprocessing

This chapter describes the data used in this thesis. We illustrate how the data were collected, give an overview of the data and explain how the data were prepared for the application of machine learning techniques described in the Chapter 3. Section 2.1 focuses on data recorded in the Pulderbos Rehabilitation Center, whereas Section 2.2 describes the data recorded in a home-like environment. At the end of this chapter, in Section 2.3, we explain the preprocessing of the data which consists of filtering and data reduction.

2.1 Pulderbos Rehabilitation Center database

2.1.1 Acquisition system

Simultaneous EEG, EOG, video and audio, ECG, sEMG and wired ACM data were recorded using the system installed in the Pulderbos Rehabilitation Center for Children and Youth, Pulderbos, Belgium. The synchronization of all signals was performed by BrainRT software (`http://www.osg.be`). A Schwarzer interface box (`http://www.schwarzer.net`) converted the analog signals obtained from the sensors to digital signals for connection with the computer. Figure 2.1 illustrates the measurement system, whereas Figure 2.2 presents the user interface of BrainRT software on the onset of an tonic-clonic seizure registered in ACM, EEG, sEMG and ECG signals. Video is synchronized with these signals and presented in a separate window, but it is omitted here due to the clarity of figure.

Figure 2.1: Acquisition setup the Pulderbos Rehabilitation Center for Children and Youth: the placements of wired accelerometers are indicated with red circles

ADXL330 accelerometers were used to convert the 3D acceleration (physical measurements) to the voltage (electrical measurements). Data were sampled at 250 Hz, and acceleration was recorded in each channel between -3g and 3g, where g=9.81 m/s^2 is the unit of Earth's acceleration.

In the developed acquisition hardware system, four 3D ACM sensors embedded into the wrist and ankle bands were attached to the pediatric patients extremities. In total there were 12 output channels (3 for each ACM sensor). sEMG was recorded on both biceps muscles using wired electrodes; the same electrodes as for EEG monitoring. For each muscle, one electrode is placed at the belly of the muscle and the other one at the tendon. The range of sEMG signals was $\pm$ 5mV and the sampling rate was 250 Hz.

The study was performed in accordance with the 1964 Declaration of Helsinki and approved by the Medical Ethical Commission of the Antwerp University Hospital, Belgium. Signed informed consent forms from all parents were obtained prior to inclusion in the study.

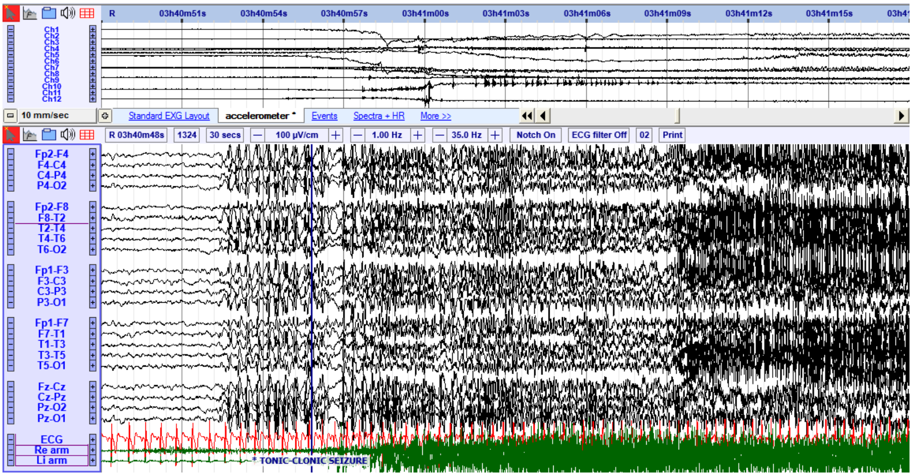

Figure 2.2: Data collected in the Pulderbos Rehabilitation Center for Children and Youth: 12 ACM channels in upper panel, 10/20 EEG configuration system (black), ECG (red) and both biceps sEMG (green) at the onset of an tonic-clonic seizure

2.1.2 Collected data

Until now, 77 children and adolescents suffering from refractory epilepsy have been monitored with the system described in Subsection 2.1.1, however the recordings of 19 of them have not yet been reviewed (no labels) and hence they are not presented in Table 2.1. In addition, over the years some difficulties with recordings were encountered (10 minutes recordings or when only one channel is working properly) which were also omitted from Table 2.1 (in total 6 nights). One of these recordings was the only recording of patient 5. Nevertheless, among the listed nights, there are recordings which contain channels which are nonfunctional or broken. A broken channel, in general, was the consequence of bad connections of the ACM sensor and cable or/and cable and signal collection point, in which case this channel only recorded the intrinsic noise of the sensor. Figure 2.3 gives an example when one ACM channel is completely broken and the other is recording on and off.

Epileptic seizures were annotated by the trained EEG specialist using the gold standard video/EEG monitoring and the International League Against Epilepsy (ILAE) seizure classification terminology described in Subsection 1.1.1. In case of doubt or disagreement regarding the occurrence or type of a seizure, two EEG experts and two neurologists agreed on the label in consensus.

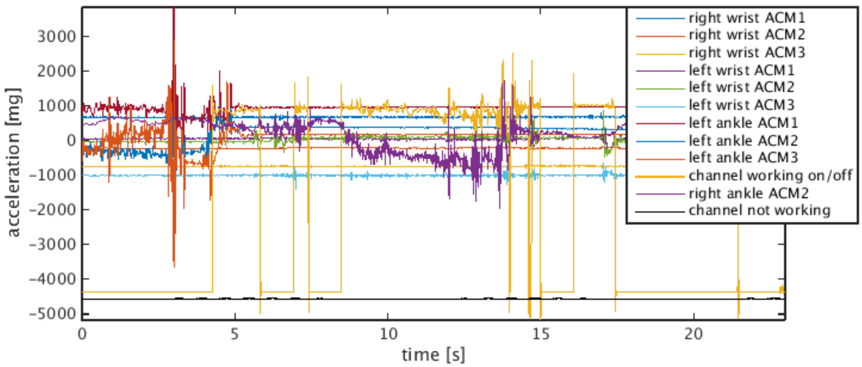

Figure 2.3: An example of ACM recording when one ACM channel is completely broken (black line) and the other is recording on and off (yellow line). Right ankle ACM3 signal (black line) is lowered for -200 mg so that this ACM channel and right ankle ACM1 signal (yellow line) can be visually distinguished when they are both not working.

Within 169 nights, 467 myoclonic, 48 myoclonic series, 104 clonic, 185 tonic, 323 epileptic spams, 18 spasm series, 31 tonic-clonic, 71 frontal-lobe seizures with hyperkinetic movements, 4 versive, 49 unclassified (unclassified due to lack of video or obstacles, atypical frontal lobe, focal seizure and other seizures), 97 subtle and 67 subclinical seizures were annotated. Even though the total number of seizures was quite high, the portion of severe seizures (like tonic-clonic, clonic and frontal lobe seizures with hyperkinetic movements) was low.

Table 2.1: Overview of Pulderbos database: patient information and labeled seizures (*The ages of the patient at the moment of the first and last recording are given. †In the group of the unclassified seizure, there are seizures which were not labeled due to the lack of video, but also all other seizure types with motor component not listed in this table (see Section 1.1.1)

Patient code	# nights	Record duration	Age*	Gender	# myoclonic	# myoclonic series	# clonic	# tonic	# epileptic spasm	# spasm series	# tonic-clonic	# frontal lobe	# versive	# unclassified†
1	7	80:56:42	9.9-10.4	F								15		
2	2	25:24:45	0.6-1.5	M					55	1				
3	22	262:22:11	5.4-10.0	F	36	2	2	7	11	1		2		2
4	3	38:55:35	3.3-4.0	M										
6	6	68:05:35	7.6-10.3	F	1							28		3
7	1	11:37:55	2.3-2.3	M					5	2				
8	1	12:06:53	13.1-13.1	M										
9	4	49:24:14	7.1-7.8	M	11			2	18					
10	1	12:31:59	2.9-2.9	F	2				1					
11	2	22:54:48	17.4-17.9	F	49			51	106		9		3	
12	1	12:21:39	5.8-5.8	M										
13	1	11:25:43	8.5-8.5	M	5			2						
14	1	13:11:57	7.4-7.4	M										
15	1	11:26:48	14.1-14.1	M										
16	1	12:49:05	6.7-6.7	F										
17	1	12:30:25	9.2-9.2	M	1			20	9					2

Patient code	# nights	Record duration	Age*	Gender	# myoclonic	# myoclonic series	# clonic	# tonic	# epileptic spasm	# spasm series	# tonic-clonic	# frontal lobe	# versive	# unclassified†
18	3	34:28:09	12.8-13.5	M										1
19	1	11:09:30	10.3-10.3	F	2							2		
20	8	88:03:22	6.7-7.5	F				1				2		
21	5	63:26:49	9.2-10.6	M				17	3					
22	3	35:49:26	11.9-12.5	M			1		1	3				
23	3	34:04:49	7.0-7.6	F										10
24	5	61:14:12	3.6-4.5	M	14		2		4	1	1			
25	2	26:03:06	1.3-1.5	M	1									9
26	4	49:32:31	3.0-3.5	F	9		1		1					
27	2	22:37:00	15.2-15.2	M								3		
28	3	36:51:54	10.3-10.8	M	2				4					1
29	2	23:19:27	6.1-6.2	M										
30	5	59:09:26	15.0-15.7	M	1	1	6		1					
31	1	11:03:58	17.6-17.6	F										
32	5	59:30:42	10.5-11.4	M	8			3	9					
33	1	12:15:15	6.8-6.8	M										
34	2	23:02:23	12.0-12.0	M										
35	7	87:06:44	6.3-8.6	M	69		6	14	25	4	2			1
36	1	11:18:15	1.2-1.2	M										
37	1	11:11:37	18.0-18.0	F										

Patient code	# nights	Record duration	Age*	Gender	# myoclonic	# myoclonic series	# clonic	# tonic	# epileptic spasm	# spasm series	# tonic-clonic	# frontal lobe	# versive	# unclassified†
38	8	99:42:08	6.6-8.3	F								8		
39	4	50:09:48	2.1-3.0	M	5			40	31	2				
40	4	47:13:59	4.8-5.5	M	4		13	6	11					2
41	2	22:01:43	7.1-7.1	M										
42	2	21:44:39	9.5-9.5	M										
43	2	24:19:57	3.9-4.0	M										
44	3	33:00:42	2.0-2.2	M										
45	2	23:55:56	3.6-3.8	M										
46	3	40:52:56	2.3-3.0	M	137								1	1
47	3	35:59:17	11.7-12.1	M			1							
48	2	25:17:53	12.5-12.7	M					9		1			
49	1	11:04:10	14.1-14.1	M										
51	3	33:43:53	2.6-3.6	M	1		48							
53	2	20:26:00	16.2-16.5	F										6
54	1	12:12:59	2.6-2.6	M	324	45	17		8	4				
57	1	12:19:29	3.6-3.6	M	40			3	2		3			
58	2	21:54:26	8.4-8.5	F										11
64	1	11:36:09	11.5-11.5	M								2		
65	1	11:00:29	9.0-9.0	M	1							9		
67	2	22:32:24	8.1-8.7	F	33		5	8	7		5			

	Patient code	♯ nights	Record duration	Age*	Gender	♯ myoclonic	♯ myoclonic series	♯ clonic	♯ tonic	♯ epileptic spasm	♯ spasm series	♯ tonic-clonic	♯ frontal lobe	♯ versive	♯ unclassified†
	72	1	10:00:13	18.5-18.5	M	11		2	11	2		10			
57 patients		169	2010:33:59	0.6-18.5	41M/16F	767	48	104	185	323	18	31	71	4	49

2.2 Home monitoring database

2.2.1 Acquisition system

The Movement Acquisition System (MAS) was placed in a home-like bedroom and it recorded and detected the nocturnal movements. The multisensory setup was used containing a camera with near infrared (IR) vision and IR light source, a radar based motion sensor (both attached to a tripod placed in a corner of the room) and four wireless ACMs attached to the wrists and ankles of the patient.

The tripod is connected to a laptop and a software application developed in LabVIEW (National Instruments, Texas, `http://www.ni.com`) which stores all the movements recorded by either camera, radar or ACM. When one or more sensors detect motion, data of all sensors are recorded for this event. Moreover, for each event, the three preceding and three trailing seconds are also recorded and stored. If two or more events occur within a time frame of six seconds, these events will be clustered into one segment. Figure 2.4 illustrates this process of clustering movement events into segments. At the end we obtain for each monitored night a dataset which consists of multiple segments containing nocturnal movement events, instead of continuous data as in the previous case (Section 2.1).

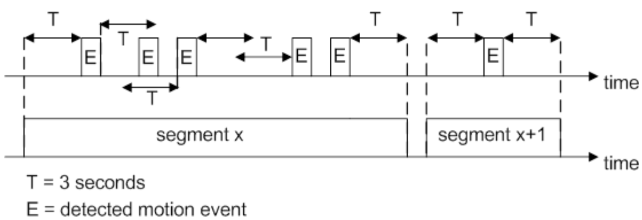

Figure 2.4: Clustering of movement events into movement segments

Four 3D ACM (Freescale MMA7260Q 1.5/2/4/6g MEMs accelerometer) within elastic blankets and wireless communication (class 2 Bluetooth Radio) were used to capture the motion. The Shimmer2 platforms underwent a battery replacement (from 280mAh into 480mAh) which increased the autonomy from approximately 7h to up to more than 10 hours. This was necessary to be able to stream the ACM data during a complete night. The sampling rate was set to 51.2 Hz. This sample frequency allows receiving and processing the data from all four Shimmer platforms concurrently. Each of the four three-axis accelerometers is calibrated so that the recorded ACM signals are expressed in g (g=9.81 m/s^2). Acceleration was recorded in each channel between -2g and 2g. Figure 2.5 illustrates the Movement Acquisition System Graphical User Interface.

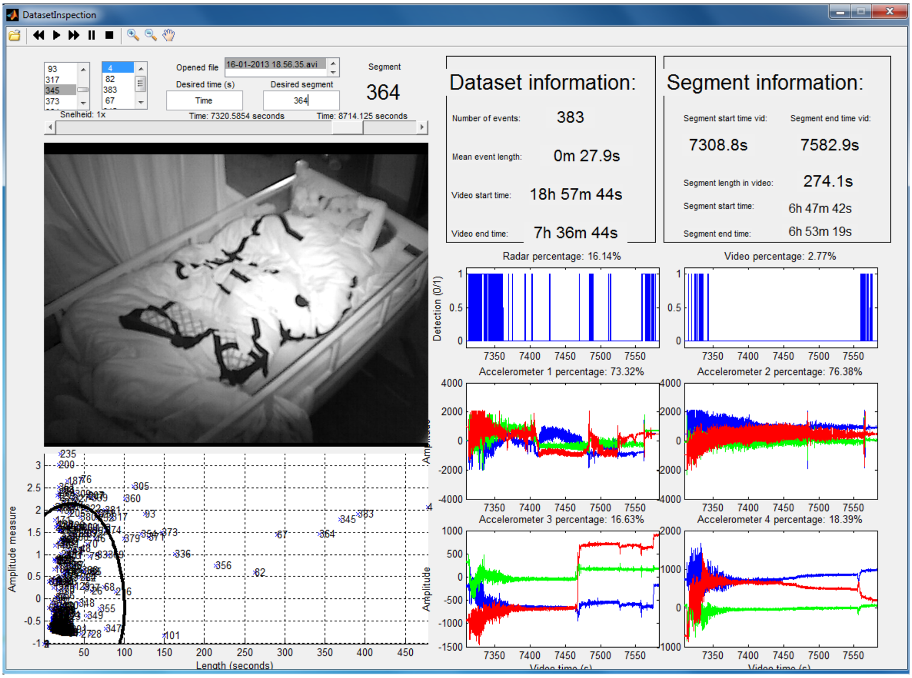

Figure 2.5: Movement Acquisition System Graphical User Interface (GUI) of the screening tool: Segment 364 contains a tonic-clonic seizure which starts at 6:47:42 am. GUI displays the video and ACM signals for the chosen segment. In addition, the movement detection is performed both with video and radar and the results are present within the GUI. Graph in the down left corner suggests the longest and the most intensive events.

2.2.2 Collected data

The described acquisition system was allocated for one month to four patients residing in the Pulderbos Rehabilitation Center, which were already monitored before with a wired ACM and video/EEG system (Subsection 2.1.2). However, since the patients do not reside seven days a week in the epilepsy center and due to the fact that data were lost during the measurements, only 59 nights of good data quality of all patients were collected. The loss of data can be assigned to one of the following three categories: 1) learning curve of the caregivers in the operation of the MAS (67%), 2) technical problems (12%), 3) and corrupted data (21%). Altogether, 71% of the data from the four patients was useful and could be analyzed. Table 2.2 provides an overview of the data.

Since there were no gold standard video/EEG recordings available, the clinical reports composed by the caregivers who observed the patient on a semi-continuous basis were used as a control set for comparison with the output of the automated algorithm. These caregivers are familiar with the patient's behavior and are experienced in epileptic seizure recognition. Nevertheless, data presented in Table 2.2 shows that 19% of seizures were not found in the data, whereas almost 100% of extra seizures are found in reviewed data (possibly there can be more seizures).

Table 2.2: Overview of Home monitoring database: patient information, number of seizures and labels reported by nurses, corresponding seizures and their labels found in the data and extra seizures found within the longest and most intensive movements (*The ages of the patient at the moment of the first and last recording are given. †In this group, we added the seizures for which the caregivers did not specified the seizure class or there were the suspicion of the seizure occurrence (scream, noise)).

Patient code	# nights	Record duration	Age*	# seizures	# myoclonic	# myoclonic series	# clonic	# tonic	# tonic series	# epileptic spasm	# spasm series	# tonic-clonic	# frontal lobe	# unspecified†
19	25	274:22:48	13.5-13.8	3 (nurses)										3
				2 (data)									2	
				6 (extra)						1			5	
35	9	114:03:59	9.4-9.4	11 (nurses)	1	1		1		1		6		1
				6 (data)					1		1	4		
				3 (extra)								3		
65	10	126:49:39	9.1-9.1	58 (nurses)										58
				47 (data)									47	
				56 (extra)									56	
67	15	189:29:20	8.4-8.5	22 (nurses)								21		1
				21 (data)			10					11		
				10 (extra)	2		5					3		
	59 nights	6142:46:28		94 (nurses)	1	1		1		1		27		63
				76 (data)			10		1		1	15	49	
				75 (extra)	2		5			1		6	61	

2.3 Data preprocessing

Preprocessing was performed to remove the artifacts and to reduce the data for further processing. In this section we explain the preprocessing performed on ACM and sEMG signals.

2.3.1 Preprocessing of accelerometry signals

Figure 2.6 depicts the consecutive steps of preprocessing of ACM signals.

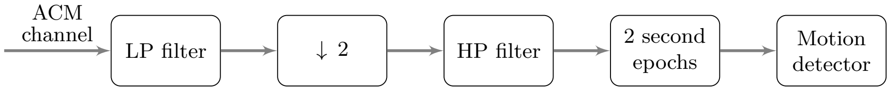

Figure 2.6: Schematic overview of preprocessing steps of ACM signals that result in motion epochs

First a Chebyshev type II low-pass (LP) filter with 47 Hz as cut-off frequency is applied as anti-aliasing filter and to remove the power-line frequency of 50 Hz and higher frequencies. After downsampling ACM signals by a factor 2, a Chebyshev type II high-pass (HP) filter of 0.2 Hz cut-off frequency was applied to remove the baseline drifts, i.e. the gravitational component of acceleration [48]. The preprocessed data were divided into 2 second epochs with 75% overlap. The epochs of 2 seconds are used since the characteristics of the seizures are rapidly changing with time. Moreover, some seizure classes, like myoclonic and epileptic spasm, are quite short and longer epochs would not be appropriate for their detection. An epoch containing more than 50% seizure activity was labeled as a seizure epoch. Finally, a simple motion detector was applied to remove all epochs during which the child was not moving; these epochs do not include any relevant seizure activity.

In Chapter 4, whenever the standard deviation in all ACM channels was lower than 10 mg, the corresponding epoch was removed from further analysis. The value of 10 mg was experimentally determined by measuring the smallest movements of the limbs [49]. This *movement detection* resulted in a 79.96±15.97% reduction of the initial number of epochs per recording. In case of detection of clonic and tonic-clonic seizures (Chapters 5 and 6), the threshold was raised to 30 mg, resulting in an 88.00±7.64% reduction of the initial number of epochs per recording. The threshold was chosen based on the standard deviation values during clonic seizures and the clonic phase of tonic-clonic seizures in ACM signals.

2.3.2 Preprocessing of surface electromography signals

Figure 2.7 depicts the consecutive steps of preprocessing of EMG signals.

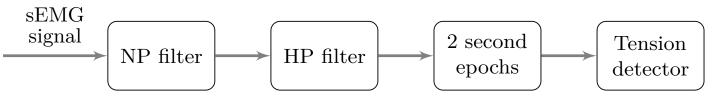

Figure 2.7: Schematic overview of preprocessing steps of sEMG signals that results in motion/tension epochs

A notch (NP) filter was used to remove power-line interference from sEMG signals. In addition, a high-pass filter of 20 Hz cut-off frequency was applied to remove the movement artifacts and baseline noise contamination [56]. As in case of ACM signals, the preprocessed sEMG data were divided into 2 second epochs with 75% overlap. An epoch containing more than 50% seizure activity was labeled as a seizure epoch. Finally, whenever the standard deviation in all sEMG channels was lower than 30 μV, the corresponding epoch was removed from further analysis. This *tension/activity detection* resulted in a 91.46±9.28% reduction of the initial number of epochs per recording. The threshold was chosen based on the standard deviation values during the tonic phase of tonic-clonic seizures in ACM signals.

Chapter 3

Machine learning techniques

A scientific field is best defined by the central question it studies. The field of machine learning seeks to answer the following question "How can we build computer systems that automatically improve with experience, and what are the fundamental laws that govern all learning processes?" [145]. This question covers the broad range of disciplines and tasks. Speech and face recognition, surveillance, motor control, brain-computer interface, finance, fraud detection and web search are just some of the applications.

We program the computers to optimize a performance criterion using example data or past experience [8]. We defined a model up to some parameters, and learning is the execution of computer program which optimize the model parameters using the training data or past experience. The model can be predictive, in case it makes predictions in the future, or it can be descriptive when it extracts the knowledge from the available data.

In machine learning, a feature is an individual measurable property of a phenomenon being observed [17]. Choosing informative, discriminating and independent features is a crucial step for effective models in pattern recognition, classification and regression. Extracting or selecting features is a combination of art and science. Combining the intuition and knowledge of the domain expert is a good starting point. However, many problems at hand are too complex given only a small number of examples and a large variability. Here we can benefit of the use of various developed feature selection methods. Feature selection techniques are able to explore multiple possibilities and the combination of a large number of features in automated way.

In the following sections we give the mathematical formulation of two feature selection methods and a binary classification technique that are applied in this thesis.

3.1 Notation and definitions

Before explaining the fundamental and mathematical formulations of machine learning methods employed through this thesis, we briefly introduce used notations and definitions.

From each movement epoch i of the training set (see Subsections 2.3.1 and 2.3.2), a feature value is calculated from each channel and stored in a single feature row vector of size $1 \times N_{ch}$ ($N_{ch} = 12$ for ACM and $N_{ch} = 2$ for sEMG modality). For N epochs, a single feature matrix $\mathbf{X}^j$ of size $N \times N_{ch}$ for each feature j is built, $j = 1, \ldots, N_f$. Hence, the total feature matrix with N_f features can be written as follows $\mathbf{X} = \left[\mathbf{X}^1, \mathbf{X}^2, \ldots, \mathbf{X}^{N_f}\right]$. The same matrix can be rewritten as follows $\mathbf{X} = [\mathbf{x}_1; \mathbf{x}_2; \ldots; \mathbf{x}_N]$ where $\mathbf{x}_i = [x_{i1}, x_{i2}, \ldots, x_{id}]$ is the i-th row vector ($d = N_f \times N_{ch}$). Corresponding column containing labels is denoted as $\mathbf{y}$. Henceforth, the defined notation is used to describe methods used in this thesis.

3.2 Feature selection methods

The initial set of features can be redundant and too large to be managed. Therefore, a preliminary step in many applications of machine learning and pattern recognition consists of selecting a subset of features, or constructing a new and reduced set of features to facilitate learning, and to improve generalization and intepretability. This process is called feature selection [18, 104, 223].

In general, we can distinguish three groups of feature selection methods: filter, wrapper and embedded methods [61]. In the following subsections, the main characteristics of these methods are described.

3.2.1 Filter feature selection methods

Filter methods include methods performed in the preprocessing phase on the training data, as an initial analysis of the feature's relevance, and afterwards the selected features are fed to the classifier. Hence, these methods filter the features independently of the classification algorithm. They are kept simple and therefore have a low computational cost. Features are ranked according to a predefined criterion, such as a $\chi 2$ test, information gain criterion, mutual information, cross-entropy measure, Fisher discriminant criterion, Pearson correlation coefficient or the Kruskal-Wallis test. Apart from these simple ranking critera, there are more advanced methods such as FOCUS and Relief [7, 103].

In this thesis, a feature selection method based on mutual information proven to outperform the others methods was applied, which is described in the next subsection.

Filter feature selection based on mutual information

The applied filter feature selection method based on mutual information, called maximal relevance minimal redundancy (mRMR), aims to identify the feature subset within which each selected feature has the highest mutual information with target class (i.e. label given by the EEG expert) and minimal mutual information among themselves [60, 166]. Starting from the empty set of chosen features $\mathbf{S} = \emptyset$ and the full set of N_f features $\mathbf{X} = \left[\mathbf{X}^1, \ \ldots, \ \mathbf{X}^{N_f}\right]$, first feature $(j = 1)$ was chosen as follows

$$\mathbf{S}^1 = \left\{\mathbf{X}^i \left| \max I\left(\mathbf{X}^i; \mathbf{Y}\right) \right.\right\}, \ \mathbf{X}^i \in \mathbf{X} \tag{3.1}$$

where $\mathbf{Y}$ is the label matrix constructed from the label column $\mathbf{y}$ which was repeated to match the size of the feature matrix and I is the mutual information defined as

$$I\left(\mathbf{u}, \mathbf{v}\right) = \sum_{i,j} p\left(\mathbf{u}_i, \mathbf{v}_j\right) \log \frac{p\left(\mathbf{u}_i, \mathbf{v}_j\right)}{p\left(\mathbf{u}_i\right) p\left(\mathbf{v}_j\right)} \tag{3.2}$$

with $p(\mathbf{u})$, $p(\mathbf{v})$ and $p(\mathbf{u}, \mathbf{v})$ probability density functions. Probability density functions were approximated by diffusion-based kernel density estimation, and adaptive kernel density estimation. They have been proven to outperform existing methods in terms of accuracy and reliability [22].

In case $j \geq 2$, an incremental search is performed using the following condition:

$$\mathbf{S}^j = \left\{\mathbf{X}^l \left| \max_{\mathbf{X}^l \in \mathbf{X} \setminus \mathbf{S}^{j-1}} \left(I\left(\mathbf{X}^l; \mathbf{Y}\right) - \frac{1}{j-1} \sum_{\mathbf{X}^k \in \mathbf{S}^{j-1}} I\left(\mathbf{X}^l; \mathbf{X}^k\right) \right) \right.\right\} \tag{3.3}$$

where $\mathbf{S}^{j-1}$ is the set of already chosen $j-1$ features.

Equation 3.3 ranks the features and the main question is when to stop the search. Generally, there are two options. We can keep the first n most relevant features. The choice of n will highly depend on the original number of features N_f. The other option is to pit a threshold on the argument of the max function on Equation 3.3. In both cases, some redundancy was inevitably kept within the chosen feature subset. Both stopping strategies were employed in this thesis as mentioned further on in individual studies details included.

Ding et al. demonstrated that the mRMR feature selection method is especially useful for large-scale feature selection problems [60]. Moreover, prior application of mRMR can enhance the wrapper feature selection method, achieving better classification performances [166].

3.2.2 Wrapper feature selection methods

The weakest property of the filter feature selection methods is that the impact of the classification algorithm is completely ignored. Therefore, the feature selection procedure should take the learning algorithm into account [99]. This leads to the second category of selection methods: feature selection techniques using the wrapper technique [104].

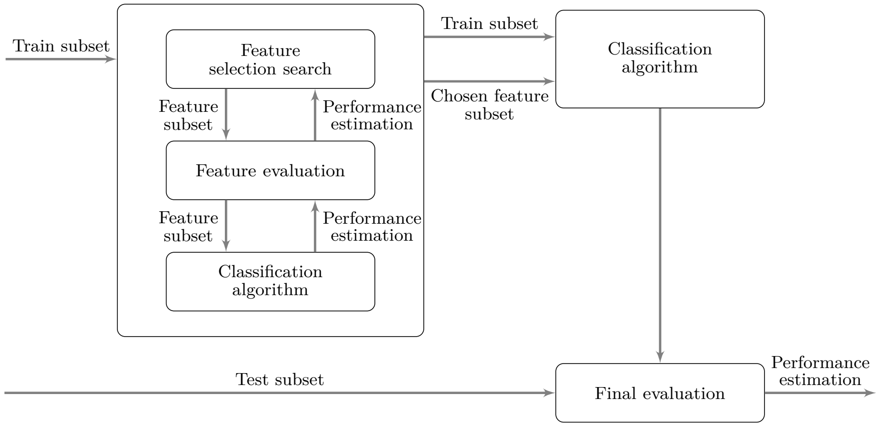

Figure 3.1: The wrapper approach for feature selection. The classification algorithm is used as a "black-box". From [104].

Wrapper methods regard the classification algorithm as a black box [104]. The classification performance is used as a criterion for the feature subset selection.

Thus, the obtained subset is optimized for the particular classification algorithm. Figure 3.1 illustrates this process. An exhaustive search can be performed if the number of features is low. However, with an increase of the number of features, a full search quickly becomes computationally unfeasible. Therefore, heuristic search strategies are employed using forward search or backward elimination. In the forward selection, features are incorporated one by one into the larger subsets, until the performance metrics start to saturate. On the other hand, a backward elimination strategy starts with all features and progressively eliminates the least significant feature until the performance metrics start to degrade. Main disadvantage of this strategy is that with an increasing number of features, the computational cost significantly increases.

For the purpose of this thesis, a wrapper feature selection method with previously described forward and backward search strategies was implemented using the least-squares support support machines (LS-SVM) classifier as a black box (see Subsection 3.3.1). The $F_1 score$, defined as the harmonic mean of the sensitivity and positive predictive value (equation 3.16), was used as an optimization and feature subset evaluation metric. Figure 3.2 illustrates the feature selection process in more detail.

The training data $\mathbf{X}$ are divided into the LS-SVM training $\mathbf{X}_{TR_w}$ and test $\mathbf{X}_{TE_w}$ sets with N_f features (N_f is added as superscript to indicate the number of features). In Figure 3.2, double subscript w is omitted for reasons of clarity, however we want to emphasize that these test data are not the final independent test data used to test the classifier.

3.2.3 Embedded feature selection methods

Apart from the filter and wrapper methods, also embedded methods exist. Embedded methods are performed in the training phase and these methods are usually specific to the given classification algorithm and computationally demanding. For example, least absolute shrinkage and selection operator (LASSO) computes weights for each variable according to their importance using a regularization procedure [208]. Recursive feature elimination (RFE) in conjunction with support vector machines is also a popular embedded method [82]. Since none of embedded methods was used in this thesis, we refer the reader to an overview of other integrated techniques in [18].

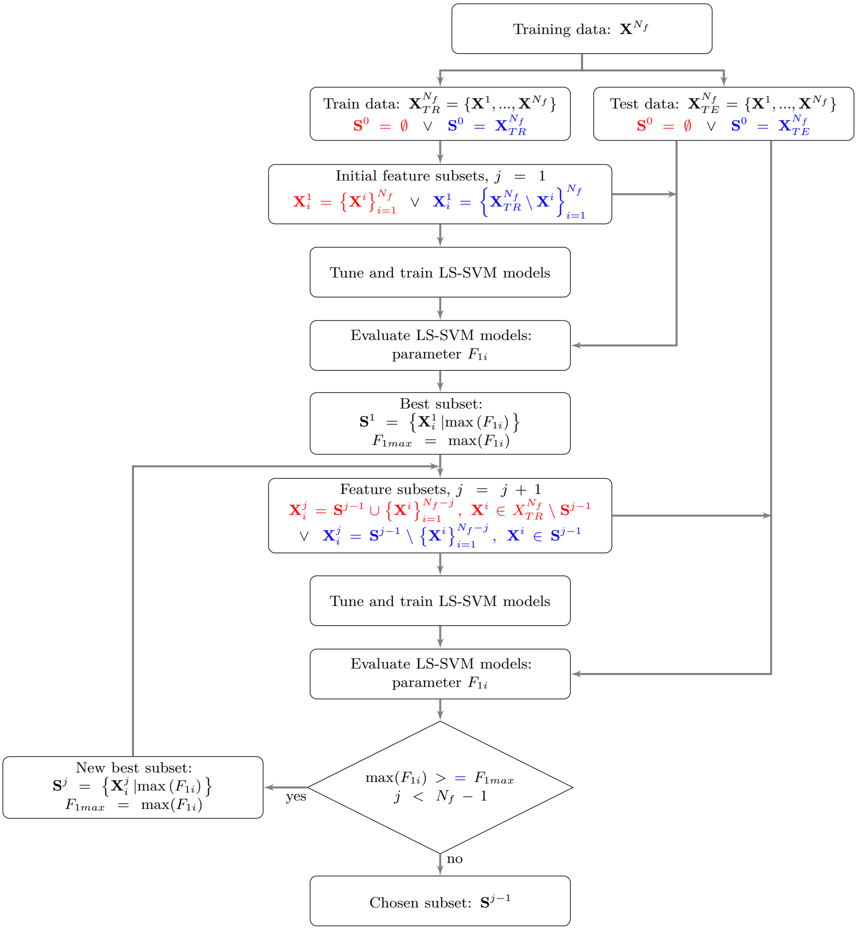

Figure 3.2: Wrapper feature selection methods with forward search (red track) and backward elimination (blue track) strategies. Prior to feature selection, the set of chosen features $\mathbf{S}^0$ is empty for forward search, whereas it contains all N_f features for the start of backward elimination. $\mathbf{X}_i^j$ are $i = 1, \ldots, N_f - j$ feature sets in iteration j which are built by adding/removing 12-dimensional features $\{\mathbf{X}^i\}_{i=1}^{N_f-j}$ to/from previous feature set $\mathbf{S}^{j-1}$. LS-SVM models are built for each $\mathbf{X}_i^j$ feature set and F_{1i} parameters are obtained (see equation 3.16). The feature set with the highest F_{1i} is selected and the procedure is continued until F_{1i} of the chosen set is higher or equal to F_{1max} from previous iteration $j - 1$ or all features are added/removed.

3.3 Supervised binary classification

Throughout this thesis, we only considered supervised classification methods, since the EEG experts annotated all signals. Hence, all available datasets were labeled. Moreover, we only considered two classes: seizure and non-seizure. Therefore, classification is restricted to binary classification here. Only one classifier was tested, namely least-squares support vector machines classifier, which is explained in the following subsection.

3.3.1 Least-squares support vector machines classifier

Support vector machines (SVM) are modern machine learning methods which use kernels to construct a linear hyperplane in a higher dimensional space for separation of two different classes [219].

If the training data set is denoted as $\{\mathbf{x}_i, y_i\}_{i=1}^{N}$, with $\mathbf{x}_i \in \Re^d$ being the input vector of features and $y_i \in \{-1, +1\}$ the class labels, SVMs map the d-dimensional input vector $\mathbf{x}$ into the d_h-dimensional space using a (non-)linear function $\varphi(\cdot) : \Re^d \to \Re^{d_h}$. Then, $\mathbf{w}^T \varphi(\mathbf{x}) + b = 0$ defines the separating hyperplane where $\mathbf{w} \in \Re^d$ is an unknown weighting vector, $b \in \Re$ a constant. Starting from the following formulation

$$y_i \left(\mathbf{w}^T \varphi(\mathbf{x}_i) + b\right) \geq 1, \quad i = 1, \ldots, N, \tag{3.4}$$

the classifier output is defined as

$$f(\mathbf{x}) = \operatorname{sign}\left(\mathbf{w}^T \varphi(\mathbf{x}) + b\right). \tag{3.5}$$

In real-life applications, perfect separation is not often possible, thus a certain number of misclassifications around the separation hyperplane should be tolerated. In this case, the resulting optimization problem becomes:

$$\min_{\mathbf{w},\xi,b} J_1(\mathbf{w}, \xi) = \frac{1}{2}\mathbf{w}^T\mathbf{w} + C\sum_{i=1}^{N} \xi_i, \tag{3.6}$$

such that

$$y_i \left(\mathbf{w}^T \varphi(\mathbf{x}_i) + b\right) \geq 1 - \xi_i, \quad \xi_i \geq 1, \quad i = 1, \ldots, N, \tag{3.7}$$

where C is a positive regularization constant which defines the trade-off between a margin size and misclassification error. Equation 3.5 can be equivalently written in the dual space using the Lagrange multipliers of support vectors α_i and chosen kernel matrices K:

$$f(\mathbf{x}) = \text{sign}\left(\sum_{i=1}^{\#\text{SV}} \alpha_i y_i K(\mathbf{x}, \mathbf{x}_i) + b\right), \tag{3.8}$$

with $K(\mathbf{x}, \mathbf{x}_i) = \varphi(\mathbf{x})^T \varphi(\mathbf{x}_i)$ and #SV number of support vectors. This relation is often called the kernel trick since no explicit construction of the mapping $\varphi(\cdot)$ is needed. This enables SVMs to work in a high-dimensional (or infinite-dimensional) feature space, without actually performing calculations in this space. One can choose from various types of kernel functions:

- linear SVM: $K(\mathbf{x}, \mathbf{x}_i) = \mathbf{x}_i^T \mathbf{x}$
- polynomial SVM of degree d: $K(\mathbf{x}, \mathbf{x}_i) = (\tau + \mathbf{x}_i^T \mathbf{x})^d$
- radial basis function (RBF) kernel: $\exp\left(-\frac{\|\mathbf{x}-\mathbf{x}_i\|_2^2}{\sigma^2}\right)$
- multi-layer perceptron (MLP) kernel: $\tanh\left(\kappa_1 \mathbf{x}_i^T \mathbf{x} + \kappa_2\right)$

where $K(\cdot, \cdot)$ is positive definite for all σ values in the RBF kernel case and $\tau \geq 0$ values in the polynomial case, but not for all possible choices of κ_1, κ_2 in the MLP case.

Many obtained α_i values are equal to zero, meaning that those training points do not contribute to the separation hyperplane. Only the training points close to the boundary are important for its creation ($\alpha_i \neq 0$) and are called support vectors. Therefore, skewed data will not affect the separating hyperplane.

Least-squares support vector machines (LS-SVM) are a modification of SVM methodology, by introducing a least square loss function and changing the inequalities in equation (3.4) into equalities [202]. Now instead of solving a quadratic programming problem, we need to solve only the set of linear equations. Therefore, this modification leads to a significant reduction in complexity and computational cost. A LS-SVM classifier optimizes the following problem:

$$\min_{\mathbf{w}, e, b} J_2(\mathbf{w}, e) = \frac{1}{2}\mathbf{w}^T\mathbf{w} + \gamma\frac{1}{2}\sum_{i=1}^{N} e_i^2, \tag{3.9}$$

subject to

$$y_i\left(\mathbf{w}^T\varphi\left(\mathbf{x}_i\right)+b\right)=1-e_i,\quad i=1,...,N, \tag{3.10}$$

where $e=[e_1,\ e_2,\ ...,\ e_N]^T$ is a vector of error variables. The classifier is again defined by (3.5) or (3.8), but now all Lagrange multipliers are different from 0; therefore all training points contribute to the construction of the separating hyperplane. However, the contribution of remote points is negligible (really low Lagrange multipliers) for the construction of the hyperplane.

Throughout this thesis solely RBF kernels were used. Even though linear kernels were also tested, their performance were always significantly lower compared with RBF kernels, suggesting a non-linear separation boundary was needed for separation of epileptic convulsions from other movements. LS-SVMlab [165] was used to perform all LS-SVM calculations in Matlab. The regularization parameter C and the width of the RBF kernel are obtained using a state-of-the-art global optimization technique Coupled Simulated Annealing (CSA) [227], which determines the parameters according to a given criterion.

3.3.2 Imbalanced dataset

A dataset is imbalanced if the classes are not approximately equally represented. We can say that usually real-word datasets are predominately composed of "normal" examples and a small percentage of "abnormal" examples. In case of seizure detection, the data are highly skewed; the seizures are rare events which should be distinguished from all other human motion and normal nocturnal movements. Generally, the cost of misclassification of an abnormal event is much higher than the cost of the reverse error. Traditional classifiers normally perform poorly on imbalanced datasets because they are designed to generalize from sample data and the model that best fits the data.

The machine learning community has addressed the issue of class imbalance in three ways. One is to assign different class-related costs to training examples [62,163]. The second is to resample the original dataset, either by over-sampling the minority class and/or under-sampling the majority class [29,96,110,116]. The last option is a combination of the previous two strategies [5,222].

In this thesis, the majority class was randomly under-sampled, whereas instead of minimizing the misclassification error which is the typical choice for LS-SVM training, we maximize the F_1score metric [170], which is the harmonic mean of the sensitivity and positive predictive value of epoch detection. If we compare the misclassification error

$$\sum_{i=1}^{N} e_i^2 = \frac{FP + FN}{TP + TN + FP + FN}, \tag{3.11}$$

with the $1 - F_1 score$

$$\sum_{i=1}^{N} e_i^2 = 1 - F_1 score = \frac{FP + FN}{2TP + FP + FN}, \tag{3.12}$$

we can see that optimizing the LS-SVM boundary by minimizing the full classification error can result in negligible classification error of non-seizures (low FN, high TN) and high misclassification of seizures (high FN, low TP). Switching to the maximization of $1 - F_1 score$, TN is removed from the denominator, whereas TP now contributes twice more to the sum.

3.4 Evaluation metrics

A very important aspect of building classifiers or the development of classification algorithms is the evaluation of their performance [2]. Starting from a confusion matrix for two class classification (Table 3.1), the developed classification models are evaluated in terms of

- Sensitivity is the percentage of the detected positive samples compared to the total number of positive samples:

$$SEN = \frac{TP}{TP + FN} \tag{3.13}$$

- Specificity is the percentage of the detected negative samples compared to the total number of negative samples:

$$SPEC = \frac{TP}{TN + FP} \tag{3.14}$$

- Positive predictive value (PPV) is the percentage of the detected positive samples compared to the total number of samples detected as positive:

$$PPV = \frac{TP}{TP + FP} \tag{3.15}$$

- F_1score is the harmonic mean of the sensitivity and positive predictive value:

$$F_1score = 2\frac{SEN \cdot PPV}{SEN + PPV} \tag{3.16}$$

- False detection rate (FDR) is the number of false detections divided by the total time of the measurement. It is expressed as the number of false alarms within 12 hours (one night).

- Latency detection or alarm delay is the time elapsed between the clinical seizure onset according to the labeling and the moment the detection system is setting off the alarm.

- While the aforementioned metrics are calculated for the specific decision threshold (bias term b in equation 3.10 in the case of LS-SVM classifier) obtained within the training process, the Receiver Operating Characteristic (ROC) curve is a function of sensitivity vs. 1-specificity obtained by varying the decision threshold. The area under the ROC curve can give a better insight on the distribution of the decisions. Area under the receiver operating characteristic curve (AUC) is often used to assess the overall performance of the developed classier. A classifier that gives random predictions results in an AUC of 0.5, whereas a perfect performance corresponds to an AUC of 1.

TP and TN are the number of correctly identified seizure (positive events) and non-seizure (negative events) epochs, respectively. FN represents the number of seizure epochs classified as non-seizure epochs, and FP the number of non-seizure epochs classified as seizure.

Table 3.1: A confusion matrix

		Detection algorithm output	
		TRUE	FALSE
EEG expert's annotations	TRUE	TP (True Positive)	FN (False Negative)
	FALSE	FP (False Positive)	TN (True Negative)

Metrics can be calculated on the level of the epochs (see Subsections 2.3.1 and 2.3.2) or on the level of events. In the latter case, some post-processing was performed. To eliminate possible false detection of short periods, a temporal constraint was applied to the LS-SVM output. The constraint only allowed detection of a seizure after the LS-SVM had classified a number of consecutive epochs containing seizure activity. In general, this post-processing greatly reduces the number of false positives, but also leads to a decreased sensitivity and increased detection latency. The post-processing (number of consecutive epochs needed for positive detection) highly depends on the use of the algorithm. Specific set-ups are described for each study.

Chapter 4

Feature selection methods for epileptic seizures

First, a literature overview of existing epileptic seizure detectors is given in Section 4.1. Subsequently we explore two feature selection methods, filter and wrapper. In Section 4.3 we describe the results of a comparison between models when no feature selection is used, when only a filter method is used, and when a wrapper method is applied after the filter algorithm (hybrid approach) with both forward search and backward elimination. The obtained results and conclusions of this study, submitted to [142], have motivated us to use only a filter method based on mutual information in the next studies. The results are discussed in Section 4.4. Finally, conclusions are drawn in Section 4.5.

4.1 Introduction

In the last decade, efforts were made to build a system for long-term home monitoring of epileptic patients which should offer an alternative to the gold standard video/EEG only performed in specialized hospitals. Main focus was on detection of convulsions related to the epileptic seizures using different single modalities or their combinations: video, ACM, gyroscopes, magnetometers and sEMG. Many research groups have been trying to develop a monitoring or/and alarm system based on some of the aforementioned sensors [11, 26, 37, 39, 48, 49, 108, 118, 153, 154, 170, 192]. The process of development of these systems is rather slow due to many reasons. The collection of data is a tedious process with slow progress due to the small number of available monitoring systems and small number of seizures. Data annotation is a laborious and expensive task. The detection system should be comfortable for the patients, easy to use for caregivers, and working with a perfect detection rate. However, this joint performance is difficult to achieve, mostly due to lack of data and huge inter- and intra-patient variability regarding the number, class and clinical manifestation of the epileptic seizures.

Many systems have been proposed, but still there is no perfect solution. Research groups employed different motion sensors and their combinations to detect specific seizure classes. Most of the algorithms were based on the use of a classification algorithm, such as SVM. Different features were fed to a chosen classifier and performance metrics were extracted [11, 39, 153, 170]. The number and type of features varied significantly from study to study. Various criteria were used to choose the features. Features were selected by 1) mimicking the expert's knowledge while screening and annotating the data, 2) visualization of feature space and the separation of the different classes, or 3) the features were borrowed from similar studies. All these approaches have their disadvantages. Experts rely on video/EEG data to determine seizure occurrence, and then video and motion sensor (in most cases ACM) data to determine the classes of epileptic seizures. Examining only motion data, the experts would not be able to correctly identify and characterize seizures. Visualization of feature space becomes demanding as the number of features grows. Moreover, the chosen features can be redundant and used sets are not optimized for the employed classification method. Thus, minimal experimentation has been performed in relation to finding the most informative features for this application.

A recent study [119] investigated the performance of 65 features in terms of EEG-based seizure detection performance and computational complexity. The goal of this work was to perform a similar analysis on the largest ACM database with 1498 labeled nocturnal epileptic seizures of pediatric patients. Instead of examining each feature individually, as in [119], features were combined in this study. Additionally, in order to overcome aforementioned feature selection disadvantages, feature selection approaches, filter and hybrid, were applied. The latter approach consisted of filter and wrapper feature selection methods applied one after the other. The filter method removes a high number of irrelevant and redundant features, allowing the application of the wrapper method. The main goal was to determine a significantly smaller subset of relevant features that preserved the performance metrics at the same level as when all features were used. As a consequence, this will result in the reduce of the overall computational complexity of the detection algorithm. In total, 140 features were taken from publications which considered detection of epileptic seizures, EEG-based seizure detection and ACM-based activity detection. The feature selection analysis was performed for each epileptic seizure class separately and then jointly. As a part of a long-term project [48, 50], this study should provide new insights into ACM-based seizure detection which would facilitate the further design of methods for home monitoring of pediatric patients.

4.2 Materials and Methods

Figure 4.1 depicts the consecutive steps of the entire procedure involved in feature selection, training and testing. The following sections describe each step in detail.

4.2.1 Data collection and partition

In this study, first 51 children and adolescents monitored in the Rehabilitation Center for Children and Youth in Pulderbos, Belgium participated (see Table 2.1). At the moment of this research, 143 nights were available. After excluding the patients without seizures and with frontal lobe seizures with hyperkinetic movements (analyzed in [48]), 1498 labeled seizures of 25 patients were kept. Table 4.1 summarizes the number and classes of seizures per patient. In addition, 18 of 83 recordings were excluded from analysis; they contained nonfunctional (or broken) channels. In order to exclude the influence of broken channels, these recordings were removed from the analysis.

The clinical characteristics of the seizure classes found in Table 4.1 are explained in Subsection 1.1.1, whereas some examples of clinical manifestations in ACM signals of main seizure classes are illustrated in Appendix A. From Table 4.1 we can see that the number of seizures and classes of seizures per patient vary significantly.

Figure 4.1 illustrates the performed analysis which is applied to all seizure classes individually (clonic, tonic, spasms and myoclonic) and then jointly (i.e. epileptic seizures). The number of tonic-clonic seizures is significantly lower than the number of other seizure classes, therefore the separate feature selection and classification was not performed for this class of seizures. Nevertheless, these seizures (and corresponding recordings) were added as test data to the clonic seizure detection algorithms, as it was expected that the algorithm would be able to detect the clonic part of a tonic-clonic seizure. In the case of clonic and tonic seizures, the continuous data till the end of the 5th seizure of each patient were used for both feature selection and building the LS-SVM classifier (i.e. training). The remaining data were used to test a seizure detection algorithm with a reduced number of features on the independent data. Due to the higher

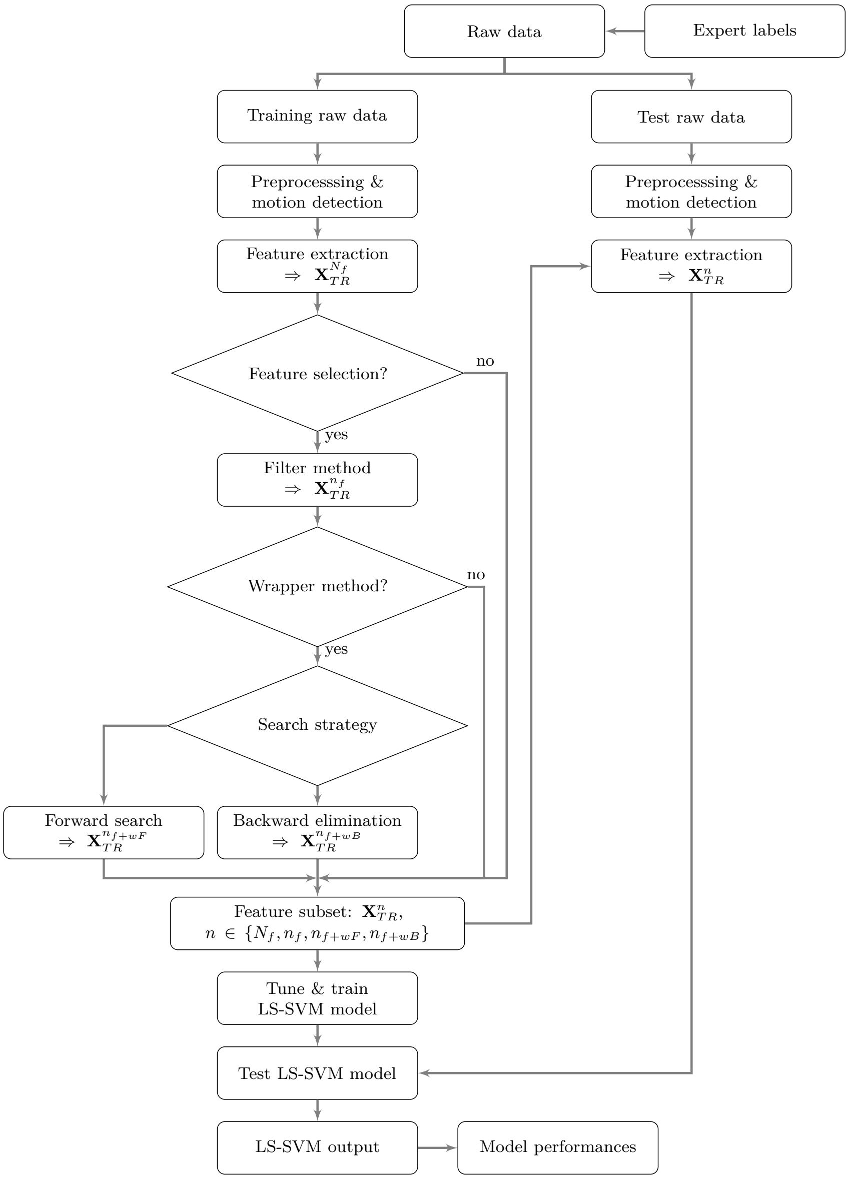

Figure 4.1: Methodology scheme: no feature selection, only mRMR feature selection, and hybrid feature selection method when wrapper method is applied with forward search and backward elimination strategies.

Table 4.1: Database overview: in addition 21 patients (31 nights) did not have seizures and 5 patients had only frontal lobe seizures (56) during 29 nights

	Complete recordings		Incomplete recordings	
Patient code	Epileptic seizures*	# nights	Epileptic seizures*	# nights
2	55S, 1S series	2		
3	26M, 2C, 1T, 9S, 1S series, 2FL, 2U	18	3M, 1M series, 3T	2
7	5S, 1S series	1		
9	7M, 2T, 15S	3	4M, 3S	1
10	2M, 1S	1		
11	9M, 3TC, 3V	1	40M, 51T, 106S, 6TC, 3V	1
13			5M, 2T	1
17			1M, 20T, 8S, 2U	1
18	1U	2		
19	2M, 2FL	1		
21	17T, 3S	5		
22	1C, 1S, 2S series	2	1S series	1
24	10M, 4S, 1S series	3	4M, 2C, 1TC	2
25	1M, 8U	2		
26	9M, 1C, 1S	4		
28	2M, 3S	2	1S, 1U	1
30	6C, 1S	3	1M, 1M series	2
32	1M, 3T, 5S	4	7M, 4S	2
35	11M, 3T, 10S, 2S series, 1TC, 1U	2	11M, 3T	1
39	1M, 24T, 1S	2	1M, 1T	1
40	2M, 13C, 5T, 10S	2	2M, 1T, 1S, 2U	2
46	23M	1		
47	1C	1		
48	9S, 1TC	2		
51	49C	1		
25 patients	106M, 73C, 55T, 73S, 8S series, 5TC, 3V, 4FL, 12U	65	78M, 2M series, 2C, 81T, 123S, 1S series, 7TC, 3V, 3U	18

*M = Myoclonic, S = epileptic Spasm, T = Tonic, C = Clonic, TC = Tonic-Clonic, V = Versive, FL = Frontal Lobe seizure, U = Unclassified seizure, M/S series = Myoclonic/Spasm series number of seizures, for epileptic spasms, myoclonic and epileptic seizures (all seizure classes together), the first 15 seizures were used for training and the rest for the testing. These divisions were chosen in order to select enough data for reliable feature selection and training, and still keep some data for testing. As a consequence, the number of test seizures was always higher than the number of training seizures, except for myoclonic seizures (see Table 4.2). Tuning of the parameters (width of RBF kernel and generalization parameter) was performed in 5-fold cross-validation procedure using grid-search approach. Once the data were divided into the training $\mathbf{X}_{TR}$ and test $\mathbf{X}_{TE}$ sets, the analysis was performed as indicated in Figure 4.1. Following blocks will be explained in the subsequent subsections.

Table 4.2: Number of seizures in training and test sets per seizure class

Seizure class	# seizures in training set	# seizures in test set
Myoclonic seizures	86	19
Epileptic spasms	79	420
Tonic seizures	24	31
Clonic seizures*	19	53C + 5TC
Epileptic seizures	316	551

*C = Clonic, TC = Tonic-Clonic seizures

4.2.2 Preprocessing and feature extraction

The preprocessing consisted of filtering, downsampling and data reduction which are explained in Subsection 2.3. The final output of the preprocessing is motion epochs from which various features are extracted.

Systematic literature review was performed in order to gather possible features for detection of epileptic seizures. Papers related to ACM-based seizure detection algorithms were taken into consideration [11, 39, 48, 153, 154, 170]. In addition, features used in EEG-based seizure detection [119, 205] and ACM-based activity detection algorithms [100, 175] were added to the list. All these features which had been fully described and were applicable to ACM measurements were included into the initial feature subset. In total $M = 140$ features from each ACM channel were included: 33 in the time domain, 33 in the frequency domain, 10 derived from the continuous wavelet transform (CWT), 62 from the packet wavelet transform (PWT) and 2 from a recurrence plot (RP) analysis. The final feature vector consisted of $12 \times 140 = 1680$ variables. The full list and definitions of features are given in Appendix B.1 (first 140 features).

4.2.3 Feature selection

In this study, we focused on two feature selection methods, an mRMR filter method based on mutual information (Subsubsection 3.2.1) [60, 166] and a wrapper method based on a LS-SVM classifier (Subsection 3.2.2). Wrapper method was programmed to work both with forward search and backward elimination strategies. These methods were combined in the two-stage process, here called hybrid feature selection method. First, the filter method was applied to quickly remove a high number of irrelevant and redundant features, and then the significantly smaller subset was even more reduced by applying the wrapper method both with forward selection and backward elimination. Both feature selection methods were extended to work with multivariable features, taking all 12 ACM channel values as one feature and evaluating their relevance as a whole (we started from $12 \times N_f, N_f = 140$ feature vector and in the end we had $12 \times n$, where n is the number of selected features). Since the number of seizures and their classes significantly vary over the different patients, a bootstrap technique was applied [81]; each feature selection algorithm was run 50 times on different randomly-chosen subsets of data points (500 seizure epochs and 2500 non-seizure epochs) and the importance of each feature was evaluated using the number of its appearance in these 50 optimal feature subsets. The features which appeared more than 75% of the number of runs (i.e. in more than 35 times of the 50 runs) were kept for further analysis.

4.2.4 Evaluation metrics

To evaluate the chosen features, the following metrics were calculated: the area under the ROC curve for epoch detection which gives a better insight on the distribution of the decisions; seizure detection sensitivity when at least one epoch within the seizure was detected, false detection rate per hour, and detection delay between the first positively detected epoch and the clinical onset of the seizure. The value of false detection rate per hour is calculated as the number of successively grouped FP epochs.

All metrics obtained with the complete feature set, the feature subset after the filter method, the feature subsets after hybrid method (filter plus wrapper method) when wrapper method is applied with both forward search and backward elimination were statistically compared using Friedman paired test and Tukey's HSD (honestly significant difference) test. The Friedman test is a non-parametric paired test working with ranks. The assumption of normality is not acceptable. When multiple significance tests are performed, the chance of finding a significant difference just by chance increases. Tukey's HSD test is one of several methods of ensuring that the chance of finding a significant difference in any comparison (under a null model) is maintained at the alpha level of the test. In addition, the purpose of Tukey's HSD test is to determine which groups in the sample differ. While a Friedman test can tell whether groups in the sample differ, it cannot tell which groups differ.

4.3 Results

The features obtained with the filter method using mutual information are listed in Table 4.3. The number of chosen features for different seizure classes ranged from 15 to 28. Some features, such as complexity, laminarity and some PWT features were relevant for multiple seizure classes, while others were seizure class-specific. CWT features used in many ACM-based seizures were completely excluded [11, 153], opposite to DWT features which contain similar information [39].

Table 4.3: mRMR filter method: selected features per seizure class (*See the definition of individual features in Appendix B.1; **PWT1 features are based on the sum of the absolute PWT coefficients, while PWT2 on the energy of these coefficients; DAA3 are the detail coefficients of approximation of approximation of an input signal)

Domain	Feature names*	Myoclonic seizures	Epileptic spasms	Tonic seizures	Clonic seizures	Epileptic seizures
Time	25th percentile value			×	×	
	50th percentile value				×	
	75th percentile value			×	×	
	Range of x	×			×	
	Range of x_{fst}	×				
	Entropy		×			
	Variance of x''				×	
	Skewness	×	×			
	Kurtosis			×	×	×
	Zero-crossing rate of x		×	×		
	Zero-crossing rate of x''			×		×
	Mobility	×	×		×	
	Complexity	×	×	×	×	×

Frequency	Dominant frequency				×	×
	1st local peak in spectrum		×			
	3rd local peak in spectrum	×				
	4th local peak in spectrum	×	×		×	×
	Spectral centroid					×
	Spectral edge frequency 10%			×	×	
	Spectral edge frequency 85%		×			×
	Power in 12-14 Hz band	×				
PWT1**	AAD3			×	×	
	DAAA4		×	×		×
	DDDA4			×		
	AAAD4				×	
	DAAD4			×	×	×
	DDAD4		×	×	×	×
	DDDD4				×	×
PWT2**	AD2	×		×		×
	DAA3	×	×	×		×
	ADA3			×	×	
	DDA3			×		
	AAD3	×	×	×	×	
	DAD3	×	×	×	×	
	DDD3	×	×	×	×	
	DAAA4	×		×	×	×
	ADAA4	×		×		
	DDAA4			×		
	AADA4			×	×	
	DADA4	×		×	×	
	DDDA4			×	×	
	AAAD4			×	×	
	DAAD4			×	×	
	DDAD4				×	
RP	Entropy	×	×			
	Laminancy	×	×	×	×	×
	# features (n_f)	18	16	28	28	15

Next, a wrapper feature selection method incorporated with a LS-SVM classifier was performed on the feature subset obtained by the filter method. Both strategies, forward search and backward elimination, were applied. Table 4.4 contains the chosen features. In general, more features were selected by backward elimination strategy, since it takes into consideration the relation between the different features. Most of the features were time-domain features, which in general have a low computational complexity (time needed to calculate the feature) [119]. Epileptic seizures which contain twitch-like contractions (myoclonic and clonic seizures) can be detected with simple statistical features, mobility and complexity. For the detection of tonic seizures, two features based on zero-crossing rates were the most optimal features.

Comparisons between LS-SVM models built upon the complete feature set, mRMR subset and mRMR and LS-SVM wrapper forward and backward subsets were performed by means of the defined metrics on the test data and statistical analysis. Area under the ROC curve for epoch detection (AUC), sensitivity when at least one epoch per seizure was detected, latency of the first detected epoch compared to the clinical onset of the seizure and false detection rate per hour (FDR/h) are presented in Figure 4.2. Due to the small number of test data, reliable statistical comparisons were not possible for myoclonic and tonic seizure classes.

AUC on epoch-detection level gives the overall performance of the classifier. AUC for (tonic-)clonic seizures did not significantly degrade with the reduction of the number of features, however the median values dropped from 0.72 to 0.68. On the other hand, in the case when all epileptic seizures were joined, AUC significantly decreased with feature reduction ($p < 0.001$) which is probably due to the increased diversity. Sensitivity of one epoch detection varied significantly from patient to patient. In the case of (tonic-)clonic seizures, sensitivity values cover the range from zero to 100, since many patients had only one test seizure which was detected or missed. Median latency per patient was quite low for detected tonic, myoclonic and spasm seizures, while for clonic and tonic-clonic seizures latency mounted up to 25 seconds. False detection rate per hour was quite high for most of the patients and in the case of (tonic-)clonic and epileptic seizures it increased with feature reduction ($p < 0.01$ and $p < 0.001$ respectively).

Table 4.4: Hybrid method - selected features per seizure class and search strategy

		Myoclonic seizures		Epileptic spams		Tonic seizures		Clonic seizures		Epileptic seizures	
Domain	Feature names*	F	B	F	B	F	B	F	B	F	B
Time	Range of x							×	×		
	Entropy		×	×	×						
	Skewness		×								
	Zero-crossing rate of x				×	×	×				
	Zero-crossing rate of x''					×	×				×
	Mobility	×	×	×	×			×	×		
	Complexity								×		×
Frequency	Spectral edge frequency 10%								×		
	Spectral edge frequency 85%									×	×
PWT1	DAAA4										×
RP	Entropy				×						
	# features (n_{f+w})	1	3	2	4	2	2	2	4	1	4

*See the definition of individual features in Appendix B.1

**Wrapper search strategy: F for forward search and B for backward elimination

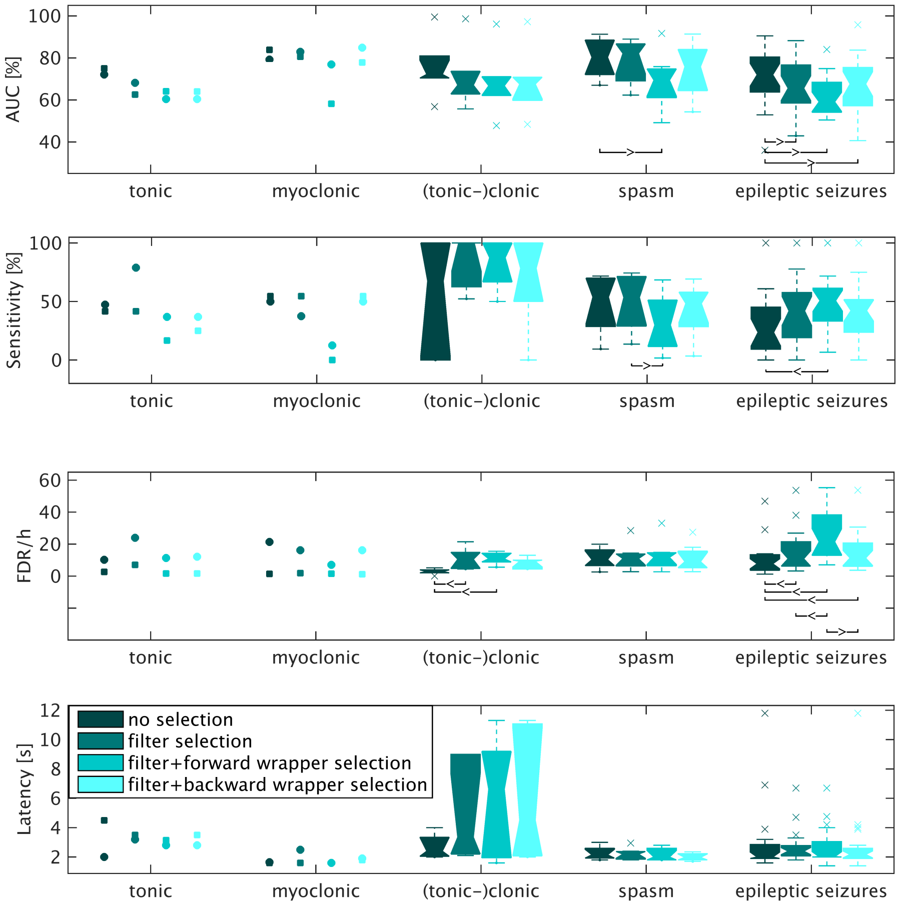

Figure 4.2: Seizure detection performance: area under the ROC curve, sensitivity (at least one epoch detected), median latency and false positive rate per hour for all test datasets when complete feature set is used, after the filter method, after the hybrid methods (wrapper method was applied with both for forward search and backward elimination). The significant differences between the groups are annotated with $>$ or $<$ depending on the relation between the groups. In the case of myoclonic and tonic seizures, two test patients are denoted here by a square and a circle.

4.4 Discussion

In this work, two feature selection algorithms were investigated. Filter method was applied individually and in the cascade with the wrapper method, composing the hybrid feature selection method. While the mRMR filter method gave the most relevant non redundant feature subset, the LS-SVM wrapper gave the suboptimal subset of features optimized for the LS-SVM classifier. With the first method, the number of features was significantly reduced, from 140 to 15-28 features, which enabled the application of a wrapper method.

In many publications, the three-axis of an ACM sensor are often combined into an acceleration magnitude (root mean square of the sum of squared channel values) which is further used for feature extraction [11, 39, 48, 49, 170]. In that case, one can apply feature selection methods to reduce both the number of features and the number of sensors. This approach was tested and it resulted in inconsistency over the features and sensor locations. We opted to keep the original information available within ACM channels for distinction of epileptic seizures from other movements. In addition, considering 12 values calculated from all ACM channels as one feature could be the input for tensor learning algorithms which are able to take into account the spatial relations between the channels [88]. A separate study will be performed to assess if the incorporation of the structural information from multichannel ACM recordings improves the detection of epileptic seizures.

Similar studies which used ACM (in combination with other modalities) never used 140 features together; however the number of features was significantly higher compared to the number of feature after the application of feature selection in this study. In previous publications mostly wavelet-decomposition derived features were used, alone or in combination with other features [11, 39, 153, 154]. Only PWT features were found relevant. However, it was unfeasible to test the importance of all PWT features from [39]. We could only calculate features within a two second epoch until the 4th level of decomposition (instead of the 6th level as done in [39]) using Daubechies 5 wavelets.

Using cascade feature selection, mostly time domain features had been obtained, facilitating faster algorithms. This methodology confirmed the importance of zero-crossing rate (ZCR) as a feature for distinguishing the nocturnal epileptic convulsions and normal in-bed movements, since ZCR has already been used for sEMG-based detection of tonic-clonic seizures [37]. Apart from ZCR, Hjorth's parameters (mobility and complexity) had been recognized as relevant features. To our knowledge, these parameters were never used for ACM-based seizure detection. Other chosen features had already been employed in previous publications, but as part of much larger feature sets [11, 153].

In case of hybrid feature selection approach, the classification performances significantly depended on the chosen wrapper search strategy. This difference was in the direct relation to the number of chosen features. In the case of backward elimination, the number of chosen features was always higher or equal compared to the ones obtained by forward search. Using forward search a single feature was permanently removed in each iteration. Thus, the effects of combined features were not always taken into consideration. However, the least degradation in all performances was observed using only the mMRM method, except in the case of latency for (tonic-)clonic seizures. When all features were used, the sensitivity for some patients was zero, while these seizures were detected when the mRMR feature selection method was applied, although with a higher latency.

The obtained results suggest that seizure class specific models have better performance. Moreover, some seizure classes are more easily detected with accelerometry. For instance, accelerometry is not suitable for the detection of tonic seizures since these seizures manifest themselves in a slow change of limb posture and usually there is not much acceleration activity during these seizures. On the other hand, it is easier to detect seizures such as (tonic-)clonic ones using accelerometry due to the specific rhythmic movements of the limbs.

In general, the number of seizures per patient used for the feature selection, LS-SVM training and testing was limited. Moreover, patients with a small number of seizures did not participate in the testing. We chose to build one algorithm on semi-patient-specific data (smaller number of patient-specific seizures and larger number of other-patient seizures) as a compromise between algorithm performance and computational load (computational time). Nevertheless, the bias induced with this strategy sometimes resulted in large differences in classification performances between test patients. However, this is not the only reason for the inconsistency over the patients. Seizures from a same patient were sometimes clinically diverse, and the trained models were not able to perform well for all possible clinical manifestations. One possible solution is to make subgroups of ACM-similar seizures within one seizure class and build the models for each subgroup.

Other groups tried to detect epileptic seizures. Nijsen et al. investigated the detection of myoclonic seizures by means of accelerometers [154]. Various methods were tested, resulting in a maximal sensitivity of 80%, but all with a high FDR. While in [154] the algorithm was tested on segments containing seizures, normal movements and no movements, we used all data of two test patients reaching only 50% sensitivity. More test data are needed to assess the real value of the model. Conradsen et al. [39] used a multimodal approach to detect simulated tonic-clonic seizures. A sensitivity of 100% with a FDR between 0 and 18 h^{-1} were obtained using ACM, magnetometer, gyroscope and sEMG data. Developed models still have to be tested on real data. Poh et al. [170] developed a wrist-worn electrodermal activity and ACM biosensor to detect generalized tonic-clonic seizures. 15 of 16 generalized tonic-clonic seizures are detected with 130 false alarms (0.74 alarm/h). We joined clonic and tonic-clonic seizures, and median sensitivity using only features obtained with the mRMR method was 100%, although for some patients only half of the seizures were correctly identified. Within our database we observed large inter- and intra-patient seizure morphology which is not present in simulated and generalized tonic-clonic seizures which generally have stereotypical patterns. In addition, the latter two publications used a multimodal approach which takes into consideration more aspects of epileptic seizures.

Generally, the obtained FDR was significantly higher than in aforementioned publications, which is the consequence of the way this metric was estimated. Each segment of false positive successive epochs was considered as one false alarm even when there are two segments only a few seconds apart. Thus, the output of the classifier was treated the same both for sensitivity and FDR estimation, which was not the case in other publications [39].

As mentioned in Section 4.2.1, 22 recordings (18 patients) with 631 seizures had been removed from the feature selection analysis. These valuable data had to be removed in order to exclude the influence of missing values and used imputation techniques on the feature selection. A separate study has to be performed to evaluate the influence of missing values and missing value imputation techniques on the feature selection and classification.

Although reached performances are not clinically acceptable, this study showed that using solely an mRMR feature selection algorithm, which is not computationally demanding, led to no significant degradation of classification performance. The best performances were obtained for (tonic-)clonic seizures which are the main candidate for a future alarm system, since they can potentially lead to physical and brain injuries.

4.5 Conclusion

The aim of this study was to investigate the use of feature selection methods within machine learning framework for detection of epileptic seizures using accelerometry. We proposed a two-stage feature selection strategy, including mRMR filter and LS-SVM wrapper selection methods applied one after the other. However, applying only a filter feature selection method, the obtained classification results had comparable performance with respect to the complete feature set. There was no need for the application of a wrapper method which is computationally demanding. Leading performances were obtained for (tonic-)clonic seizures, with median sensitivity of 100%, but a high FDR. The proposed methodology and obtained results should be further validated by adding new data and within the real-time seizure detection algorithm.

Chapter 5

Accelerometry-based detection of prolonged epileptic seizures

In the previous chapter the feature selection for ACM-based detection of epileptic seizures was discussed. The obtained results were used to build automated detection of tonic-clonic and clonic seizures, which is presented in this chapter. First an overview of the literature is given in Subsection 5.1.1. Proposed methodology is described in Subsection 5.1.2. In Subsection 5.1.3 the results of patient-independent algorithms are presented using the Pulderbos datasets (published in [139]). The results are discussed in Subsection 5.1.4. Finally, conclusions are drawn in Subsection 5.1.5. In Section 5.2 methods developed in the Section 5.1 are applied on data recorded in a home-replacement environment when only the observations of professional caregivers are available (to be submitted to [141]). The results of patient-independent, patient-specific and semi-patient-specific algorithms are presented in Subsection 5.2.3. They are discussed in Subsection 5.2.4. Finally, conclusions are drawn in Subsection 5.2.5.

5.1 ACM-based detection of epileptic seizures through a machine learning approach

5.1.1 Introduction

Existing literature on epileptic seizure detection using solely ACM data or in the combination with other modalities, widely vary in approach, intentions and outcome [12, 39, 48, 108, 118, 170, 192]. Individual research groups have been investigating their own particular databases using their own device(s) and their own data collection protocols, and have been applying a wide variety of algorithms and methods. Therefore, it is difficult to make significant comparisons or draw meaningful conclusions except that ACM shows promise in registration and detection of epileptic seizures.

Most of the studies use one accelerometer fixed on the wrist or on the upper arm [12,39,108,118,170,192]. A smaller number of studies tried to use multiple accelerometers attached to the wrists, legs, chest and/or head [12,48]. The use of a larger number of ACMs is likely to provide a higher accuracy in terms of epileptic seizure classification. However, such a system is also likely to be too cumbersome and inconvenient for long-term monitoring of epileptic patients.

A variety of classification methods have be tested. A small number of publications have focused on the development of simple threshold-based algorithms or rule-based heuristic methods [12, 192]. Other researchers employ automatic machine learning methods including the most popular support vector machines and others [39, 48, 170]. It is not clear which of these methods is most effective for this particular application, since these methods are mostly tested on simulated data and/or preselected data [12, 39, 192]. Hence, the reported results are too optimistic.

This study investigates the application of machine learning techniques to construct patient-independent classifiers capable of detecting seizures with high accuracy. Unlike previous efforts, which do not make a distinction between adults and children, we evaluate our patient-independent classifiers on epileptic seizures in pediatric patients. These seizures even though classified as severe do not always last as long as in adults. Moreover, they are sometimes subtle.

Within the discriminative framework we choose to solve a binary classification problem, despite the fact that the underlying physiological activity is multiclass. We do so because it is neither easy nor practical for an algorithm to identify and label all subclasses of seizure and non-seizure events. Moreover, not all seizure classes are suited for the alarm system; frequent short seizures are not harmful for the child well-being; however, prolonged and heavy seizures require an alarm as early as possible after the EEG onset of the seizures, so that proper actions could be conducted. The focus is on the distinction of (tonic-)clonic seizures from all other movements since these seizures are mostly prolonged and dangerous and they contain rhythmic components most suitable for the ACM-based registration and detection.

In the current setup we use four 3D accelerometers attached to the wrists and ankles to register leg and arm movements. The key part of this study is a completely automated process for contracting a feature vector selecting the most relevant and discriminative features through use of a feature selection process. We used the entire real-life recordings, without rejection of any data. Moreover, in evaluating our approach to seizure detection, we avoided testing the methodology that might result in overly optimistic results. Since, seizures are rare events and patient-specific seizure detectors are often very costly to develop, we present a patient-independent approach which is more appropriate for practical use and newly epilepsy-diagnosed patients.

5.1.2 Materials and Methods

Figure 5.1 depicts the consecutive steps of the entire procedure involved in the construction of patient-independent algorithms. The following sections describe each step in detail.

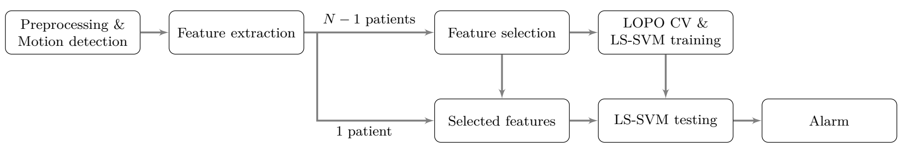

Figure 5.1: Schematic overview of the patient-independent algorithms. Abbreviations used in figure: leave-one-patient-out (LOPO) cross-validation (CV), least-squares support vector machines (LS-SVM), N is number of patients

Data collection and preprocessing

In this study only data of patients with (tonic-)clonic seizures were used. Table 5.1 gives the overview of the number of labeled seizures, their median duration and number of nights per pediatric patient. Even though patient 54 (see Table 2.1) had clonic seizures, he was removed from the analysis since the child's limbs were constantly restrained. In addition, two clonic seizures of patient 67 were removed since the ACMs were detached at the occurrence of these seizures; hence nothing was recorded. All the data from each recording were included in the analysis regardless on the record length and quality, whether the child was awake or asleep. A total of 237:09:11 of ACM data were analyzed.

Table 5.1: Database overview: C for clonic and TC for tonic-clonic seizures

Patient code	♯ seizures	♯ nights	Median seizure duration [s]
3	2C	1	11.9
11	9TC	2	7.9
22	1C	1	33.6
24	2C+1TC	1	4.3
26	1C	1	14.2
30	6C	1	14.4
35	6C+2TC	4	10
40	13C	1	10.3
47	1C	1	32.3
48	1TC	1	62.2
51	48C	1	1.8
57	3TC	1	57.4
67	3C+5TC	2	45.6
72	2C+10TC	1	35.8
Total	85C+31TC	19	8.4

In general, (tonic-)clonic seizures have stereotypical clinical manifestation. At the onset of the seizure, after short body tension in the case of tonic-clonic seizures, a child's limbs develop fast and uncontrollable rhythmic activity. However, in our large-scale database, limbs involved and the duration of this rhythmic activity highly differs across different patients and also within each patient which is illustrated on Figure 5.2. Seizure A is generalized prolonged clonic seizure, whereas seizure B is (clinically) focal prolonged clonic seizure. Finally seizure C, although labeled as clonic, is short and involves only the right arm, same as seizure B. Figure 5.3 presents the histogram of seizure duration.

The preprocessing consisted of filtering, downsampling and data reduction which are explained in Subsection 2.3. The final output of the preprocessing are motion epochs from which various features are extracted.

Feature extraction and selection

Same 140 features used in Chapter 4 were calculated from each ACM channel [11, 39, 48, 100, 119, 153, 154, 170, 175, 205]. The final feature vector consisted of

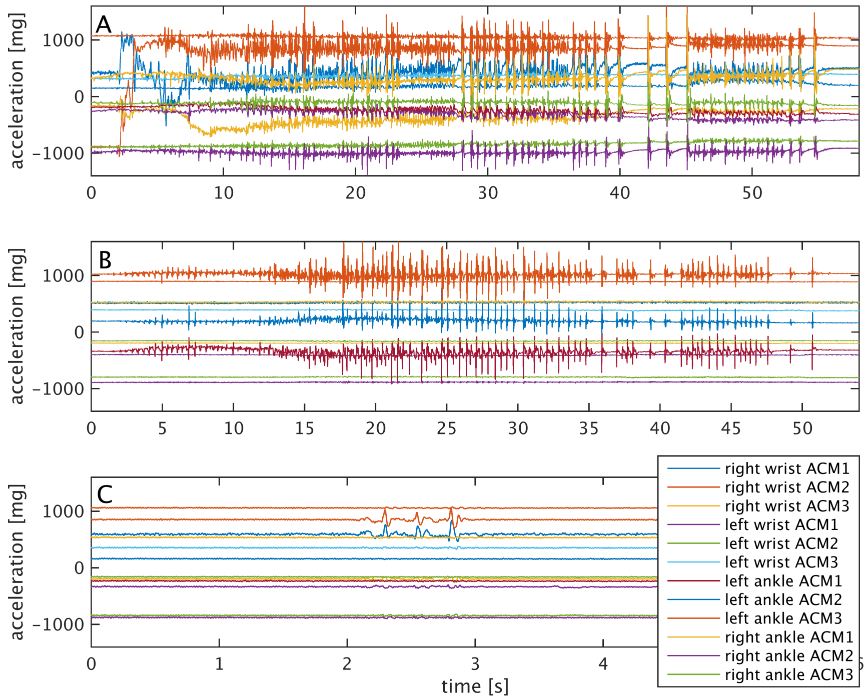

Figure 5.2: Three clonic seizures of the patient 51 during one night: Seizure A is a generalized prolonged seizure, seizure B is a focal prolonged seizure and seizure C is short focal seizure

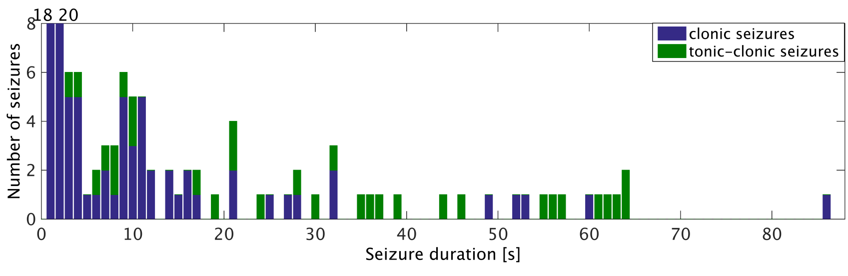

Figure 5.3: Histogram of (tonic-)clonic seizure duration. In total, there are 38 seizures shorter than 2 seconds (only of patient 51).

$12 \times 140 = 1680$ variables. The full list and definitions of features are given in Appendix B.1 (first 140 features).

In chapter 4, we found that applying only a filter feature selection method, called maximal relevance minimal redundancy (mRMR) [166], the obtained classification results had comparable performance with respect to the complete feature set. Moreover, there was no need for the application of a wrapper method which is computationally demanding. In this study, we use the mRMR filter feature selection methods to select the most informative features for distinction of (tonic-)clonic seizures versus all other movements. All features for which the difference between the mutual information between that feature and the target class and the mean mutual information between that feature and already chosen features was positive (see equation 3.3) were kept for further analysis.

Classification

Features obtained using mRMR feature selection methods were fed to the LS-SVM classifier (see Subsection 3.3.1). In real-life applications, the most practical procedure would be if the existing classification model built on the previous patients could be used on a newly arrived epileptic patient. Thus, within this study, the training is performed on all patients' data except one, which is left out for the testing of the built model (leave-one-patient-out (LOPO) testing). Due to the high inter-patient variability, we can expect that for some patients, a classification model developed on other patients will not work with acceptable accuracy.

Evaluation metrics

The patient-independent classifiers were evaluated as seizure alarm systems. An alarm was set every time the cluster of successive positive epochs was longer than half the minimal duration of the seizures we wanted to detect. For instance, if we want to detect all seizures longer than 10 seconds, at least 5 consecutive seconds of the seizure need to be accurately identified in order to set an alarm. The system performance was evaluated for the detection of seizures longer than 10, 15, 20 and 30 seconds. Sensitivity, FDR/h and detection latency were calculated (see Section 3.4).

5.1.3 Results

As detection algorithms, the feature selection is also performed in the LOPO manner. Therefore, 14 subsets are obtained. Features like zero-crossing rate of second derivative (appeared 14 times in the subsets), Shannon entropy of the spectrum signal (14), the first peak location in the spectrum (13) and power in 1-13 scales of a continuous wavelet transform of the ACM signal using db5 wavelet (12) are found in almost all subsets, making them the most important features for detection of (tonic-)clonic seizures. In addition, cross-recurrent plot laminatry (6) and total power of CWD of ACM signal (2) describe the differences between the patients' data.

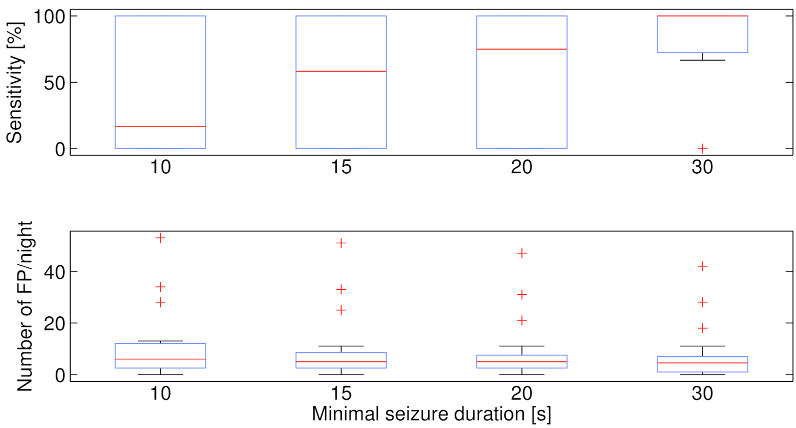

Figure 5.4: Seizure detection sensitivity and number of false alarms per night (FDR/12h) for systems developed for detection of seizures lasting more than 10, 15, 20 and 30 seconds

Using the aforementioned feature subsets, LOPO models are built for detection of prolonged (tonic-)clonic seizures. Figure 5.4 presents the results of the patient-independent algorithms for different minimal seizure duration (10, 15, 20 and 30 seconds). Corresponding median alarm delays are 10, 11, 12.9 and 15.2 seconds. The algorithm performance represents the trade-off between the number of correctly identified seizures (sensitivity) and number of false alarms. If the minimal duration of seizures increases more seizures are detected, and less false alarms are triggered.

Tables 5.2, 5.3, 5.4 and 5.5 list the numerical values of sensitivity and FDR/12h for each patient separately for different minimal seizure duration. Values of both parameters are significantly vary over the patients.

Table 5.2: Classification results: seizure longer than 10 seconds

Patient code	♯ seizures	Sensitivity [%]	TP (extra)	FDR/12h
3	2	0.00	-	6.68
11	1	100.00	4	3.14
22	0	-	-	1.01
24	1	0.00	-	1.03
26	1	0.00	-	4.77
30	5	40.00	1	4.03
35	4	75.00	6	6.63
40	6	0.00	-	8.15
47	1	100.00	-	0.99
48	1	0.00	-	13.72
51	4	75.00	-	3.10
57	3	100.00	-	0.97
67	8	62.50	-	10.12
72	12	100.00	1	40.79
	49	61.22	12	7.01

Table 5.3: Classification results: seizure longer than 15 seconds

Patient code	♯ seizures	Sensitivity [%]	TP (extra)	FDR/12h
3	0	-	-	6.68
11	1	100.00	3	3.67
22	0	-	-	1.01
24	1	0.00	-	1.03
26	0	-	-	3.81
30	3	66.67	1	3.02
35	2	50.00	6	5.68
40	3	0.00	-	8.15
47	1	100.00	-	0.99
48	1	100.00	-	6.40
51	4	75.00	-	3.10
57	3	100.00	-	0.97
67	7	71.43	-	8.52
72	12	100.00	1	40.79
	38	76.32	11	6.16

5.1.4 Discussion

Within this study, we presented a machine learning methodology for detection of prolonged seizures in epileptic children. Employing a feature selection method

Table 5.4: Classification results: seizure longer than 20 seconds

Patient code	♯ seizures	Sensitivity [%]	TP (extra)	FDR/12h
3	0	-	-	6.68
11	0	-	3	3.67
22	0	-	-	1.01
24	1	0.00	-	1.03
26	0	-	-	3.81
30	2	50.00	1	3.02
35	2	50.00	6	5.68
40	2	0.00	-	8.15
47	1	0.00	-	0.99
48	1	100.00	-	6.40
51	4	75.00	-	3.10
57	3	100.00	-	0.97
67	5	100.00	-	7.45
72	11	100.00	2	38.39
	32	78.13	12	5.95

Table 5.5: Classification results: seizure longer than 30 seconds

Patient code	♯ seizures	Sensitivity [%]	TP (extra)	FDR/12h
3	0	-	-	5.72
11	0	-	2	3.14
22	0	-	-	1.01
24	0	-	-	0.00
26	0	-	-	3.81
30	0	-	2	3.02
35	1	100.00	6	5.21
40	0	-	-	8.15
47	1	0.00	-	0.99
48	1	100.00	-	6.40
51	3	100.00	-	3.10
57	3	100.00	-	0.97
67	5	100.00	-	6.92
72	9	100.00	4	35.99
	23	95.65	14	5.53

based on mutual information, the most relevant features for distinction between seizure and non-seizure epochs are obtained. LS-SVM nonlinear models are built for the data of all patients except one, whose data is used as the test data. We only focused on the detection of seizures longer than 10 seconds. Detection of shorter seizures (see Figure 5.2, seizure C) would require that an alarm is triggered for each epoch classified as seizure, making the algorithm useless for home nocturnal monitoring. Moreover, these seizures are not harmful for the child and administration of medication is not required. Figure 5.4 demonstrates that it is possible to detect 19 of the 23 seizures longer than 30 seconds with 0.39 false alarms per hour.

Other groups also tried to develop an algorithm for detection of (tonic-)clonic seizures. Becq et al. [12] used a rule-based algorithm applied to acceleration norm entropy and reached 80% sensitivity with 95% specificity. However, the algorithm was tested only during a short period of time encompassing the seizure. This way of testing does not provide a realistic performance of proposed algorithm. Poh et al. [170] developed a wrist-worn electrodermal activity and ACM biosensor to detect generalized tonic-clonic (GTC) seizures. 15 of 16 GTC seizures are detected with 130 false alarms (0.74 alarm/h). Conradsen et al. [39] used a multimodal approach to detect simulated tonic(-clonic) seizures. A sensitivity of 100% with a false detection rate between 0 and 18 h^{-1} were obtained using ACM, magnetometer, gyroscope and sEMG data.

In addition, two commercial wrist-worn motion sensors, the SmartWatch [118] and EpiLert [108], have been evaluated for the detection of tonic-clonic seizures. The SmartWatch was tested on a group of 40 patients. Seven of eight tonic-clonic seizures and 204 non-seizure events were detected. On the other hand, the EpiLert had a very low rate of false detection (8 in 1692 hours), while 20 of 22 seizures are detected. However, many seizure-like movements were excluded from testing, which could explain the low false alarm rate. Both devices employed proprietary algorithms that were not described in aforementioned publications, making it difficult to compare with other algorithms.

The aforementioned publications make no distinction between children and adults. However, from data available within these publications, we can infer that the majority of patients are adults and that their (tonic-)clonic seizure are long (around and more than 1 minute) and stereotypical. However, the majority of seizures in children are shorter, while longer and stronger seizures are rare events (see Figure 5.3). Thus, a direct comparison between our and other publications is not possible. Although for the alarm system detection of seizures lasting more than 30 seconds is acceptable, if this system is to be used to infer the seizure frequency and effect of prescribed therapy, shorter seizures should also be detected.

We see that patient independent classifiers can exhibit impressive performances when restricted to analyzing seizure classes that vary little across patients. Longer (tonic-)clonic seizures in most cases have stereotypical rhythmic patterns which with the right choice of features can be detected with an acceptable number of false alarms. However, patient-independent classifiers exhibit poor accuracy when the seizures of the test patient differ from the ones in the training set. For those cases, gradually adding patient-specific data into the training set would, in theory, improve the accuracy, which is the topic of future research.

5.1.5 Conclusion

This study offers a significant step towards the realization of a system for epileptic seizure detection from accelerometry data. Patient-independent detectors detected 19 of the 23 seizures longer than 30 seconds with 0.39 false alarms per hour. Apart from being an alarm system, the utilization of this system in the non-clinical environment will enable the registration of the number of seizures the patient encountered in a given time frame. This information can improve clinical insight on how well the prescribed treatment is working.

5.2 Long-term accelerometry-triggered video monitoring and detection of prolonged epileptic seizures in a home environment

5.2.1 Introduction

Epilepsy is a condition in which seizures often occur in an unprovoked and unwarned way. Mainly for safety reasons, many patients and their family are looking for a seizure detection system that is efficient, comfortable and easy to use. This implies that such a system should have a high sensitivity and low false alarm rate, it should be unobtrusive, and should allow long-term use in a home situation in the absence of professionals.

Alarming for safety reasons or reassurance is already used in fall detectors for the elderly, babyphones (reacting to sound or movement) and glucose monitors for diabetics [28, 69]. In addition to alarming, a detection system could allow offline storage or online streaming of (selected) data, allowing follow-up on treatment efficacy respectively emergency support.

The goal of this research is to test the efficacy of the recording system (Subsection 2.2.1) and algorithm for (tonic-)clonic seizures (Section 5.1) compared to semi-continuous monitoring by professional caregivers, as well as the independence, robustness, comfort and user-friendliness of the system. Therefore the measurements were performed in a home replacement environment rather than in a video/EEG Monitoring Unit, and the system needed to be able to store the data and to allow retrospective visual verification of detected events. This is why a camera was added to the accelerometry system. In addition, radar was added for movements in the direction of the sensor and measurements through sheets.

5.2.2 Materials and methods

Data collection and preprocessing

Two patients with (tonic-)clonic seizures were monitored for one month in their rooms in an epilepsy center in Flanders, Belgium. As they returned home for the weekends and because of the slow learning curve of the caregivers, at the end a mean of 12 nights per patient was obtained. For this purpose Bonroy et al. [21] developed a system that can record and store all nocturnal movements of a child and provided a simple interface to evaluate these recordings. A Movement Acquisition System (MAS) consisted of four wireless accelerometers, camera and radar. A screening tool allowed a clinical expert to screen the recorded events. It also could also select a reduced set of nocturnal events which contained the most interesting (abnormal) movements of the evaluated night. This allowed the expert to quickly screen, in a reduced time, (abnormal) nocturnal movements without evaluating the whole night.

Professional caregivers were asked to describe all seizures the patients had, with time occurrence and description. They were trained to recognize epileptic seizures and they were familiar the patient. They were awake during the whole night and usually they were semi-continuously supervising on average four patients though a video surveillance, only leaving if one of them needed care. The observations of the caregivers were compared to the ACM-triggered video segments [21]. A margin of error of five minutes had been taken into account for the seizure reporting. As the caregiver might report a seizure after having rushed to the patient, we assumed the seizure may have been noticed five minutes before or after the actual time in the notes. Most of these seizures were found in the recorded data.In addition, 5% of (abnormal) nocturnal movements with the highest amplitude and duration were reviewed by a clinical expert. Table 5.6 gives the overview of the number of seizures reported by the caregivers, but also number of the extra seizures found in reviewed data. Since not all nocturnal movements were analyzed, some seizures might be undetected. Note that these are the same patients as in the previous study (see Table 5.1).

Monitoring for 24 nights for these two patients resulted in 9515 movement segments of which 322 segments (3.4% or 15 minutes) were discarded before the

Table 5.6: Overview of home monitoring database: two patients with (tonic-)clonic seizures, seizures reported by nurses, seizures reported by nursed and found in the data, extra seizures found within the longest and most intensive movements and number of nights

Patient code	♯ nights	Seizures* (nurses)	Seizures* (data)	Seizures* (extra)
35	9	1M, 1M series, 1T, 1S, 6TC, 1U	1T series, 1S series, 4TC	3TC
67	15	21TC, 1U	10C, 11TC	2M, 5C, 3TC
Total	24	1M, 1M series, 1T, 1S, 27TC, 2U	1T series, 1S series, 10C, 15TC	2M, 5C, 6TC

*M = Mycoclonic, T = Tonic, S = epileptic Spasm, C = Clonic, TC = Tonic-Clonic, U = Unspecified

algorithm was applied because at least one of the ACM channel recorded less than 1 second of data or was completely missing. Since the sampling rate was quite low, only a high-pass filter was applied on each segment to remove the gravitational component as in the case of the Pulderbos dataset (see Subsection 2.3). The final output of the preprocessing stage were motion epochs of two seconds from which various features were extracted.

Detection algorithms

Data recorded in a home replacement environment were only used to test the algorithm. We used the labeled data registered during video/EEG monitoring to built the detection algorithms. First we applied the patient-independent algorithms built in the previous study [139] and described in Section 5.1. Since the sampling rates of the recording systems were different, Pulderbos data (Table 5.1) were first downsampled to 50 Hz, features were recalculated[1] and the rest of the methodological scheme represented in Figure 5.1 was executed.

Since both patients had a substantial number of seizures registered during video/EEG monitoring, we decided to build additionally patient-specific algorithms and test the hypothesis that they perform better than patient-independent algorithms. In order to be comparable, the same number of seizures was used for training for both patients, i.e. seven seizures. The optimization of the parameters was performed in a leave-one-seizure-out cross-validation approach.

[1]Some features, like CWT or DWT features, had to be removed from the list, since the frequency content of ACM signals was significantly reduced

Finally, to allow the LS-SVM to learn from previous examples of seizures of the test patients, a generic model was built including all patients having (tonic-)clonic seizures monitored using wired ACM system and video/EEG (see Table 5.1). Since the algorithm was not trained solely on data from a particular test patient but included examples from all other patients, this approach is called semi-patient-specific [170]. In our case, basically only one model was built using all patients, and then it was evaluated on both test patients.

Evaluation metrics

All detection algorithms were evaluated as seizure alarm systems. An alarm was set every time the cluster of successive positive epochs was longer than seven seconds, since the goal is to detect all seizure longer than 10 seconds. Hence shorter seizures are not counted when calculating detection performance. An alarm within one minute after a previous one is ignored. A future real-time alarm system should allow the system being turned off by the caregiver when checking an alarm, and one minute is considered too short for the caregiver to have checked and left the patient's room after the first alarm. Alarms caused by the caregiver waking or handling the patient (medication administration) and installing (evening) or removing (morning) the system and accelerometers are ignored. Again, at these times the future real-time alarm system should be turned off by the caregiver. Sensitivity, FDR/night and detection latency were calculated (see Section 3.4) and used to evaluate the algorithms.

5.2.3 Results

The results of the patient-independent and semi-patient-specific approach can be found in Tables 5.7 and 5.8. True positives (TP) are detected seizures. The extra seizures detected by the algorithm but not the caregiver are put between brackets. False negatives (FN) are seizures reported by the caregiver but not detected by the algorithm. To calculate sensitivity, the formula TP/(TP+FN) was used.

The patient-independent approach resulted in a sensitivity of 90% and FDR of 1 per night for patient 67 and a sensitivity of 33% and FDR of almost 2 per night for patient 35. The semi-patient-specific approach gave somewhat better results with a sensitivity of 93% and FDR slightly more than 1 per night for patient 67 and a sensitivity of 40% and FDR of 1 per night for patient 35. The patient-specific algorithms performed poorly. While seizures missed by previous two models were detected in case of patient 67, this was compensated by missing other seizures and increased an FDR (more than 10 false alarms per

Table 5.7: Detection results for the patient-independent approach

Patient code	TP (extra)	FN	Sensitivity [%]	FP	FDR/night
35	3 (1)	6	33.33	17	1.88
67	29 (11)	3	90.62	15	1
Mean			61.97		1.44

TP = True Positive, FN = False Negative, FP = False Positive

Table 5.8: Detection results for the semi-patient-specific approach

Patient code	TP (extra)	FN	Sensitivity [%]	FP	FDR/night
35	4 (2)	6	40	9	1
67	30 (11)	2	93.75	20	1.33
Mean			66.87		1.16

TP = True Positive, FN = False Negative, FP = False Positive

night). On the other hand, for patient 35, there were five false alarms, but only two seizures were correctly identified. In general, when a seizure were correctly identified it was done between 10 and 35 seconds from the clinical onset of the seizure depending of the seizure type and characteristics on the onset of the seizure.

5.2.4 Discussion

The semi-patient-specific algorithm gave the best results, including 13 extra seizures detected (31%) and eight seizures missed (19%) compared to professional caregivers' observations. Of these eight, six were not even recorded in any of the movement data (five for patient 35 and one for patient 67). Possible explanations include a temporary defect in the system, mistakes in reporting by the caregiver (one seizure was reported at 5:20 am but detected at 6:20 am and counted as extra seizure) or short seizures involving only the head (not attached to an accelerometer). This discrepancy can explain the low sensitivity of patient 35.

Apart from being compared to the report of substandard quality of the professional caregivers, the detection algorithm (whether it is patient-independent or semi-patient-specific) has it own limitations. It is not able to detect tonic seizures or the tonic phase of tonic-clonic seizures. The algorithms are not trained nor tuned to detect these seizures. If the clonic seizure or clonic phase of the tonic-clonic seizure is too short, the seizure will be missed. The alarm is only set after seven seconds of positive detection, but if clonic phase of tonic-clonic seizures is 5-6 seconds and whole part is detected, still the alarm is not set off. Finally, asymmetric (tonic-)clonic seizures during which the movements of the limbs are not synchronized and seizures with lower clonic jerks are often missed since the spatial and frequency content of these seizures are different than majority of training seizures. This can be solved by making sure that each subclass is equally represented in the training set or or by having a separate model for each subclass.

It seems that combining the large amount of data of many (other) patients, instead of using limited amount of data of one specific patient, yields better classification results. This can be explained be the higher data variability. For instance, in case of patient 67, only two nights of recordings were available for training of the patient-specific algorithm, which resulted in a high FDR. On the other hand, for patient 35, four nights used for training gave a lower FRD compared with other approaches.

We compared the results of the semi-patient-specific algorithms with the screening tool of Bonroy et al. [21] where the most intense and long movement events were visually inspected for seizures using the same database. The comparison results are presented in Table 5.9. As Bonroy et al. [21] only included 12 nights of patient 67, three nights were left out from the semi-patient-specific analysis, and as the former counted only one FP per segment, this was adjusted for the latter as well. Compared to the screening tool, the semi-patient-specific algorithm missed five seizures but detected 14 more. Because "abnormal" events were selected, this automatically resulted in more false positives, so comparison of FDR is not relevant. Moreover, 11 of the 16 false alarms were due to a system failure (broken channel or high frequency noise), hence clustered alarms can be used to indicate these kinds of events.

The recording system and screening tool can be used before a diagnose is made to report abnormal nocturnal behavior, including seizures. Once the patient is diagnosed we can change the functionality of the same hardware into an alarming system. This implies that we have to reduce the FDR and increase the sensitivity. This study shows preliminary results of automated ACM-based seizure detection algorithms on two patients.

It is difficult to compare this study and obtained results with other publications, mainly because the gold standard video/EEG was not used to annotate the data. Furthermore, we did not review all movement segments and some of the observations reported by the professional caregivers were not even found in the data. Therefore, the presented results are just the estimation of the algorithm's performances.

Table 5.9: Comparison of the semi-patient-specific algorithms to the screening tool [21]

Patient code (# n)	Screening tool [21]				Semi-patient-specific algorithm			
	TP (e)	FN	Sen [%]	FDR	TP (e)	FN	Sen [%]	FDR
35 (9)	7 (3)	4	63.63	9.88	4 (2)	6	40.00	1.00
67 (12)	13 (6)	11	54.16	20.33	25 (9)	2	92.59	0.58
Mean			58.89	15.10			66.29	0.79

n = nights, TP = True Positive, e = extra TP, FN = False Negative, Sen = Sensitivity, FRD = FRD/night

A major advantage of our system is that it allows video storage. Of the commercially available seizure detection systems reported by Van de Vel et al. [212] some keep a log of the detected seizures: EpiWatcher stores the time and duration of up to 20 detections, SmartWatch keeps the time, duration and movement pattern, EpiCare saves the time and duration of an unspecified number of detections and the mobile phone application EpDetect logs the raw accelerometer data. None of them records and stores video data of the detected seizures. Few studies [50, 101, 182] report on video-based seizure detection but a disadvantage is the difficulty to measure through bed sheets.

In the future, we plan to verify how many accelerometers give the best results and to reduce its number, to provide the caregiver with less set-up steps and to include measurement of other body signals in order to improve sensitivity.

5.2.5 Conclusion

This study presents the first clinical results of an algorithm for detection of (tonic-)clonic seizures tested on two epileptic patients monitored in a long-term home replacement environment with the MAS system. Four wireless accelerometers were used for detection of prolonged epileptic seizures. Compared with the professional caregivers' observations, a mean sensitivity of 61.97% and FDR of 1.44 per night was obtained with the patient-independent approach and a mean sensitivity of 66.87% and FDR of 1.16 per night with the semi-patient-specific approach. While privacy protection needs to be taken into account, video as a part of the MAS system allowed retrospectively (offline) verification of detected events and should be used in the monitoring of epileptic patients.

Chapter 6

Automated detection of tonic-clonic seizures using accelerometry and surface electromyography

Chapter 5 discussed the detection of (tonic-)clonic seizures based on one modality, namely accelerometry. This chapter compares accelerometry and surface electromyography for detection of tonic-clonic seizures. Furthermore, it investigates if combining these modalities improves the detection performance. Section 6.2 elaborates on the used methodology and the way the modalities are combined. In Section 6.3 first sensor number reduction analysis is presented, and then the uni-modal and multi-modal seizure detection algorithms are compared. The results are discussed in Section 6.4. Finally, conclusions are drawn in Section 6.5. This study is also described in [140].

6.1 Introduction

Several studies have been investigating the detection of different epileptic seizure classes using different recording systems. The main focus has been on the detection of (generalized) tonic-clonic (TC) seizures [14, 26, 37–39, 108, 118, 170, 192]. As described in Subsection 1.1.1, a TC seizure is a combination of tension resulting in a change of posture followed by a series of jerk-like contractions of agonist and antagonist muscles that regularly occurs with frequency of 0.2-5 jerks/s [124].

Conradsen et al. used sEMG and an algorithm based on the zero-crossing rate to detect the tonic phase of the TC seizure [37, 38]. On the other hand, other groups used ACM, usually by means of one wrist-worn sensor, to detect the rhythmic pattern of a TC seizure. Applied algorithms ranged from simple thresholding [192], to the use of machine learning techniques [39, 170].

In general, the research tended to focus more on the adult population, rather than on children. Only [170] used data recorded solely from children, whereas other publications did not make a distinction between adults and children; however latter were always underrepresented.

In this study, we investigated the detection of TC seizures in pediatric patients using ACM and sEMG in both uni- and multi-modal approaches. First ACM and sEMG-based alarm systems were compared, and afterwards these two modalities were merged using late integration. In the latter case, the goal is to increase the probability of detection of seizures with short tonic and clonic phases (which are not detected with unimodal approaches) and by imposing the stricter detection constraints to decrease the FDR compared to unimodal seizure detection. In contrast to the aforementioned publications, which reported seizure duration above 1 minute, some TC seizures within our dataset last only a few seconds. Detection of short events in general leads to the trade-off between detection sensitivity and false detection rate (FDR). In addition, children tend to move more than adults, resulting in a higher number of false alarms compared to the adult population. Taking into consideration the above described challenges, this study compares machine learning based methodology using ACM and sEMG signals to detect TC seizures in pediatric patients.

6.2 Materials and Methods

Figure 6.1 depicts the consecutive steps of the entire procedure involved in construction of classification algorithms in uni-modal approach. We can see that the same methodology was applied in Chapter 5, therefore only the alterations and additions are mentioned.

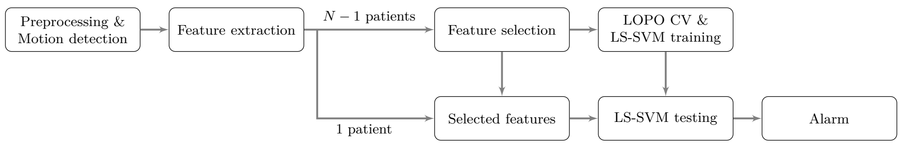

Figure 6.1: Schematic overview of the algorithm. Abbreviations used in figure: leave-one-patient-out (LOPO) cross-validation (CV), least-squares support vector machines (LS-SVM), N is number of patients

6.2.1 Data collection and preprocessing

Seven pediatric patients had in total 31 TC seizures registered both in the ACM and sEMG signals. Table 6.1 gives the overview of the patients and number of TC seizures. These data were used to develop the classification algorithms.

Table 6.1: Overview of patients with TC seizures

Patient	♯ TC seizures	♯ nights	Record duration
11	1/9*	2	22:54:48
24	1	5	61:14:12
35	1/2*	7	87:06:44
48	1	2	25:17:52
57	3	1	12:19:29
67	5	2	22:32:24
72	10	1	10:00:13
7 patients	22/31*	20 nights	241:25:43

*Number of TC seizures longer than 10 seconds over total number of TC seizures. For other patients all seizures were longer than 10 seconds.

Apart from seven patients with TC seizures, 49 patients with other or no seizures were monitored during 148 nights (patients from Table 2.1 except patient 54 who was restrained due to the too violent movements), adding around 1757 hours of data to the analysis. These data were used to better estimate FDR of the developed methodology. Full recordings were included in the analysis regardless of the record length and quality[1], whether the child was awake or asleep.

[1]There were 46 recordings during which one to maximally three of 12 channels were partially or totally not working. This is the consequence of bad connection between the sensor and the cable or the cable and the collection point.

The preprocessing consisted of filtering, downsampling and data reduction which are explained in Subsection 2.3. The final output of the preprocessing are motion epochs from which various features are extracted.

6.2.2 Feature extraction and selection

Apart from zero-crossing rate used in [37] for detection of TC seizures using sEMG, we added frequently used features for description of sEMG signals [136], [196]. The full list and definitions of features of sEMG features are given in Appendix B.2. A range of parameters has been used for epileptic seizure classification, from simple time domain, entropy, spectral, wavelet to cross-recurrence plot features [11, 39, 48, 100, 119, 153, 154, 170, 175, 205]. In addition, entropy measures frequency used to characterized to sEMG signals [196] were added to the ACM feature list (see Appendix B.1).

Starting from $N_f = 149$ ACM and $N_f = 87$ sEMG signal features respectively, a mRMR [60, 166] (see Subsection 3.2.1) was applied in the same set up as in Chapter 5.

6.2.3 LS-SVM classification

LS-SVM classifier (subsection 3.3.1) was applied in LOPO testing approach since the number of seizures per patient was very low, disabling the building of patient-specific models. Moreover, some patients were monitored for only one night also limiting the number of normal movements. In real-life applications, patient-independent algorithms are most practical to seizure detection since the existing detectors built on the previous patients could be applied on the newly arrived epileptic patient.

Since the tonic and clonic phases are morphologically different both in ACM and sEMG signals, we preselected tonic and clonic segments for sEMG and ACM-based seizure detection algorithms, respectively. The training epochs were randomly chosen from these segments for each modality individually. For each patient maximally 250 seizure and 1000 non-seizure epochs were chosen for training.

In case of uni-modal seizure detection, only post-processing, explained in Subsection 6.2.4, was performed. Additionally we tested a multimodal approach using late integration by fusing the LS-SVM decisions (see equation 3.5) of ACM (f_{ACM}) and sEMG (f_{sEMG}) modalities. The integration was performed using the inclusive disjunction operation:

$$f_{ACM+sEMG}(\mathbf{x}_i) = f_{ACM}(\mathbf{x}_i) \vee f_{sEMG}(\mathbf{x}_i), \quad (6.1)$$

$i = 1, \ldots, N$. By merging these two decisions the seizure detection probability increased, as shown in Subsection 6.3.2.

6.2.4 Evaluation metrics

To eliminate possible false detection of short periods, a temporal constraint was applied to the LS-SVM output. The constraint only allowed detection of a seizure after the LS-SVM had classified a number of consecutive epochs containing seizure activity. In general, this post-processing greatly reduces the number of false positives, but also leads to a decreased sensitivity and increased detection latency. The post-processing (number of consecutive epochs needed for positive detection) highly depends on the use of the algorithm. Since ACM is only capable of detecting the clonic phase of the seizure, whereas sEMG the tonic phase, for uni-modal TC seizure detection seven consecutive seconds were required to be positively classified by the LS-SVM classifier as a seizure. On the other hand, it was assumed that both phases were detected with the multi-modal approach, and therefore the alarm was put on after 10 seconds.

The performances of the developed seizure detectors were characterized in terms of sensitivity, false detection rate per 12 nocturnal hours and detection latency. Sensitivity gives the percentage of test seizures identified by the algorithm. Only TC seizures longer than 10 seconds were taken into consideration for the alarm system, since shorter seizures are not dangerous. False detection rate (FDR) refers to the number of times, over the course of a full night (12 hours), that the detector declared the onset of seizure activity in the absence of an actual TC seizure. In case other seizure classes were the cause of an alarm, this alarm was counted as an extra seizure detected. In addition, when nurse/parent's interference led to an alarm, those false alarms were omitted. Examples of these events were nurse bringing, putting on, removing and testing the system, or handling the child (medication administration, changing the diapers, (un)dressing the child and similar events). At these moments, the real-time alarm system should be turned off beforehand. Latency refers to the delay between expert-marked clinical onset of the seizure and alarm set off by the detection algorithm during the seizure activity.

6.3 Results

Previously described methodology was applied to identify TC seizures using ACM or/and sEMG signals. First we checked each modality individually and then late integration was applied to the ACM and sEMG detections. In addition, within each modality, since the number of sensors was large, different sensor combinations were compared regarding the sensitivity and FDR over patients with TC seizures.

6.3.1 Unimodal seizure detection

Table 6.2 illustrates the classification performances over all seven patients with TC seizures, when different numbers of ACM and sEMG sensors and their combinations within each modality were employed. In addition, the numbers of selected features are added in the table.

When all four ACM sensors were used to build a classifier, 16 of 22 TC seizures were detected, with on average one false alarm per night. Combining three ACM sensors if two of which were wrist sensors sensitivity increased, however the false detection rate also significantly increased. Left wrist and right ankle ACM positions resulted in the identification of 19 TC seizures (the highest sensitivity), but also false detection rate increased by two compared with the use of the complete ACM-based measurement system. Finally, using only one wrist ACM sensor caused too many false positives to be used for an alarm system.

In general, the following features were found to be relevant for ACM-based distinction of TC seizures from other movements: number of local maxima in the signal [205], Shannon entropy of diagonal line lengths in cross-recurrence plot [130, 170], frequency of the first local peak in the spectrum and power within scale range 5-11 (corresponding pseudo-frequency range 9-22.5 Hz) from continuous wavelet transform obtained using Morlet mother wavelet [11]. There were slight differences when different ACM sensors were used, but in case the highest sensitivity was reached (two ACM sensors) and in case the lowest FDR was accomplished (all ACM sensors), all aforementioned features were chosen for all patients (in a LOPO procedure).

Table 6.2 suggests that the detection of TC seizures with only one sEMG sensor was not reliable both regarding sensitivity and false detection rate. Combining right and left biceps sEMG data, 18 TC seizures were detected with 3 false alarms within 5 nights, outperforming ACM-based TC seizure detection. The most relevant feature for detection of TC seizures was Wilson amplitude [136],

Table 6.2: ACM/sEMG sensor combination vs seizure detection performance

Sensor(s)*	Sensitivity [%]	FDR/12h	♯ features†
RW	68.18	4.97	3-5
LW	63.64	6.16	4-5
LA	68.18	2.73	6-9
RA	72.73	1.64	3-5
RW+LW	63.64	6.16	4-4
RW+LA	68.18	1.84	3-5
RW+RA	68.18	1.09	3-4
LW+LA	77.27	2.29	4-5
LW+RA	**86.36**	**1.94**	**4-4**
LA+RA	68.18	3.13	3-6
RW+LW+LA	81.82	3.13	4-4
RW+LW+RA	77.27	4.27	4-4
LW+LA+RA	68.18	1.04	4-5
RW+LW+LA+RA	**72.73**	**0.99**	**4-4**
RB	63.64	1.14	1-4
LB	45.45	2.09	1-3
RB+LB	**81.82**	**0.60**	**1-2**

*RW = right wrist ACM, LW = left wrist ACM, LA = left ankle ACM, RA = right ankle ACM, RB = right biceps sEMG, LB = left biceps sEMG;
†Feature selection was performed for each patient by excluding that particular patient. Therefore the number of selected features and selected features were often different among the patients.

then the zero-crossing rate of the second derivative and the number of local maxima [205] in sEMG signals.

Since the seizure detection and FDR vary significantly over the patients, the results for each patients with TC seizure(s) and each modality are presented in Tables 6.3, 6.4 and 6.5.

Sensitivity per patient was either 0 or close to 100%, meaning that the seizure detection depended on the seizure characteristics and used modalities. For instance, patient 35 had only one seizure, and although the seizure was 21 second long, it had a clonic phase shorter than the algorithm's requirements for ACM-based detection (around 6 seconds and only three jerks). The opposite was

Table 6.3: Unimodal classification results: four ACM sensors

Patient	Sensitivity [%]	Latency [s]	FDR/12h
11	100	7.3	0.00
24	0	-	1.96
35	0	-	0.55
48	100	15	1.42
57	0	-	0.00
67	100	13.2	0.00
72	90	20.5	3.60
	72.73	15.55	0.99

Table 6.4: Unimodal classification results: two ACM sensors (left wrist and right ankle)

Patient	Sensitivity [%]	Latency [s]	FDR/12h
11	100	7.3	0.00
24	0	-	5.49
35	0	-	0.96
48	100	15	1.90
57	66.67	22.8	0.00
67	100	13.4	0.00
72	100	20.5	0.00
	86.36	19.4	1.94

valid for the TC seizure of patient 24, with short tonic phase (around 4 seconds). Patient 57 experienced TC seizures of around 1-minute, however due to the obstruction of the limbs the clonic pattern was disrupted and discontinuous (child was lying in supine position and was trying to get up). One seizure of patient 24 was never detected, probably due to the low frequency of the jerks.

Values of FDR were influenced by patient-specific behavior. Children with epilepsy tend to have a specific pattern of behavior, which was sometimes similar to the seizure patterns. For instance, patients 24, 35 and 48 before falling to sleep, frequently started clapping, they uncontrollably rubbed or shacked the hands. Patient 72 in early morning hours started trembling, similarly to the clonic pattern of TC seizures. Previously mentioned behavior most often

Table 6.5: Unimodal classification results: two sEMG sensors

Patient	Sensitivity [%]	Latency [s]	FDR/12h
11	0	-	5.76
24	0	-	0.00
35	100	7.3	0.00
48	100	10.5	0.00
57	66.67	7.3	0.00
67	80	12.2	0.00
72	100	14	1.20
	81.82	10.5	0.60

resulted in false alarms in ACM-based seizure detectors. On the other hand, sEMG was sensitive to stretching and tension-line turning which were typical for patient 11.

As shown in Table 6.5, detection latency was on average lower for sEMG-based seizure detection compared with the ACM system. This result was logical, since the clonic phase detected by ACM was preceded by the tonic phase detected by sEMG modality. However, the latency differences were not large, since mainly all TC seizures were short seizures.

We repeated the whole methodology scheme (Figure 6.1) using seven patients with TC seizures. The obtained algorithm was tested on 49 patients who did not experience TC seizures. The number of test nights per patient ranged from 1 to 22 nights. Same subsets of features were obtained as in LOPO procedures for both modalities. Figures 6.2 and 6.3 display the histograms of FDR/12h for these patients using ACM- and sEMG-based seizure detection, respectively.

The results strongly suggested that sEMG was less sensitive to the false alarms (overall 46 false alarms in 1998.3 hours). In contrast, dispersion of FDR histogram was increased for ACM-based seizure detection, whether four or two ACM sensors were used. For the majority of the patients the FDR was 0, however for some patients due to the high FDR other solutions have to be found.

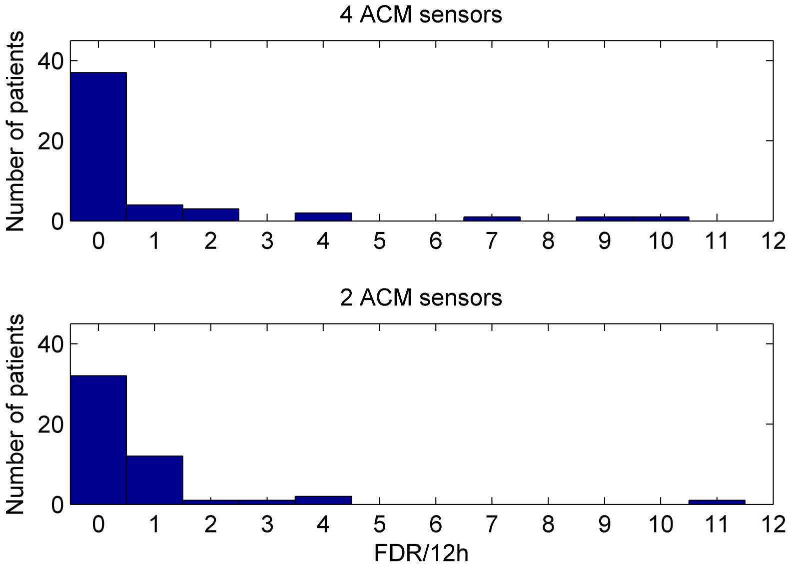

Figure 6.2: Unimodal classification results: Histogram of FDR/12h for patients without TC seizures when all four ACM sensors are used, and when only left wrist and right ankle ACM sensors are used.

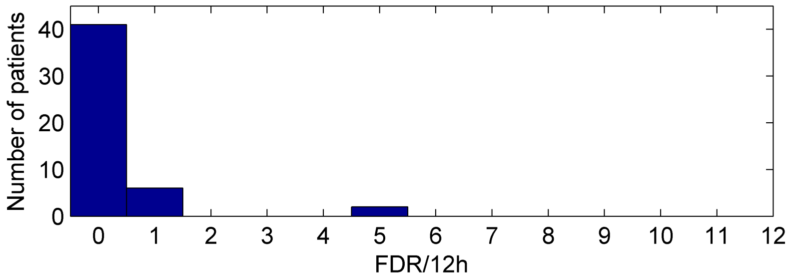

Figure 6.3: Unimodal classification results: Histogram of FDR/12h for patients without TC seizures when two sEMG sensors attached to the child's biceps are used

6.3.2 Multimodal seizure detection

We chose to perform the late integration of the outputs of two ACM and two sEMG sensors, since the performance between two and four ACM sensors was not significantly different whereas the number of sensors makes a big difference. More weight was given to sensitivity over FDR. 20 of 22 TC seizures were correctly identified and there were nine false alarms within 20 nights of patients with TC seizures. Table 6.6 displays algorithm performances per patient. In addition, Figure 6.4 shows the histogram of FDR/12h over the patients without TC seizures. Including sEMG, one extra seizure was correctly identified, while the number of false alarms dropped from 162 to 83. Still this was twice as much the number of false alarms using only the sEMG modality (in total 46 false alarms).

Table 6.6: Multimodal (AMC and sEMG) classification results

Patient	Sensitivity [%]	Latency [s]	FDR/12h
11	0	-	0.00
24	0	-	1.18
35	100	7.3	0.28
48	100	10.5	0.47
57	100	15	0.00
67	100	8.7	0.00
72	100	14	0.00
	90.91	10.5	0.45

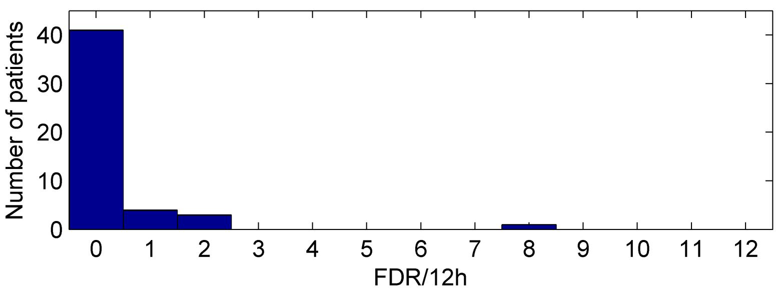

Figure 6.4: Multimodal classification results: Histogram of FDR/12h for patients without TC seizures when left wrist and right ankle ACM sensors are combined with two sEMG sensors

6.4 Discussion

In this study, we investigated the use of sEMG and ACM sensors for the detection of TC seizures in pediatric patients. Since the number of sensors was high, an analysis was performed to assess the relevance of the number and position of sensors. In case of ACM modality, a two sensor set-up was found to not significantly degrade the algorithm performance compared with the full setup. Left wrist (i.e. generally non-dominate hand) and right ankle were identified as the optimal positions for ACM sensors. In case of sEMG sensors, it was not possible to reduce the number of sensors to only one. One possible explanation would be that the biceps muscles are not the best positions for TC seizure registration and detection [37].

Based on the available data, sEMG was significantly less sensitive to false alarms, while only one TC seizure was not identified by sEMG when compared with the ACM modality. Over all patients, sEMG experienced 46, whereas 152 and 162 false alarms were observed within 1998.3 hours using four and two ACM sensors, respectively. Although, the total number of false alarms obtained from ACM signals were 3.3 and 3.5 times higher using four and two ACM sensors, 40 and 45% of these events were "events of interest". Most of these events were of one particular child hitting the pillow with the head (typical strange behavior of this child), as pulling the EEG electrodes, falling off the bed, trying to remove the sensors, and similar dangerous situations, when assistance was needed. On the other hand, sEMG was insensitive to these kind of events, except to pulling off the EEG electrodes. Applying late integration on two ACM and sEMG sensors classification decisions, not only the sensitivity increased, but also the FDR decreased. Out of 83 false alarms, we observed 43 events in which assistance was needed.

As seen in Table 6.2, depending which sensor combination was employed, the number and features chosen in LOPO testing approach often differed. When complete set or two ACM sensors (left wrist and right ankle) were employed, the number and chosen features did not depend on the patient who was excluded from the data. This is highly practical for the development of generic algorithm for detection of TC seizures. It also suggests that chosen features have universal relevance for TC seizure detection using ACM signals. However, this was not the case when two sEMG signals were used to detect TC seizures. The Wilson amplitude appeared in all feature sets. The second feature was the zero-crossing rate of the second derivative which appeared four times, whereas the number of local maxima appeared only in one feature set. It would be interesting to investigate if the fixed feature set (use always these three features or only the Wilson amplitude) for all patients significantly influence the detection performance.

Apart from TC seizures, within the used database 164 extra seizures longer than 10 seconds were annotated by the EEG expert. The majority of the seizures were frontal lobe seizures with hyperkinetic movements (66), atypical frontal (23), tonic (22) and clonic (18) seizures. Using the developed TC detection algorithms, other seizure classes were also detected. Using sEMG, 31 extra seizures were identified; predominantly tonic seizures (14), frontal lobe seizures with hyperkinetic movements (10) and three TC seizures shorter than 10 seconds. The same number of extra seizures was registered using two ACM sensors; among them there were 12 frontal lobe seizures with hyperkinetic movements, four clonic, four tonic and two TC seizures shorter than 10 seconds. Even though the methods were not trained to detect other classes of epileptic seizures, on average 18% of them were detected. We expected to detect more clonic seizures (at least using ACM modality), since the clonic phase and clonic seizures are similar. In general, the clonic phase of TC seizures was intensive with high-frequency jerk-like movements, whereas clonic seizures encountered in our database had different movement frequency making it difficult to detect them from the features optimized for TC seizures with high frequency jerk-like movements. In case of tonic seizures, a large number of tonic seizures were correctly identified by the sEMG-based TC seizure detector even though Conradsen et al. [41] found that sustained muscle activation during the tonic phase of TC seizure is different from that during tonic seizures. The tonic phase of TC seizures is characterized by an increased amplitude whereas tonic seizures are produced by a significant increase in the frequency of the signal.

Table 6.7: Comparison of studies involving ACM and sEMG-based TC seizure detection methods

Publication	Kramer (2011) [108]	Poh (2013) [170]	Beniczky (2013) [14]	Milosevic (2015)	Conradsen (2012) [37]	Conradsen (2012) [38]	Milosevic (2015)	Milosevic (2015)
Sensor(s)	1 ACM	1 ACM + EDA*	1 ACM	2 ACM	1 sEMG	1 sEMG	2 sEMG	2 ACM + 2 sEMG
Population [y]		9-14.2	6-68	0.7-18.5	11-62	34-48	0.7-18.5	0.7-18.5
# patients†	15/31	7/80	20/73	7/56	11/60	2/4	7/56	7/56
# seizures	22	16	39	22	22	7	22	22
Seizure classes‡	T, C, TC	GTC	GTC	TC	GTC	GTC	TC	TC
Seizure duration	≥20 s	≥60 s		≥10 s		≥50 s	≥10 s	≥10 s
Record duration	1692h	4213h	4878h	1998h	776h	298h	1998h	1998h
Sensitivity	91% (20/22)	94% (15/16)	90% (35/39)	86% (19/22)	100% (22/22)	57% (4/7)	82% (18/22)	91% (20/22)
FDR♮	0.11/24h	0.74/24h	0.2/24h	0.97/12h	0.04/24h	0.07/24h	0.28/12h	0.5/12h
Median latency	17 s	31.4 s	55 s	19.4 s	13.7 s	24.5 s	10.5 s	10.5 s

*EDA = ElectroDermal Activity;
†Number of patients with seizures over total number of patients;
‡TC = tonic-clonic, GTC = generalized tonic-clonic, T = tonic, C = clonic seizures;
♮While other studies monitored the patients day and night, we did it only during the night, hence different FDR measurement units

Finally, we compared the obtained results with publications reporting on TC seizure detection (alarm system) using one or more body-attached sensors (ACM or sEMG) that used real-life data and did not preselect the data. Table 6.7 contains the study information regarding the listed publications. Sensitivity obtained within this study using an unimodal approach was a bit lower, whereas our multimodal approach had comparable sensitivity in the range of detection rates reported by other publications [14, 37, 108, 170]. On the other hand, the FDRs for both approaches were much higher than in other studies. FDR of 0.28/12h obtained using two sEMG sensors is comparable to 0.74/24h obtained using a biosensor based on ACM and electrodermal activity [170]. In both cases, pediatric patients were monitored, which generally tend to move more than adults. This could explain the higher FDRs. Median detection latency on average was higher using ACM sensors [14, 108, 170] compared with the sEMG [37, 38]. Using ACM sensors, we obtained a detection latency either comparable or much lower than other studies, whereas using sEMG sensors the latency was always lower. The seizures recorded in Pulderbos Rehabilitation center in general were short seizures which led to building the alarm system with short detection latency. Increasing the latency, FDR would decrease. However, in that case, only the longest seizures would be detected by the alarm system.

In the future, we plan to investigate the influence of fixed feature set for all patients calculated from sEMG signals on the detection performance, compared with the features obtained within LOPO procedure used in this study. In addition, the measurements of other body signals (like ECG) individually or in the combination with other modalities will be studied in order to improve the sensitivity for the patients whose seizures were difficult to detect with patient-independent algorithms based on ACM or sEMG signals.

6.5 Conclusion

Within this study, the detection of tonic-clonic epileptic seizures was accomplished with the use of 3D accelerometry and surface electromyography. It was shown that the use of two ACM sensors (non-dominant arm wrist and one leg) gave comparable performances compared to the full set of four ACM sensors attached to the wrists and ankles. Over all patients, sEMG showed lower susceptibility for false alarms compared with the ACM signals. However, high inter-patient variability was observed regarding FDR values, with a majority of patients experiencing no or a really small number of false alarms, indicating the need for a patient-specific measurement system for detection of epileptic seizures based on prior knowledge on patient's seizure characteristic and his/her typical non-epileptic behavior.

Chapter 7

Conclusion and future work

Section 7.1 summarizes the most important findings of this dissertation, whereas in 7.2 an outlook on interesting topics for future research is given.

7.1 Concluding remarks

The goal of this thesis was to investigate the application of accelerometry and surface electromyography for the automated detection of epileptic seizures in pediatric patients. The main focus was on tonic-clonic and clonic seizures. ACMs attached to the limbs register the movements of the patients, whereas sEMG recorded biceps activity.

The first research area provided us with valuable information regarding the use of feature selection methods within the machine learning framework for epileptic seizures detection using accelerometry. For this purpose, a large number of features was collected from the literature. Classification performances were compared when no feature selection method was applied, when only a filter method was applied and when wrapper following a filter method (hybrid approach) was applied using both forward search and backward elimination strategies. The results showed that the filter method significantly reduced the number of features but did not degrade the classification performance compared with the complete feature set. The presented feature selection was tested on each epileptic seizure class separately and by all including epileptic seizures. Better results were achieved if we focused on a single epileptic seizure class instead of various seizure classes. In addition, detection of more violent and longer seizures (here (tonic-)clonic seizures) resulted in the highest classification performance, making them the main candidates for an alarm system.

In the second study, we focused on the development of algorithms for (tonic-)clonic seizure detection in pediatric patients. ACM signals were used to detect the rhythmic component of clonic seizures and the clonic phase of tonic-clonic seizures. Since the number of seizures per patient was small, patient-independent algorithms were built using the findings from the previous study. The analysis of 14 patients showed high inter-patient variability regarding the seizure detection performance. In addition, the results depended on the time constraint impose on the output of the classifier. The same methodology was tested in patient-independent, patient-specific and semi-patient-specific approaches on two patients monitored long-term in a home-replacement environment. Patient-independent and semi-patient-specific models outperformed patient-specific models. Compared with the professional caregivers' observations, a mean sensitivity of 61.97% and FDR of 1.44 per night was obtained with the patient-independent approach and a mean sensitivity of 66.87% and FDR of 1.16 per night with the semi-patient-specific approach. However, the sensitivity values improve significantly if we remove the seizures reported by caregivers but not found in the data. In addition, more than 50% of false alarms was clustered and due to a system failure, hence they can be used to indicate these kinds of events.

The purpose of the last study was to compare the ACM- and sEMG-based tonic-clonic seizure detection in pediatric patients. While ACM signals were used to detect the rhythmic component of clonic phase, sEMG was used to detect the tension during the tonic phase of tonic-clonic seizures. The same methodology was applied as in the second study. First, we investigated if it was possible to reduce the number of sensors for both modalities. Only in case of ACM, this reduction was possible. Two ACM sensors (left wrist and right ankle) gave comparable classification results when tested on 56 pediatric patients. Next, ACM- and sEMG-based tonic-clonic seizure detection algorithms were compared. ACM and sEMG are equally useful for seizure detection; however sEMG was less sensitive to false alarm (46 vs. 162 in 1998.3 hours). Nevertheless, 45% of false alarms were events for which assistance was needed; most of these events were of one particular child hitting the pillow with the head (typical strange behavior of this child), as pulling the EEG electrodes, falling off the bed, trying to remove the sensors, and similar dangerous situations. Finally, late integration was applied at the classification outputs which resulted in improved sensitivity (91% vs. 86% for ACM vs. 82% for sEMG), however the false detection rate was still higher than sEMG-based seizure detection, since many ACM events were detected (0.5/12h vs. 0.28/12h). The results in this study suggest that there is a need for a patient-specific measurement system for detection of epileptic seizures based on prior knowledge on patient's seizure characteristic and his/her typical non-epileptic behavior.

The research presented in this thesis is one step towards the automated monitoring which was initiated based on the need from parents with epileptic children to have a better tool for monitoring the epilepsy.

7.2 Future perspectives

The research area related to detection of epileptic seizures is wide and there are many possibilities. However, there are some limitations. In general, the main focus is to increase the detection performances whether through methodological changes or adding extra sensors/modalities. But there is a trade-off between the number of sensors and the comfort of the patient, unless contact-less sensors are used. Still, it is possible to integrate multiple sensors in one node (e.g. the sensors for measuring the skin conductivity and the heart rate can be integrated in the wrist band that already measures the acceleration of the arm), therefore reducing the number of total sensor nodes attached to the patient's body.

7.2.1 Epileptic seizures that should/can be detected

Ideally, a neurologist would like to have an estimation of the number of seizures a patient had in a certain time interval. By tracking this number over a longer period of time, he could accordingly adapt the therapy. However, at this moment, this is not realistic. Currently, detection systems, that can be used at home, are not able to detect all seizures. For example, although ACM sensors register myoclonic jerk, there is no algorithm with acceptable performance for their detection; these seizures are just too short to be reliably detected with low false detection rate during long-term monitoring.

Therefore, one should try to detect and set an alarm for prolonged epileptic seizures that can potentially lead to physical injuries. The methods described in this thesis mainly focused on detection of clonic and tonic-clonic seizures using ACM and/or sEMG. In Chapter 6, it was show that ACM-based algorithms for detection of tonic-clonic seizures also detected a large number of frontal lobe seizures with hyperkinetic movements. Detected seizures were patient-specific and associated ACM patterns were similar to clonic seizures. In addition, sEMG-based algorithms detected a surprisingly large number of tonic seizures. We should investigate if the detection reliability improves by adding other seizure classes (frontal lobe, tonic) in the training set. To conclude, an alarm system should be extended to detect clonic, frontal lobe (ACM), tonic (sEMG) and tonic-clonic (ACM, sEMG) seizures.

Apart from epileptic seizures with motor component (convulsive seizures), there are seizures with subtle or no clinical signs (non-convulsive seizures) which can cumulatively affect cognitive functions [6]. We should explore the possibilities of detecting these seizures using ECG (i.e. HR).

7.2.2 Improvement of detection algorithms

Within this thesis, mainly patient-independent algorithms were investigated. In many studies, this was the only option, since the number of seizures per patient was limited. Furthermore, for some patients, there were no many non-seizure examples. In that case, patient-specific algorithms actually performed worse than patient-independent algorithms. In the Section 5.2, we also tested a semi-patient-specific model built on the data of all patients. This model gave slightly better classification results compared with patient-independent algorithms. Furthermore, to increase the performance of the classification it is possible to update the model by adding more patient-specific data as it is recorded. This updating procedure should be investigated in more detail.

Apart from inter-patient variability which can be resolved by constructing patient-specific algorithms, we often observe intra-patient variability in seizure morphology or spatial localization. In that case, placing one generalized (whole body involved in seizure) and one focal (e.g. only one are involved in seizure) in the training set, can confuse both the feature selection and classification methods resulting in poor detection results for both seizure subclasses. The same holds for different seizure morphologies. Therefore, we should explore the possibilities of splitting the problem of seizure detection into a subset of seizure detectors based on the seizure characteristics (see first two lines of Figure 7.1). Seizures can be clustered by visual inspection or using unsupervised learning techniques [92].

7.2.3 Integration of multiple modalities

Using a monitoring system based on accelerometry and surface electromyography, only epileptic seizures distinctively present in these modalities can be registered and potentially detected. This means that we can monitor only a subgroup of patients with this system. Patients suffering from epilepsy sometimes present disturbed motion patterns which resemble the epileptic seizures, but they are not related to the epilepsy. These non-epileptic movements are hard to

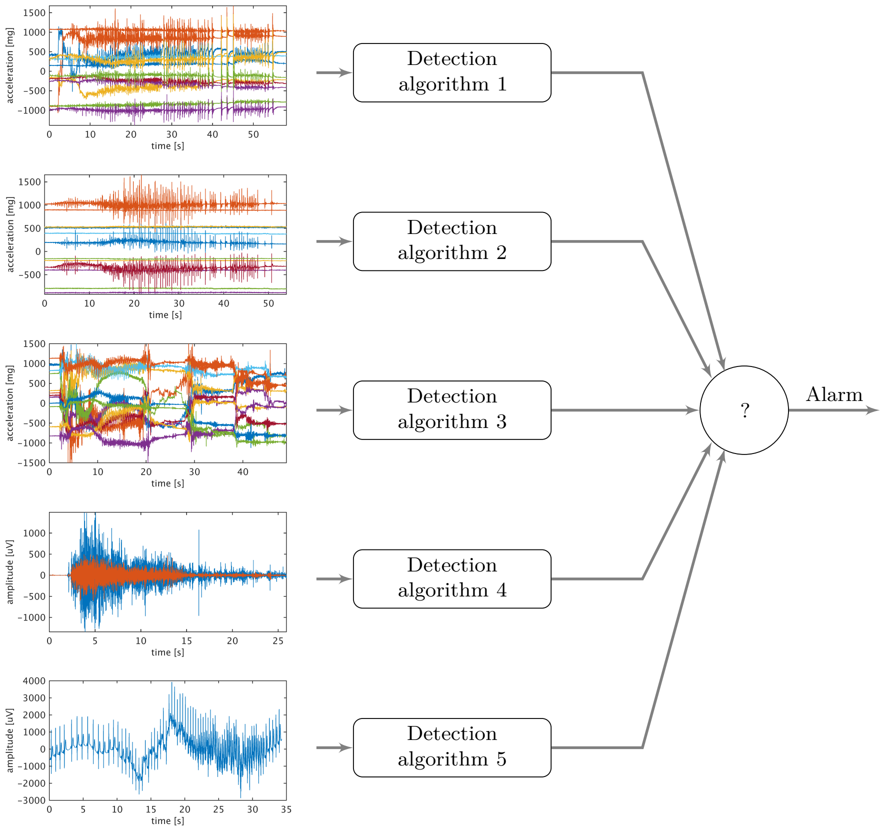

Figure 7.1: Detection of epileptic seizures: divide and conquer strategy

distinguish from epileptic ones without any knowledge of other physiological parameters. Beniczky et al. found several differences in the sEMG signal between the convulsive epileptic and psychogenic non-epileptic seizure activity [13]. Nevertheless, sEMG-based tonic-clonic seizure detection poorly performed when patient exhibited tension-like non-epileptic movements. A possible solution for non-epileptic movements and detection of non-convulsion seizures is trying to integrate multiple modalities.

As described in Subsection 1.2.2, a large number of modalities can be employed for long-term (home) monitoring. Nevertheless, to build the algorithms, data (with seizures) have to be collected and annotated which is a laborious task. Hence, until new sensors and new data are recorded, only the modalities used in the Pulderbos Rehabilitation Center are taken into the consideration: video, audio extracted from video and ECG. Cuppens investigated the use of video for the detection of myoclonic and frontal lobe seizures with hyperkinetic movements [46]. Video was recently tested as seizure screening tool in a home-like environment [21]. Further on-line testing should assess the reliability of the developed methods. ECG (i.e. HR) looks like the most promising extra modality for the on-line detection of epileptic seizures [55]. In addition, using advanced methods like kernel PCA, it is possible to derive respiration from the ECG signal [224], which could have an added value for seizure detection. However, this method and ECG-based seizure detection algorithms are still highly sensitive to muscle artifacts present in ECG signal.

Figure 7.1 presents an overall solution for the detection of epileptic seizures employing modalities present in recording system used in the Pulderbos Rehabilitation Center. The problem of epileptic seizure detection is divided into smaller problems, which focus on a subset of seizures with unified specific seizure characteristics and appropriate detection algorithms. In addition, different modalities can be applied to detect different seizure classes. The question is how to fuse all these detections. The fusion of the algorithms will depend on the used modalities and the characteristics of applied algorithms. Figure 7.1 shows five different seizure detection algorithms where three algorithms are based on ACM signals (two algorithms for generalized and focal seizures with rhythmic pattern and one algorithm for frontal lobe seizures with hyperkinetic movements) and the others are based on sEMG and ECG. It is possible that we will need two separate algorithms for detection of generalized and focal seizures based on ECG signal. Breaking the overall problem of epileptic seizure detection into smaller subproblems can result in large number of parallel detection algorithm in Figure 7.1, however in reality a patient has only a small variety of seizure classes which could be detected with smart choice of sensors. The goal should be a tailored patient-specific seizure detection system that takes into account prior clinical knowledge, so that per individual patient the best seizure detection is achieved and it is also suitable for home monitoring purposes.

Appendix A

Seizure examples in accelerometry

In this Appendix, examples of seizures in accelerometry (ACM) are given. Due to the clarity reasons, only wrist ACM signals are plotted.

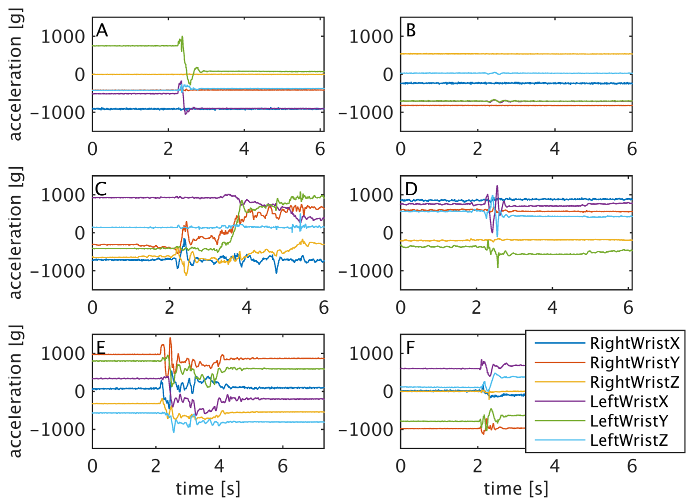

Figure A.1: Examples of individual myoclonic seizures starting at 2 seconds. Seizure B is almost subtle in accelerometry, whereas after seizure C there is a movement.

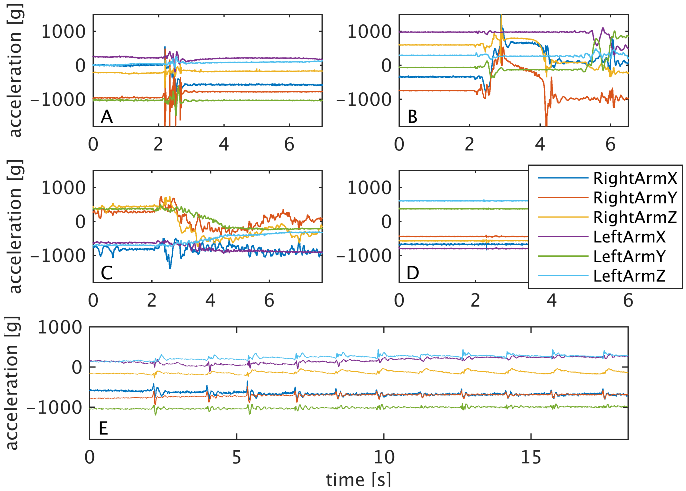

Figure A.2: Examples of individual epileptic spasms starting at 2 seconds (A-D) and one series of epileptic spasms (E). Spasm D is almost subtle in accelerometry, whereas after seizures B and C there are movements.

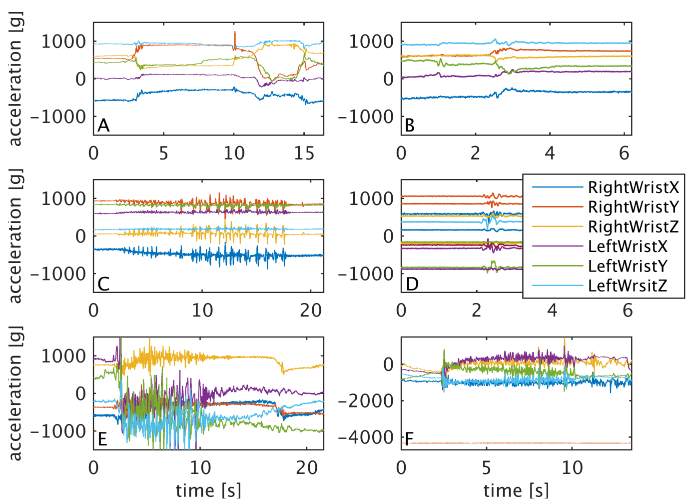

Figure A.3: Examples of individual tonic (A-B), clonic (C-D) and tonic-clonic (E-F) seizures starting at 2 seconds. Seizure A is typical tonic seizures: we can observe block-wise ACM shape. Clonic seizure D contains only few jerks and lasts only two seconds. During seizure F, one channel is broken (ACM value is around 4g).

Appendix B

Feature list

B.1 Features extraction: accelerometry signals

Features extracted from ACM signals can be divided in six big groups: time domain features, frequency domain features, continuous wavelet transform features, packet wavelet transform features, recurrence plot analysis and entropy features. Equations and algorithms used to generate these features are described in the following subsections.

Herein each preprocessed ACM signal (i.e. channel) is denoted $x(n)$ where n is the sample index in time. N is the total number of samples in an epoch.

B.1.1 Time domain derived features

1 Signal mean [1, 11, 27, 119, 170, 175, 217] is defined as

$$\mu = \frac{1}{N}\sum_{n=1}^{N} x\,(n). \tag{B.1}$$

2-4 25, 50 and 75 percentile values of the signal amplitude [175] are calculated as the $(\alpha \times N)$-th element of a sorted array, where $\alpha = \{0.25, 0.50, 0.75\}$

5-7 Jerk (first derivative of the signal amplitude) of the slow, fast and original ACM signal $x(n)$ [153, 156] is defined as

$$J = \frac{1}{N}\sqrt{\sum_{n=2}^{N}\left(\frac{x\left(n\right)-x\left(n-1\right)}{\Delta t}\right)^{2}}. \tag{B.2}$$

The slow component (x_{slw}) is obtained by filtering the signal $x(n)$ using a Chebyshev type II filter with cut-off frequency of 1 Hz. The fast component (x_{fst}) is calculated as a difference between the original signal and slow component. Δt is the sampling interval.

8-10 Standard deviation of the slow, fast and original ACM signal [27, 120, 153, 156, 170, 175] is defined as

$$\sigma = \sqrt{\frac{1}{N}\sum_{n=1}^{N}\left(x\left(n\right)-\mu\right)^{2}}, \tag{B.3}$$

where μ is the mean value of the signal $x(n)$, defined by equation B.1.

11-12 Variance of the first and second derivative of the ACM signal [205, 207]

13-15 Range of the slow, fast and original ACM signal $x(n)$ [153, 156] is calculated as

$$R = \max(x) - \min(x). \tag{B.4}$$

16 Activity is the same as standard deviation [1, 78, 119, 205].

17 Mobility [1, 78, 119, 205] is defined as

$$\delta_x = \frac{\sigma_{x'}}{\sigma_x}, \tag{B.5}$$

where $\sigma_{x'}$ is the standard deviation of the first derivative of signal $x(n)$.

18 Complexity [1, 78, 119, 205] is defined as

$$\lambda_x = \frac{\frac{\sigma_{x''}}{\sigma_{x'}}}{\delta_x}, \tag{B.6}$$

where $\sigma_{x''}$ is the standard deviation of the second derivative of signal $x(n)$.

19-20 Number of local maxima and number of local minima in the signal [78, 88, 119, 205, 217] is estimated as the number of times the first derivative of the ACM signal crosses the zero level. The second derivative is used to determine the type of local extreme.

21-23 Number of zero-crossings in the original signal, first derivative and second derivative are calculated [1,35,37,52,78,88,114,119,205,217]. This feature is the total number of positive zero crossings within an epoch where a positive zero crossing is defined as

$$x(n) < \varepsilon \quad \text{and} \quad x(n+5) > \varepsilon. \tag{B.7}$$

Parameter ε is usually called hysteresis and here $\varepsilon = 50$ mg, where g=9.81 m/s^2.

24 Root mean square amplitude (RMSA) [27,40,41,78,88,170,205] is calculated as

$$RMSA = \sqrt{\frac{1}{N}\sum_{n=1}^{N} x^2(n)}. \tag{B.8}$$

25 Line length [35, 71, 78, 119, 205] is defined as

$$L = \sum_{n=2}^{N} |x(n) - x(n-1)|. \tag{B.9}$$

26 Signal magnitude area (SMA) [100] is defined as

$$SMA = \frac{1}{N}\sum_{n=1}^{N} |x(n)|. \tag{B.10}$$

27 Force is similar not-normalized SMA [170]:

$$force = \sum_{n=1}^{N} |x(n)|. \tag{B.11}$$

28 Signal energy [52, 119, 175, 181] is defined as

$$E = \sum_{n=1}^{N} x^2(n). \tag{B.12}$$

29 Mean nonlinear energy [78, 119, 144] is calculated as

$$NE = \frac{1}{N-2}\sum_{n=2}^{N-1} \left(x^2(n) - x(n-1)\,x(n+1)\right). \tag{B.13}$$

30 Kurtosis [1, 27, 88, 119, 205] is defined as

$$kurt = \mathbb{E}\left[\left(\frac{x-\mu}{\sigma}\right)^4\right], \tag{B.14}$$

where $\mathbb{E}$ denotes the expected value.

31 Skewness [1, 27, 88, 119, 205] is defined as

$$skew = \mathbb{E}\left[\left(\frac{x-\mu}{\sigma}\right)^3\right], \tag{B.15}$$

where $\mathbb{E}$ denotes the expected value.

32 Auto-regressive (AR) model fit or goodness-of-fit is the error of an AR model of order $d = 10$ applied on the signal $x(n)$ [24, 78, 144, 167, 205]. The AR model of order d can be written as

$$x(n) = \sum_{i=1}^{d} a_i x(n-i) + e(n), \tag{B.16}$$

where $x(n)$ is the output of the model, $x(n-1), x(n-2), ..., x(n-d)$ are the previous outputs, and a_i are the model parameters and $e(n)$ is Gaussian white noise. The model parameters, i.e a_i coefficients, are obtained via the covariance method. Auto-regressive model fit or goodness-of-fit feature is defined as the variance estimate of white noise $e(n)$:

$$ARMF = \sum_{n=1}^{N}\left(e(n) - \frac{1}{N}\sum_{i=1}^{N} e(i)\right)^2. \tag{B.17}$$

B.1.2 Frequency domain derived features

The frequency domain features are extracted from the power spectral density $S(f)$ obtained from signal $x(n)$, where f is the corresponding frequency vector. The power spectral density (PSD) is calculated from the centered epoch signal using the Welch method with default parameters: eight segments of equal length with 50% overlap.

33 Dominant frequency in the spectrum [11,78,88,119,144,170,175] is defined as

$$DF = \arg\max_{f} S(f). \tag{B.18}$$

34 Maximal power in the spectrum is defined as PSD value at the dominant frequency:

$$MP = S(DF). \tag{B.19}$$

35-38 Frequencies of the first four local maxima in the spectrum describe the shape (distribution) of signal spectrum.

39-43 Spectral edge frequencies for 10, 50, 85, 90 and 95% are calculated [11,52,119,162,205] and they are defined as

$$SEF_{\alpha} = \max_{f} \{f \,|\text{cumsum}(P(f)) \leq \alpha/100\}, \tag{B.20}$$

where $\alpha = \{10, 50, 85, 90, 95\}$.

44 Spectral centroid or mean frequency [52,78,162] is calculated as

$$SC = \frac{\sum_{f} f \cdot S(f)}{\sum_{f} S(f)}. \tag{B.21}$$

45-54 Powers in 2 Hz non-overlapping bands (0-20 Hz) [205] are calculated as follows

$$P_{\delta_f} = \sum_{f \in \delta_f} S(f). \tag{B.22}$$

where δ_f is the predefined frequency band.

55 Total power in range 0-20 Hz

56-63 Powers in 1.25 Hz non-overlapping bands (0-10 Hz) are estimated in the same way as for 2 Hz non-overlapping bands, except that the spectrum is estimated using the fast Fourier transform, as in the original publication [170].

64 Spectral entropy [78,119,120,162,175,205] is defined as

$$H_s = -\frac{1}{N_f}\sum_{f=1}^{N_f} P\left(f\right)\log P\left(f\right), \tag{B.23}$$

where $P(f)$ is the normalized estimation of the probability density function of the signal x, and in this study, it is calculated by normalizing the PSD with the total spectral power:

$$P\left(f\right) = \frac{S\left(f\right)}{\sum\limits_{f=1}^{N_f} S\left(f\right)}. \tag{B.24}$$

N_f is the number of spectral components.

65 Spectral Shannon entropy was calculated using 101 quantization levels from normalized PSD [78,119,120,162,175,205]

B.1.3 Continuous wavelet transform derived features

The continuous wavelet transform (CWT) of a continuous time signal $x(t)$ is defined as

$$CWT_{\psi}\left(a,b\right) = \frac{1}{\sqrt{a}}\int_{-\infty}^{+\infty} x\left(t\right)\psi^{*}\left(\frac{t-b}{a}\right)dt, \tag{B.25}$$

where $\psi^{*}(t)$ is the complex conjugate of the wavelet analysis function $\psi(t)$, a is the dilatation (scale) parameter of the wavelet and b is the location (time) parameter of the wavelet.

CWT features are calculated as the ratio of coefficients in a given band δ_a to the sum of all coefficients:

$$W_{\delta_a} = \frac{\sum\limits_{a\in\delta_a}\sum\limits_{b} CWT\left(a,b\right)}{\sum\limits_{a}\sum\limits_{b} CWT\left(a,b\right)}. \tag{B.26}$$

In addition, the sum of all coefficients is added as extra feature.

Using three different mother wavelets, namely the fifth Daubechies wavelet [154], a model-based matched wavelet (mod) obtained in [152] by modeling arm movements during a myoclonic seizure, and a Morlet wavelet which was used by Becq et al. [10], ACM signals are decomposed. db5 and morl wavelets are used from the Matlab continuous wavelet toolbox and the model-based matched wavelet is implemented in Matlab using the following equation from the Nijsen et al. study [152]:

$$\psi\left(t\right) = t\left(e^{-t} - \frac{1}{A}e^{-\frac{t}{B}}\right), \quad t \in [0, \infty)\,, \tag{B.27}$$

where A and B are predefined constants. Fitting the model to the clinical data, Nijsen et al. obtained the following values $A = 1.045$ and $B = 1.023$ [151]. Table B.1 lists the total number of decomposition levels, the scale-bands δ_a and pseudo-frequency bands for which the features are calculated compared to the number of levels and bands (bold values in Table B.1) from original studies. The differences can be explained due to the differences in the sampling rate and signal (epoch) lengths.

66-67 Ratio of coefficients in 2-13 and 10-32 scale ranges to the sum of all coefficients using db5 mother wavelet [154].

68 Sum of all coefficients using db5 mother wavelet for CWT [154].

69-70 Ratio of coefficients in 5-11 and 13-16 scale ranges to the sum of all coefficients using morl mother wavelet [10].

71 Sum of all coefficients using morl mother wavelet for CWT [10].

72-74 Ratio of coefficients in 2-9, 2-20 and 25-48 scale ranges to the sum of all coefficients using mod mother wavelet [151, 152].

75 Sum of all coefficients using mod mother wavelet for CWT [151, 152].

Table B.1: CWT features: scale and pseudofrequency bands

Mother wavelet	Sampling rate [Hz]	# scales	Scale bands δ_a [a.u.]	Pseudofrequency bands [Hz]
	Previous studies			
db5	100	256	**8-60, 9-39, 74-256**	1-9, 1.7-7.9, 0.3-0.9
mod	100	50	**2-8, 2-10, 10-50, 20-50**	12.5-50, 10-50, 2-10, 2-5
morl	46	> 256	2-4, 5-19, 30-?	**9-23, 2-8, 0.05-1.25**
	Current study			
db5	125	32	2-13, 10-32, 2-32	6.2-65.5, 2.5-9, 2.5-65.5
mod	125	48	2-9, 2-12, 25-48, 2-48	13-62.5, 10.4-62.5, 2.5-5, 2.5-62.5
morl	125	16	5-11, 13-16, 2-16	9-22.5, 6-8.1, 6-62.5

B.1.4 Packet wavelet transform derived features

Packet wavelet transform (PWT) is an extension of discrete wavelet transform. Instead of splitting only the low frequency signals at each decomposition level, PWT filters both an approximation (A) and a detail (D) signals on each decomposition level, providing equal frequency and time resolutions for all frequencies. Figure B.1 illustrates the process of PWT decomposition till the 4th level of decomposition. A wavelet function φ and scaling function ψ are described by the low-pass (g) and high-pass (h) filters:

$$\varphi_{j,m}(l) = 2^{j/2} g_j \left(l - 2^j m\right) \tag{B.28}$$

$$\psi_{j,m}(l) = 2^{j/2} h_j \left(l - 2^j m\right) \tag{B.29}$$

where j is the scaling factor, and m is the translation parameter. The outputs of decomposition are approximation $A_j(m)$ and detail $D_j(m)$ signals:

$$A_j(m) = x(l)\,\varphi_{j,m}(l) \tag{B.30}$$

$$D_j(m) = x(l)\,\psi_{j,m}(l)\,. \tag{B.31}$$

76-106 Absolute sum of PWT coefficients [39] is defined as

$$F_Q = \sum_{m=1}^{M} |Q(m)|, \tag{B.32}$$

where Q is the signal obtained from the PWT decomposition. The number of samples M depends on the level of decomposition. For the level j, $M = N/2^j$, where N is the length of the original signal. Due to the low number of samples in the epochs in this study, it is not possible to perform a high number of decomposition levels. Using built-in Matlab function *wmaxlev*, the maximal number of 4 levels of wavelet decomposition is obtained. Further decomposition would be unreasonable due to lack of data. However, in Conradsen et al. (2012) 1 minute epochs (with sampling rate of 120 Hz) are used for PWD with 6 levels of decomposition [39].

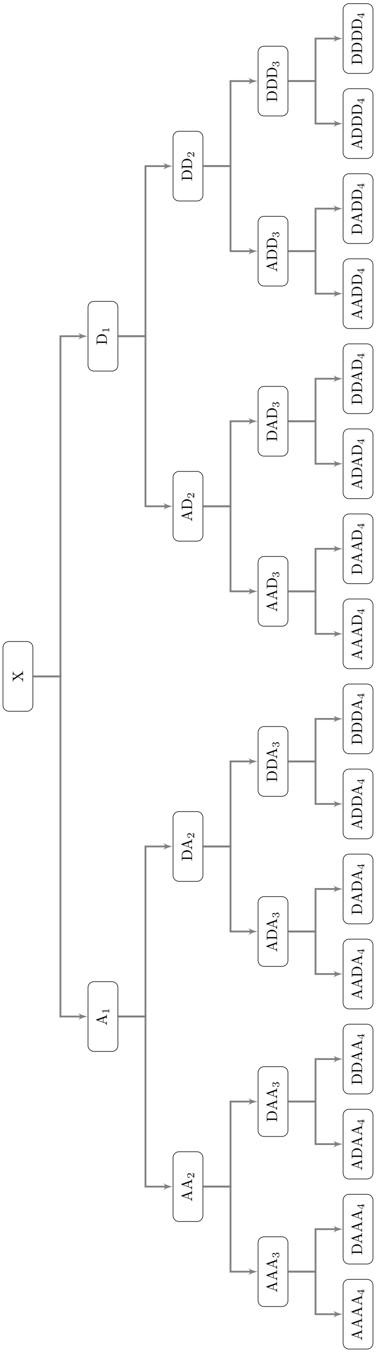

Figure B.1: Schematic representation of packet wavelet decomposition till the 4th level of decomposition

107-137 Energy of PWT coefficients

$$F_Q = \sum_{m=1}^{M} Q^2(m). \tag{B.33}$$

where Q is the signal obtained from the PWT decomposition.

B.1.5 Recurrence quantitative analysis derived features

A recurrence plot (RP) is an advanced technique for nonlinear signal analysis. The RP reveals all the time instances when the phase space trajectory of the dynamical system visits roughly the same area in the phase space. Eckmann et al. have introduced a tool to visualize the recurrence of states $\mathbf{x}_i$ in a phase space [64]. Usually, a phase space does not have a dimension (two or three) which allows it to be pictured. Higher-dimensional phase spaces can only be visualized by projection into the two- or three-dimensional subspaces. However, Eckmann's tool enables us to investigate the m-dimensional phase space trajectory through a two-dimensional representation of its recurrences. Such recurrence of a state at time instance i at a different time instance j is marked within a two-dimensional squared matrix with ones and zeros (black and white dots in the plot), where both axes are time axes. This representation is called recurrence plot. Such a RP can be mathematically expressed as

$$\mathbf{R}_{i,j} = \Theta\left(\varepsilon_i - \|\mathbf{x}_i - \mathbf{x}_j\|\right), \quad x_i \in \Re^m, \quad i,j = 1, \ldots, N, \tag{B.34}$$

where N is the number of considered states of $\mathbf{x}_i$, ε_i is a threshold distance, $\|\cdot\|$ a norm and $\Theta(\cdot)$ the Heaviside function. The signal is represented in the state (phase) space by constructing embedded vectors

$$\mathbf{x}_i = \left[x(i), \; x(i+d), \; \ldots, \; x(i+(m-1)d)\right]^T, \tag{B.35}$$

where m is the embedding dimension and d is the time delay. RP analysis is performed using the Recurrence Plot toolbox for Matlab [130] and the following parameter values $m = 5$, $d = 1$ and $\varepsilon = 1$ [170].

138 Shannon entropy of diagonal line lengths in RP [170] reflects the complexity of the deterministic structure in the system:

$$E_{RP} = -\sum_{l=l_{\min}}^{N} p(l) \ln p(l), \tag{B.36}$$

where $p(l)$ is the probability that a diagonal line has exactly length l estimated from the histogram $P(l)$ of the lengths l of the diagonal lines:

$$p\left(l\right) = \frac{P\left(l\right)}{\sum\limits_{l=l_{\min}}^{N} P\left(l\right)}. \tag{B.37}$$

139 Laminarity [170] is the percentage of the RP which is formed of vertical lines. LAM is related to the amount of laminal phases in the system (intermittency):

$$LAM_{RP} = \frac{\sum\limits_{\nu=\nu_{\min}}^{N} \nu P\left(\nu\right)}{\sum\limits_{\nu=1}^{N} \nu P\left(\nu\right)}, \tag{B.38}$$

where $P(\nu)$ is the histogram of the lengths ν of the vertical lines.

B.1.6 Entropy derived features

140-142 Shannon entropy is defined as

$$ENT = -\sum_{i} p_i \log\left(p_i\right), \tag{B.39}$$

where p_i denotes the probability of the quantization level q_i and $i = 1 \ldots N_l$. We used $N_l = 65536 = 2^{16}$ [11], $N_l = 9$ [136] and Scott's rule [194, 195] to determine the number of quantization levels. For $p_i = 0$, $p_i \log(p_i)$ is considered to be null; otherwise

$$p_i = \frac{n_i}{N_l} = \frac{\#\left(x == q_i\right)}{N_l}. \tag{B.40}$$

143-144 Cumulative residual entropy [179, 196] is defined as

$$CRE = -\int\limits_{R_+^N} p\left(|x| > \lambda\right) \log p\left(|x| > \lambda\right) d\lambda, \tag{B.41}$$

where $x = (x_1,\ x_2,\ \ldots,\ x_N)$, $\lambda = (\lambda_1,\ \lambda_2,\ \ldots,\ \lambda_N)$ and $|x| > \lambda$ means $|x_i| > \lambda_i$ and R_+^N set of non-negative numbers. Again, $N_l = 9$ quantization levels are used [136] and in another estimation Scott's rule [194, 195] was used to determine the number of quantification levels.

145 Approximate entropy [4,32,33,168] is defined as

$$ApEn(m,r,N) = \phi^m(r) - \phi^{m+1}(r), \tag{B.42}$$

where $m = 2$ is the embedding dimension of the vector to be formed, $r = 0.2\sigma$ is filter factor,

$$\phi^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} \ln C_i^m(r) \tag{B.43}$$

and

$$C_i^m(r) = \frac{1}{N-m+1} \sum_{j=1}^{N-m+1} \Theta\left(r - \|X_i - X_j\|\right) \tag{B.44}$$

is the correlation algorithm where Θ is the Heaviside function. $X_i = [x(i),\ x(i+1),\ \ldots,\ x(i+m-1)]$ for $i = 1,\ \ldots,\ N-m+1$ are delayed versions of the original signal $x(n)$.

146 Sample entropy [32,107,185] is defined as

$$SampEn(m,r,N) = -\ln \frac{\Phi'^m(r)}{\Phi'^{m+1}(r+1)}, \tag{B.45}$$

where

$$\Phi'^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} C_i'^m(r) \tag{B.46}$$

and

$$C_i'^m(r) = \frac{1}{N-m+1} \sum_{j=1}^{N-m+1} \Theta\left(r - \|X_i - X_j\|\right) \quad j \neq i. \tag{B.47}$$

The notation and used values are the same as for approximation entropy. Sample and approximate entropies are very similar. In $ApEn$, the comparison between the template vector and the rest of the vectors also includes comparison with itself. This guarantees that probabilities $C_i^m(r)$ are never zero. Consequently, it is always possible to take a logarithm of probabilities. Because template comparisons with itself lower $ApEn$ values, the signals are interpreted to be more regular than they actually are. These self-matches are not included in $SampEn$ (equation B.47).

147 Fuzzy entropy [31, 32] is defined as

$$FuzzyEn(m, r, N) = \ln \phi^m(r) - \ln \phi^{m+1}(r), \tag{B.48}$$

where

$$\phi^m(r) = \frac{1}{N-m} \sum_{i=1}^{N-m} \left(\frac{1}{N-m-1} \sum_{j=1}^{N-m} D_{ij}^m \right) \quad j \neq i \tag{B.49}$$

and

$$D_{ij}^m = \mu\left(d_{ij}^m, r\right) = e^{-\frac{\left(d^{ij}\right)^n}{r}} \tag{B.50}$$

is fuzzy membership function. The absolute distance between the vectors is

$$d_{ij}^m = \|X_i - X_j\|. \tag{B.51}$$

The notation and used values are the same as for approximation entropy.

In addition to the entropy measures, two features derived from Scott's role are added to the list:

148 Bin width is calculated using the Scott's rule [194, 195] as fallows:

$$BW = \frac{3.5\sigma}{\sqrt[3]{N}}, \tag{B.52}$$

where σ is the standard deviation calculated using equation B.3, and N number of samples in the epoch.

149 Number of bins determined from Scott's rule [194, 195] is estimated as:

$$BN = \left[\frac{R}{BW}\right] - 1, \tag{B.53}$$

where R is the signal range calculated using equation B.4.

B.2 Features extraction: surface electromography signals

Features extracted from sEMG signals can be divided in three big groups: time domain features, frequency features and entropy features. Many features are the same features as features calculated from ACM signals. Those features are just listed here, whereas only sEMG features are described in detail.

Herein each preprocessed sEMG signal is denoted $x(n)$ where n is the sample index in time. N is the total number of samples in an epoch.

B.2.1 Time domain derived features

1 Mean absolute value [136] is defined as

$$MAV = \frac{1}{N}\sum_{i=1}^{N}|x(i)|. \tag{B.54}$$

2 Median absolute value [136] is calculated as $(0.5 \times N)$-th element of the sorted elements of signal $|x(n)|$.

3-5 25, 50 and 75 percentile values of the absolute signal $|x(n)|$

6 Activity [1, 78, 119, 205]

7 Mobility [1, 78, 119, 205]

8 Complexity [1, 78, 119, 205]

9-11 Variance of the original sEMG signal, first and second derivative [205, 207]

12 Range of $x(n)$ [153, 156]

13-15 Number of local maxima, number of local minima and number of turns in the signal [78, 88, 119, 136, 205, 217]

16-18 Number of zero-crossings in the signal, first derivative and second derivative [1, 35, 37, 52, 78, 88, 114, 119, 205, 217]

19 Root mean square amplitude [27, 40, 41, 78, 88, 170, 205]

20 Line or waveform length [35, 71, 78, 119, 136, 205]

21 Mean absolute difference value [136] is normalized line length:

$$MADV = \frac{1}{N-1} \sum_{n=2}^{N} |x(n) - x(n-1)|. \tag{B.55}$$

22 Wilson amplitude [136] is defined as

$$WAMP = \sum_{i=2}^{N} \psi_i, \tag{B.56}$$

where

$$\psi_i = \begin{cases} 1, \ |x(n) - x(n-1)| > \varepsilon \\ 0, \ \text{otherwise} \end{cases} \tag{B.57}$$

It is take that $\varepsilon = 50\mu$V.

23 Signal energy [52, 119, 175, 181]

24 Mean nonlinear energy [78, 119, 144]

25 Kurtosis [1, 27, 88, 119, 205]

26 Skewness [1, 27, 88, 119, 205]

27 Auto-regressive (AR) model fit or goodness-of-fit is the error of an AR model of 4th order [136]

28-31 Auto-regressive coefficients [136]

32-40 Amplitude histogram [136, 228] is contacted using 9 equal bins and counts are used as features.

B.2.2 Frequency domain derived features

The frequency domain features are extracted from the power spectral density $S(f)$ from sEMG signal, where f is the corresponding frequency vector. The power spectral density (PSD) is calculated from the centered epoch signal using the Welch method with default parameters: eight segments of equal length with 50% overlap.

41 Dominant frequency in the spectrum [11, 78, 88, 119, 144, 170, 175]

42 Maximal power in the spectrum

43-48 Spectral edge frequencies or quartiles for 10, 30, 50, 60, 75 and 90% are calculated [11, 52, 119, 136, 162, 205].

49 Spectral centroid or mean frequency [52, 78, 136, 162]

50-58 Powers in 20 Hz bands with 50% overlap (20-120 Hz)

59-67 Normalized powers in 20 Hz bands with 50% overlap (20-120 Hz)

68-76 Frequency histogram [136, 228]: the frequency spectrum is divided into 9 segments of equal size and the percentages of the power in each of them are taken as features.

77 Spectral entropy [78, 119, 120, 162, 175, 205]

78 Spectral Shannon entropy was calculated using 101 quantization levels from normalized PSD [78, 119, 120, 162, 175, 205].

B.2.3 Entropy derived features

79-80 Shannon entropy is calculated for $N_l = 9$ [136] and Scott's rule [194, 195] is used to determine the number of quantization levels.

81-82 Cumulative residual entropy [179, 196] is calculated for $N_l = 9$ [136] and Scott's rule [194, 195] is used to determine the number of quantization levels.

83 Approximate entropy [4, 32, 33, 168]

84 Sample entropy [32, 107, 185]

85 Fuzzy entropy [31, 32]

86 Bin width is calculated using the Scott's rule [194, 195]

87 Number of bins determined from Scott's rule [194, 195]

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Curriculum

Milica Milošević was born in Belgrade, Serbia on March 4, 1984. In 2003 she started studying Electrical Engineering at the University of Belgrade, Serbia. After obtaining her Bachelor in Electrical Engineering in 2008, she started a Master of Electrical Engineering, option Telecommunication and Information Technologies, at the University of Belgrade, Serbia. In June 2010, she joined the STADIUS research group at the Department of Electrical Engineering (ESAT), KU Leuven, Belgium as a predoctoral student under the supervision of Prof. Dr. Ir Sabine Van Huffel. In April 2011, she started her PhD program under the supervision of Prof. Dr. Ir. Sabine Van Huffel and Prof. Dr. Bart Vanrumste resulting in this thesis.

Publication list

Papers in international journals

Cuppens, K., Karsmakers, P., Van de Vel, A., Bonroy, B., **Milošević, M.**, Luca, S., Croonenborghs, T., Ceulemans, B., Lagae, L., Van Huffel, S., and Vanrumste, B. Accelerometry-based home monitoring for detection of nocturnal hypermotor seizures based on novelty detection. *IEEE Journal of Biomedical and Health Informatics 18*, 3 (2014), 1026–1033.

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