Master's Thesis

Design of a Pattern Recognition Algorithm for Temporal Lobe Seizures for Future Use on a Mobile System

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Graz, July 2011

Abstract

Epilepsy is one of the most frequent neurological disorders of the brain. Patients often have to deal with a number of unpleasant restrictions during daily activities. Epileptic seizures can impair consciousness partly or completely. Once a person is ill with epilepsy the risk of experiencing a sudden seizure is always present. Therefore, patients are excluded from certain activities or they can only participate when special precautions are taken.

The reduction as well as the early detection of seizures is an important goal in order to allow patients to lead a normal life. This thesis deals with the detection of temporal lobe seizures, which constitute the most frequent subgroup of all seizure types. The detection is based on EEG and ECG signals provided by long-term monitoring. Pattern recognition is performed by an RBF-SVM.

This thesis is aiming to detect seizures close to the real onset. The detection should work on-line and in further consequence be used in combination with warning or monitoring devices.

The use of various features allows the detection of up to 88.9 % of tested temporal lobe seizures. A mean detection delay of 2.7 seconds after real seizure onset and a false alarm rate of 0.02 per hour are achieved.

Keywords: Epilepsy, Seizure Detection, Temporal Lobe, Electrocardiogram (ECG), Electroencephalogram (EEG), Support Vector Machine (SVM)

Kurzfassung

Epilepsie ist eine der häufigsten neurologischen Erkrankungen des Gehirns. Personen, die daran leiden, müssen im täglichen Leben mit einer Reihe von Einschränkungen umgehen. Durch epileptische Anfälle kann das Bewusstsein beeinträchtigt oder auch völlig verloren werden. Da einmal erkrankte Personen praktisch zu jeder Zeit von einem Anfall überrascht werden können, sind gewisse Tätigkeiten gar nicht, beziehungsweise nur unter gewissen Vorsichtsmaßnahmen möglich.

Um Patienten ein normales Leben zu ermöglichen, ist einerseits eine Reduktion, andererseits eine rechtzeitige Erkennung von Anfällen von großer Bedeutung. Diese Arbeit befasst sich mit der Detektion von Temporallappenanfällen, welche die häufigste Untergruppe epileptischer Anfälle ausmachen. Für die Detektion werden sowohl EEG als auch EKG Signale aus Langzeitmessungen ausgewertet. Die Mustererkennung wird mittels ausgewählter Features und einer RBF-SVM durchgeführt.

Ziel der Arbeit ist eine Detektion zeitlich nahe beim Einsetzen der Anfälle. Die Detektion sollte on-line funktionieren und in weiterer Folge in Warn- oder Beobachtungsvorrichtungen eingesetzt werden.

Unter Berücksichtigung unterschiedlicher Features können bis zu 88.9 % der getesteten Temporallappenanfälle innerhalb einer mittleren Verzögerung von 2.7 Sekunden detektiert werden. Dabei beträgt die Rate der falschen Alarme etwa 0.02 pro Stunde. Dies entspricht in etwa einem falschen Alarm innerhalb von zwei Tagen.

Stichwörter: Epilepsie, Anfallsdetektion, Temporallappen, Elektrokardiogramm (EKG), Elektroenzephalogramm (EEG), Support Vektor Maschine (SVM)

Statutory Declaration

I declare that I have authored this thesis independently, that I have not used other than the declared sources / resources, and that I have explicitly marked all material which has been quoted either literally or by content from the used sources.

Eidesstattliche Erklärung

Ich erkläre an Eides statt, dass ich die vorliegende Arbeit selbstständig verfasst, andere als die angegebenen Quellen/Hilfsmittel nicht benutzt und die den benutzten Quellen wörtlich und inhaltlich entnommene Stellen als solche kenntlich gemacht habe.

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Acknowledgement

First of all I would like to thank Dr. Stefan Rosenkranz and Mario Fallast who enabled the realization of this thesis at their company smaXtec product developement GmbH and supported me in every problem.

Furthermore I want to thank my mentor and assessor Dr. Gernot Müller-Putz for his support during this thesis as well as during the preceding Master's study.

Thanks also to Dr. Michael Feichtinger and especially to graduate nurse Gerda Zmugg at the University Hospital for Neurology in Graz for the time invested to collect and pre-process the patient data and also for the quick and solid replies to my questions about epilepsy.

Finally I would like to thank my parents Angelika and Franz Wolfgruber for their moral and financial support during my whole study.

Thank you very much!

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1. Introduction

About 0.5–1 % of the global population are diagnosed with epilepsy. Therefore, epilepsy is one of the most common neurological disorders of the brain [5, 58]. The following sections provide a short overview on the human brain and detailed information about epilepsy.

1.1. The Human Brain

The human brain consists of the telencephalon (cerebrum), diencephalon (thalamus, hypothalamus), brainstem (mesencephalon or midbrain, pons, and medulla oblongata), metencephalon (cerebellum), and medulla spinalis (spinal cord). A graphical overview is given in Figure 1.1 [53].

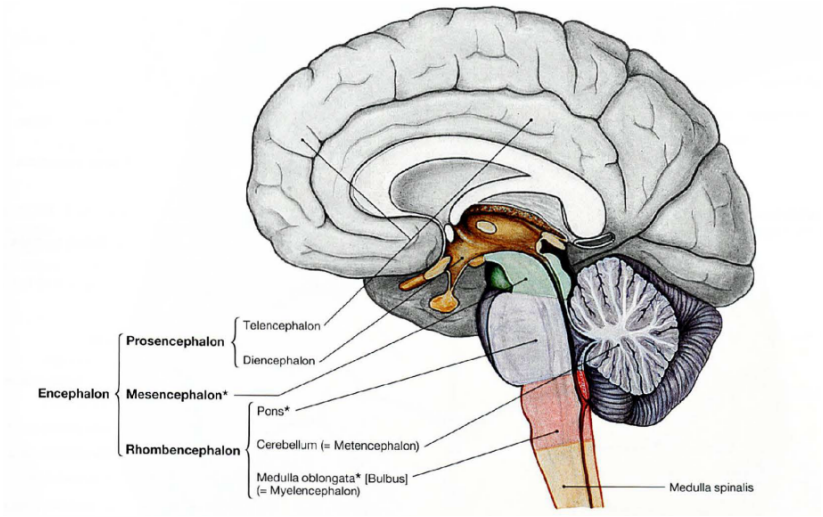

Figure 1.1.: Cross section of the human brain. Adapted from [53].

The cerebrum represents the largest part of the brain. It is split into a left and a right hemisphere and both hemispheres are further divided into four lobes: frontal, parietal, temporal, and occipital lobe. Figure 1.2 illustrates this segmentation [53].

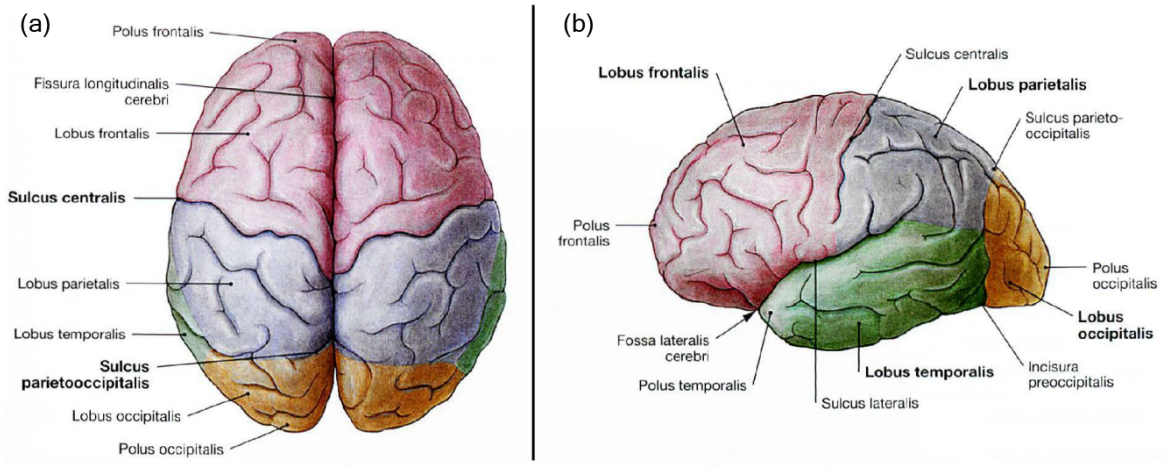

Figure 1.2.: The division of the cerebrum into four lobes: frontal lobe, parietal lobe, temporal lobe, and occipital lobe. Adapted from [53].
(a) View from above, additionally showing the division into two hemispheres. (b) Lateral view from the left side.

1.2. Epilepsy

1.2.1. Definition

The term *Epilepsy* originates from Greek "epilamvanein" which means "to be seized", "to be attacked" [23]. The International League Against Epilepsy (ILAE) provides the following definition:

"Epilepsy is a chronic condition of the brain characterized by an enduring propensity to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure." [26]

Furthermore, epileptic seizures are described as "transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain." [26] A great variety of different symptoms like changed motor and sensory functioning, altered level of consciousness, and behavioral changes may accompany the seizure [54].

1.2.1.1. Terms

Literature dealing with epilepsy makes use of certain medical vocabulary. Therefore, the most important terms used in this thesis are shortly described here:

ictal: refers to the seizure state and to events during this state [28].

inter-ictal: everything that happens between two seizures is referred to as being *inter-ictal*.

pre-ictal/post-ictal: describes the period directly before/after a seizure.

subclinical events: suggest the presence of diseases although no symptoms are visible. They may be the first indications of a developing disease. Subclinical seizures can only be noticed by characteristic changes within the electroencephalography (EEG) [62].

clinical events: are always accompanied by noticeable symptoms in contrast to *subclinical* events.

spasm: describes involuntary muscle contractions [21].

clonic (spasms): describes fast alternating muscular contractions and relaxations [21].

tonic (spasms): describes severe, longer lasting muscle contractions without relaxation [21].

paroxysmal activity: describes a brief activity that starts and ends suddenly [38].

1.2.2. Epidemiology

People of all ages can be affected by epilepsy, however, most new diseases occur during the first year of life and at an age older than 65 years [58]. The World Health Organization (WHO) provides a number of additional facts on epilepsy. They use a more restricted definition for epilepsy as the one given previously. In their definition a person is only diagnosed to have epilepsy after having experienced *at least two unprovoked seizures*. The WHO uses this adaption because up to 10 % of the world's population is facing at least one seizure during their lifetime. Of those persons about 50 million people worldwide suffer from consecutive seizures and are therefore diagnosed with epilepsy according to the WHO definition. Nearly 90 % of affected persons are living in developing countries. In [58] the rate of diseased persons (*prevalence*) is given with 5 to 10 per 1000 and the probability to develope epilepsy during one's lifetime (*cumulated incidence*) is estimated between about 2 to 5 % [5].

Epileptic disorders can be coarsely classified on behalf of their initial cause [5, 50, 58]:

Symptomatic epilepsy: About 25 % of the disease trace back to injuries of the central nervous system. These may be the result of head injuries, tumors, strokes, central nervous system infections, or perinatal complications.

Idiopathic epilepsy: Epilepsy resulting from genetic disorders is classified as *idiopathic*.

Cryptogenic epilepsy: All cases that cannot be classified as *symptomatic* or *idiopathic* are said to be *cryptogenic*. No evidence for a specific cause has been found for these cases so far.

Epilepsy is a chronic disorder, i.e., it accompanies patients for their whole lifetime. However, state of the art drug treatment is said to succeed in eliminating seizure activity in about 70 % of all applications [5].

A major problem arising in combination with the disease is the increased risk of injuries and even death as seizures might occur during critical situations, like participation in traffic, sports, cooking, handling dangerous tools, etc. Most risks can be eliminated with special care, however, the measures needed might negatively influence the quality of living. The mortality of patients that do not become seizure-free after treatment is slightly increased. Compared to healthy people, in the first nine years of the disease the mortality is about three times higher for patients with *symptomatic epilepsies* and 1.6 times higher for patients with *idiopathic epilepsies*. The higher risk for patients with symptomatic epilepsies is due to the often severe physical damage that has lead to the disease in the first place [58].

1.2.3. Seizure Types

A complete list of classified seizure types can be found in [22]. The list has been issued by the ILAE to deliver a standard guideline, however, in practice varying classifications are still in use. Table 1.1 gives a short overview of the most common seizure types.

The different seizure types are classified coarsely concerning their temporal and spatial properties.

Temporal properties: Seizure activity is either limited or unlimited in time. Self-limited seizures terminate after a few minutes at the longest, whereas continuous seizures have no specified time limit. This so-called *Status Epilepticus* is a life-threatening manifestation of epilepsy. The patient is either experiencing prolonged seizures or a number of consecutive seizures with no recovery period in between. If this condition lasts for more than five minutes, the person is in severe danger, as the brain is running out of oxygen and other metabolic products. This is due to the increased power consumption

Table 1.1.: Short list of different seizure types.

I) Self-limited seizures
- *a) Generalized seizures*
  - Tonic-clonic seizures
  - Absence seizures
- *b) Focal seizures*
  - Focal sensory seizures
    - With elementary sensory symptoms (e.g., occipital and parietal lobe seizures)
  - Focal motor seizures
    - With elementary clonic motor signs
    - With asymmetric tonic motor seizures (e.g., supplementary motor seizures)
    - With typical (temporal lobe) automatisms (e.g., mesial temporal lobe seizures)
  - Secondarily generalized seizures

II) Continuous seizures
- *a) Focal status epilepticus*
- *b) Generalized status epilepticus*

Adapted from [22].

of the brain during the heavily excitatory state of seizures. Brain damage can be the cause and eventually this condition may even lead to death [66].

Spatial properties: Both, self-limited and continuous seizures can either occur spatially limited to a certain brain region or be spread over the whole brain. A more precise description of these *focal* and *generalized* seizures is given next.

1.2.3.1. Generalized Seizures

Generalized or primarily generalized seizures are the result of synchronous neuronal discharges all over the brain starting straight at the seizure onset.

Tonic-Clonic Seizures: A common subtype of generalized seizures are tonic-clonic seizures also known as "Grand Mal". Their characteristics are best known by the layperson and therefore primarily associated with the term "seizure". Seizures start with a tonic phase that results in an *epileptic cry* as air is pushed out of the lungs [28]. Patients fall down as they lose consciousness. After that, the clonic phase begins in which extremities start to bend and relax interchangeably. The whole seizure may last for about 40 to 90 s.

Straight after the seizure the persons return to consciousness or transcend into a deep sleep (*postictal sleep*) that lasts for a few minutes or up to several hours [25, 48, 66].

Absence Seizures: Another kind of generalized seizures are absence seizures also known as "Petit Mal". Patients are unable to receive visual or acoustical inputs during the seizure as consciousness is impaired. Nevertheless, these seizures usually do not result in downfalls [48]. Absence seizures commonly last only about 5 to 10 s. Patients cannot recall those episodes after regaining consciousness [39].

1.2.3.2. Focal Seizures

Focal seizures are caused by malfunctions of a spatially restricted group of neurons. However, the seizure is not bound to start exactly at this defective focus. Depending on the malfunctioning brain region, focal seizures can be divided further (cf. Table 1.1). Focal seizures are often accompanied by distinct sensations or emotions. These experiences are called *auras*. Together with a close observation of the patient's behavior and reaction during a seizure as well as intense studying of the patient's EEG, experts are able to draw conclusions about the epileptic focus [66].

Seizures with focal onset can propagate to a large percentage of brain areas. These seizures are classified as secondarily generalized. Sometimes it is difficult to differentiate between secondarily generalized and generalized seizures because the spreading can be very fast [66].

Temporal Lobe Seizures: Temporal lobe epilepsy (TLE) is a very common type of epilepsy. Most TLEs (90–95 %) originate from the mesial temporal lobe. They roughly account for 40 % of all seizures and for 60–70 % of the focal seizures [58]. They can produce auras like rising epigastric sensations, dèjá-vus, abnormal gustatory or olfactory sensations, and psychic or mystical experiences. Additional symptoms concern heart rate, respiration and pupillary reflexes. Furthermore, motor reactions like smacking, hand automatisms and involuntary head turning are common phenomena. The aggregate of the described side effects allows professional staff to draw conclusions about the malfunctioning focus. It is quite common for temporal lobe seizures to expand to secondarily generalized tonic-clonic seizures [54, 66].

Frontal Lobe Seizures: The frontal lobe is the largest structure of the cerebrum (cf. Figure 1.2 in Section 1.1). A number of different seizure types are associated with this part of the brain. Exemplary seizures with "elementary clonic motor signs" and "asymmetric tonic motor seizures" are listed in Table 1.1. Forced movements of the head or limbs

are common while consciousness is often preserved. The EEG quite often looks normal during these seizures, therefore exact diagnosis is quite difficult in many cases [2, 54].

Occipital and Parietal Lobe Seizures: Both types are relatively rare. Occipital lobe seizures often affect the visual perception, whereas parietal lobe seizures are mostly accompanied by tingling or painful sensations [54].

1.2.4. Treatment

1.2.4.1. Anti-Epileptic Drugs (AEDs)

Two-thirds of epileptic patients benefit from anti-epileptic medicine. The success achieved by AEDs ranges from seizure reduction to total seizure elimination. AEDs operate by influencing the chemical processes in the brain that are active during epileptic seizures. Although many people benefit from AEDs this treatment is accompanied by major drawbacks. Many side effects come along with the used drugs, as they usually affect the entire brain. In some cases those side effects can be even worse than the disease they are designated to cure. Furthermore, the drugs have to be customized for each patient. The real problem causing the seizures is seldom understood completely. Therefore, the type of drug as well as the administered dosage has to be chosen in a trial and error fashion. There are about 15 different pharmaceuticals available. If, after applying more than three different AEDs, the number of seizures does not drop distinctly, other means of seizure prevention, like brain surgery or electrical stimulation, need to be examined [58, 66].

1.2.4.2. Surgery

As mentioned earlier (in Section 1.2.3), focal epilepsies are caused by a spatially constrained focus within the brain. Patients suffering from this kind of epilepsy can therefore become seizure-free by surgically resecting the epileptic focus from the brain. Resection should only include cerebral matter already damaged by numerous seizures and therefore leave the patients without additional damage. However, also functional regions might be removed from the brain which can result in post-surgical behavior changes or the decline of cognitive functions, like partial memory loss. Furthermore, surgery always carries the risk of infections. Surgical interventions range from partial or complete resection of a brain lobe to the resection of a whole hemisphere. Even in the latter case it is shown that patients can regain motor control because of the plasticity of the brain. Brain surgery is most prominently used with mesial temporal lobe epilepsy as this type seems to be especially resistant to AEDs [44, 58, 66].

1.2.4.3. Electrical Stimulation

Practically, electrical stimulation is a surgical intervention as well, but in literature it is sometimes treated as a separate topic. Brain structures are usually less damaged by this procedure. The goal of electrical stimulation is to stimulate certain brain areas in order to abort or control epileptic activity. Two different stimulation methods exist: vagal nerve stimulation (VNS) and deep-brain stimulation (DBS). Those two different electrical stimulation approaches are illustrated in Figure 1.3.

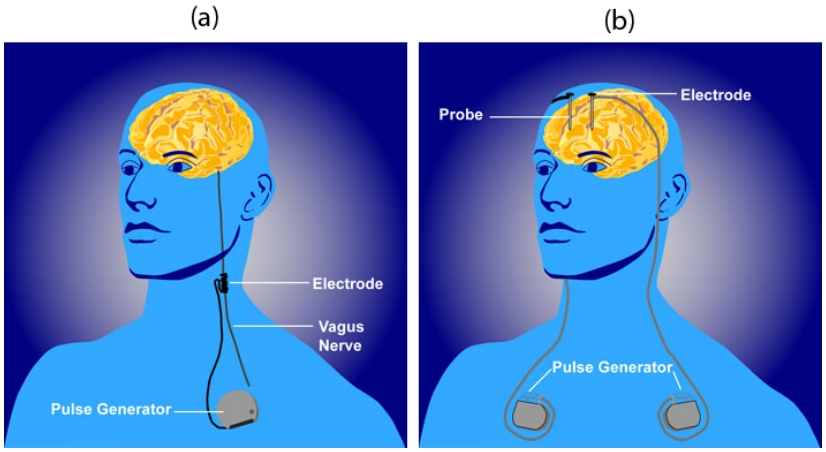

Figure 1.3.: Different methods of electrical stimulation. Adapted from [4].
(a) Vagal nerve stimulation (VNS); (b) Deep-brain stimulation (DBS).

VNS: The vagal nerve is one of the main nerves connecting internal organs to the brain. A large percentage of the vagal nerve is afferent, which enables the stimulation to almost exclusively affect the brain without the need for brain surgery. The exact dynamics behind VNS are not readily understood. Increased inhibition because of serotonin release might be an explanation [8]. VNS usually has less side effects than AEDs and it can even positively affect the patient's mood [66]. Murphy et al. [47] have investigated the long term benefits of VNS for 70 patients and have found that VNS succeeds in at least halving the number of seizures of about 50 % of these patients.

DBS: In DBS the stimuli generator is placed directly within the brain. Success rates of DBS and VNS are similar [66]. In current applications all electrical stimulations are run continuously (i.e., 7 s on, 12 s off). A new approach aims at activating the generator only in case of a seizure. Therefore, it has to be investigated whether ongoing seizures can be stopped. Furthermore, reliable seizure detection systems are needed [66].

1.3. Common Signals Used for Seizure Detection

1.3.1. Electrophysiological Brain Signals

As epileptic seizures present neuronal discharges within the brain, electrophysiological brain signals have proved useful for observing the disease. However, although great effort has been put into deciphering epileptic patterns, it is still difficult to classify brain signals correctly. Sometimes it is even impossible to separate ictal-clinical from ictal-subclinical or interictal paroxysmal activity [48].

Different methods for obtaining brain signals are available. A distinction between non-invasive, invasive, and semi-invasive signals can be made. Ictal and inter-ictal patterns look similar for these different measuring methods. However, the magnitude of the signal as well as the temporal resolution differs. Also, the influence of electromyographic (EMG) artifacts is much weaker in invasive recordings compared to non-invasive recordings. Invasive signals also provide a better signal-to-noise ratio. Furthermore, ictal patterns may be spotted earlier by invasive methods than by non-invasive methods [49]. In a number of cases, seizure activity, especially auras and subclinical seizures, can be observed exclusively by invasive techniques [42].

Non-Invasive Signals: Electroencephalography (EEG), also referred to as *scalp EEG*, provides a number of advantages compared to invasive methods. It is cheap and relatively easy to apply. Therefore, usage is widespread. Furthermore, electrode placement is standardized, which makes it easier to compare data from different patients. In epilepsy monitoring, usually long-term EEG is used. Unlike short-term EEG, electrodes are glued to the skin in order to maximize conductivity and to minimize artifacts.

Invasive Signals: Invasive methods for data mining are usually only used preceding brain surgery and therefore available data is rare. Electrodes are either placed directly on the cortex (*electrocorticography (ECoG)*) or even further inside the brain (*depth electrodes*). Spatial resolution is superior to scalp recordings, but the brain area monitored is very limited. Electrode positions are chosen individually and are therefore not comparable between different subjects. Furthermore, due to ethical reasons there exists no data from healthy subjects for comparison. Also, the electrode placement is not standardized [66].

Semi-Invasive Signals: In addition to the measurement methods discussed before, so-called semi-invasive procedures are sometimes applied in combination with scalp EEG. In [20] two different techniques are described: sphenoidal and nasopharyngeal electrodes. These electrodes penetrate through the cheek or nose and are used in focal epilepsy monitoring

in order to reach positions closer to epileptic foci. The authors do not think that those techniques offer much additional information to scalp EEG recordings although they state some benefits in focus localization accuracy.

1.3.1.1. Inter-ictal EEG Patterns

There are some typical inter-ictal EEG changes that indicate epileptic seizure disorders. Most prominent are the so-called *spikes* and *sharp waves*. However, the occurrence of such patterns in an EEG offers no strict evidence for epilepsy, as those patterns can be found within persons not having experienced a single epileptic seizure. The presence of these paroxysmal EEG changes may indicate a certain predisposition for future seizures or the presence of smaller psychological dysfunctions, though [48]. Figure 1.4 shows different manifestations of inter-ictal EEG phenomena.

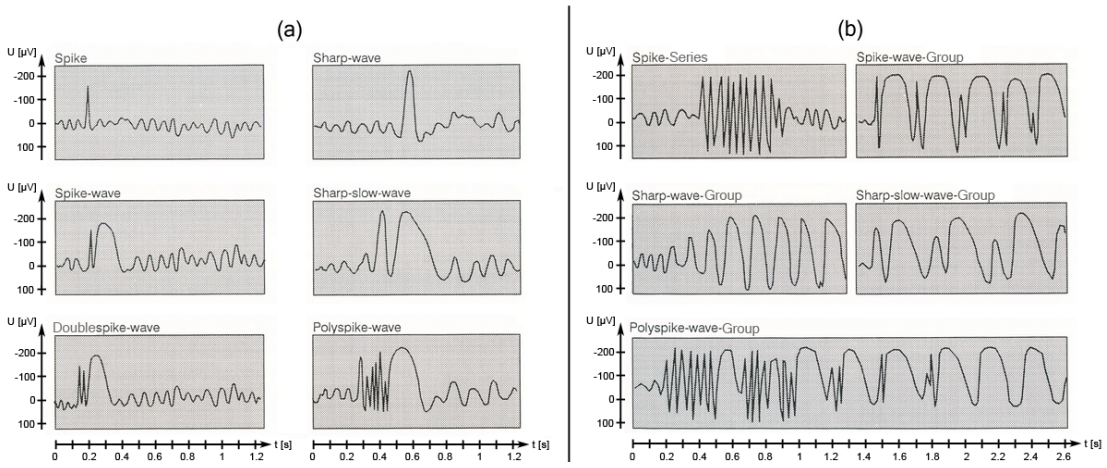

Figure 1.4.: Different inter-ictal EEG manifestations. Adapted from [15].
(a) Single potentials and complexes; (b) Series.

Spikes: Spikes are localized EEG patterns with a major negative component. A peak of a duration between 20 to 70 ms and variable amplitude can be seen in the EEG. Spike morphology can vary inter- as well as intra-individually. Evidence exists that at least some spikes are more than pure EEG patterns. Shewmon and Erwin [59] showed that spikes are capable of temporally impairing brain functionality at the region of occurrence. Furthermore, spikes are discussed to be especially present as a post-ictal phenomena [29, 48].

Sharp Waves: Sharp waves show similar morphologies as spikes. Their main component is negative as well. However, their duration is longer ($\sim$ 70–200 ms) [48].

Polyspikes or Multiple Spikes: Two or more consecutive spikes with variable duration and often large amplitudes are called polyspikes [48].

Runs of Rapid Spikes: A series of spikes may persist for 2 to 10 s and show a higher frequency than usual spikes. They have a similar morphology to some epileptic seizures but they exclusively appear during sleep [48].

Spike Wave Complex: Spike wave complexes are defined as a spike followed by a slow wave. They appear in different velocities: 1–2.5 per second, 3 per second, 4–5 per second, 6 per second. Different frequencies and foci allow to draw conclusions about the underlying epileptic seizure type. A contradictory example are 6 per second spike wave complexes with focus in the occipital lobe which do not suggest any epileptic disorder [48].

1.3.1.2. Ictal EEG Patterns

According to [31] cited in [56] most epileptic seizures show an increased EEG activity between 3 and 29 Hz at seizure onset. In [48] additional indications for epileptic EEG activity are pointed out:

Change of Frequency: Clinical seizures often cause a sudden change of frequency range. Dominant frequencies at epileptic events are usually within the alpha frequency or sometimes a bit faster or slower than that. This dominant frequency may change slowly while the seizure progresses.

Loss of Voltage: A special seizure type (*electrodecremental seizures*) manifests in a sudden strong decrease in amplitude resulting in almost a flat line. The frequency changes from very fast to slower frequencies as the EEG recovers to normal amplitude.

Increase of Voltage: A sudden increase in amplitude is noted especially during petit mal absences.

Ultraslow/Ultrafast Frequencies: Ultraslow frequencies (0–0.3 Hz) as well as ultrafast frequencies (90–1000 Hz) are carrying information about epileptic states. To capture these frequencies special EEG measuring devices are needed.

Additionally to these indications ictal EEG might just look the same as the inter-ictal patterns described in the previous subsection. The only visible difference to the inter-ictal manifestation might be a prolonged appearance.

As different inter-ictal patterns indicate different types of epilepsy the same is true for ictal patterns. In this study, the main interest lies on temporal lobe seizures. Therefore, only additional ictal EEG changes related to this type are described here.

Temporal lobe seizures show a great variety of ictal and inter-ictal patterns. Observed patterns include *serrated slow waves*, *flat-topped 4/s waves*, and *high voltage 6/s waves* [48].

As mentioned earlier (cf. Section 1.2.3) temporal lobe seizures can develop to tonic-clonic seizures. Therefore, typical patterns for this type would be interesting as well. The problem with tonic-clonic seizures is, however, that the EEG is highly contaminated by muscular artifacts. Special patterns can only be visualized by using muscle relaxants and artificial respiration which is not practicable for this thesis [48].

1.3.1.3. Difficulties concerning EEG Interpretation

Subclinical Seizures: Subclinical seizures are only traceable through EEG recordings. There is no other evidence, like auras or changed behavior signaling, that the person is experiencing a seizure. According to Babb et al. [10] the difference of subclinical to clinical seizures results from varying recruitment of synchronously firing neurons. Increased firing of about 7 % of neurons at the epileptic focus has been noticed during subclinical seizures, whereas seizures that have been accompanied by auras have had about 14 % of neurons active. Estimated 36 % firing neurons have been involved with seizures that have shown loss of consciousness and other side effects. Depending on the usage of a detection system those seizures have to be recognized as well or they can be left aside.

Inter-/Intra-subject Variations: A problematic property of seizures is their diversity. Leave alone the different seizure types, the same seizure type can produce varying EEG patterns from seizure to seizure. This is true for different patients with the same seizure type as well as for different seizures from the same person.

1.3.2. Electrocardiography (ECG)

Another signal type useful in seizure detection is the ECG. Still in literature, most research is done concerning EEG and only a small selection of studies utilizes ECG signals in detection systems. According to Leutmezer et al. [41] heart rate changes are a common phenomena at seizure onset. They have investigated 145 seizures from 58 patients. Of those 86.9 % have shown tachycardia and 1.4 % have shown bradycardia. Increased heart rate has been measured on average already 13.7 s ahead of first seizure signs within the EEG for temporal lobe seizures.

1.3.3. Electromyography (EMG)

In seizure detection electromyographic events are mostly handled as spurious artifacts. However, the EMG might carry useful information itself. A technique using EMG information and accelerometer data to detect the onset of epileptic seizures is proposed by Lorincz et al. [43]. In their study, they have used 8 sensors, one for each limb segment (upper and lower arms and legs).

1.3.4. Other Signals

In addition to the signals described before, there might be other signals indicating seizure activity, which could be exploited for detection. Some of the autonomic signals that accompany seizures are listed next [12]:

Respiratory Manifestations: Examples are hyperventilation, choking, and apnea.

Gastrointestinal Manifestations: Most prominent are epigastric auras. Occasionally seizures are accompanied by spitting or vomiting.

Cutaneous Manifestations: Examples are flushing, sweating, and piloerection.

Pupillary Manifestations: In many tonic-clonic seizures pupils are dilated.

1.4. Epileptic Seizure Detection

1.4.1. Overview

Automatic detection of epileptic seizures has been investigated by researchers for many years now. One of the first attempts has been undertaken by Gotman [29]. His system has been built to recognize seizure events during long-term EEG recordings in order to assist EEG technicians in the examination of the large amount of data that is collected. The algorithm is designed to work on-line and only seizures that show rhythmic activity within the 3 to 20 Hz range are addressed.

Gotman's features are based on so-called half-waves which he described already earlier in [30]. To get these half-waves, the EEG signal is lowpass filtered and decomposed into segments between local minima and maxima. After that, the following three features are calculated:

- *Relative average amplitude:* The average half-wave amplitude in a 2 s window is computed. The result is then related to an average value computed from a larger data segment of the recent past (sliding background window).
- *Average duration:* The average half-wave duration is calculated for each 2 s window.
- *Coefficient of variation of duration:* The ratio between standard deviation and the mean of the half-wave durations within a 2 s window is computed. This feature is used to measure the rhythmicity of the signal.

Artifact rejection is used for too large amplitudes or too short durations. For detection predefined thresholds are used for all three features.

The algorithm has been used for EEG as well as for ECoG data. Results show, that 22 % of all EEG detections and 2.5 % of ECoG detections have been correct. There is not sufficient information about missed seizures as data has only been recorded after automatic detection or after patients or staff have pressed a button. The designed detection system is intended not to miss any seizures. Therefore, the relatively large amount of false detections does not pose a big problem.

Since this first encouraging attempt, a lot of different approaches have been made to generate improved detection algorithms. In this section the different approaches and results are stated and compared to each other. However, comparison is problematic as different studies pursue different goals and therefore the experimental setup varies strongly. The following list shows a number of possible differentiations between the studies:

- *Measurement method:* scalp EEG vs. ECoG
- *Observed seizure types:* all seizure types vs. selection of seizure types
- *Detection mode:* off-line vs. on-line
- *Accuracy criterion:* no missed seizures vs. no false positives
- *Subject specificity:* subject specific vs. subject independent
- *Timing restrictions:* detect seizure no matter when vs. detect seizure at onset

Furthermore, differing electrode settings are used and the amount of analyzed data can differ to a great degree.

1.4.2. Quality Measures

As mentioned earlier, requirements for seizure detection systems can vary strongly. Depending on the designated application, classifiers need to behave differently. The quality of a classifier can be calculated with a number of different measures. Most of these measures rely on values of the so-called "confusion matrix" shown in Table 1.2. Formulas for the most important measures are given next.

Table 1.2.: Confusion Matrix. Juxtaposition of assigned and actual classification

	assigned positive	**assigned negative**	
actual positive	true positive (TP)	false negative (FN)	$P = TP + FN$
actual negative	false positive (FP)	true negative (TN)	$N = FP + TN$
	$P' = TP + FP$	$N' = FN + TN$	$PN = P + N$ $= P' + N'$

Adapted from [6].

Sensitivity [%]: Indicates how many of the presented seizures are detected.

$$\text{Sensitivity} = \frac{TP}{TP + FN}\,[\%] \tag{1.1}$$

Specificity [%]: Gives information about how many non-seizure events are falsely detected as seizures.

$$\text{Specificity} = \frac{TN}{TN + FP}\,[\%] \tag{1.2}$$

Accuracy [%]: Shows the proportion of correctly classified events.

$$\text{Accuracy} = \frac{TP + TN}{PN}\,[\%] \tag{1.3}$$

Cohen's Kappa (κ) [19]: The real classification accuracy $\mathbf{p_0}$ is compared with the accuracy at random $\mathbf{p_e}$. For imbalanced classes this measure provides a better insight about the quality. Values close to zero indicate poor accuracy. In case all samples are classified correctly κ equals 1.

$$p_0 = \frac{TP + TN}{PN} \tag{1.4}$$

$$p_e = \frac{P}{PN} \cdot \frac{P'}{PN} + \frac{N}{PN} \cdot \frac{N'}{PN} \tag{1.5}$$

$$\kappa = \frac{p_0 - p_e}{1 - p_e} \tag{1.6}$$

False Detection Rate (fdr) $\left[\frac{1}{\mathbf{h}}\right]$, $\left[\frac{1}{\mathbf{d}}\right]$: False detections are often stated in relation to a time interval (i.e., number of false detections per hour or per day).

$$\mathrm{fdr} = \frac{\mathrm{FP}}{\mathrm{T}} \left[\frac{1}{\mathrm{h}}\right] \tag{1.7}$$

Detection Delay: Time that elapses between seizure onset $\mathbf{t_s}$ and detection $\mathbf{t_d}$. This value can also be negative, in case the seizure is detected ahead of the real onset.

$$\mathrm{Detection\,Delay} = \mathrm{t_d} - \mathrm{t_s}\,[s] \tag{1.8}$$

The measures *Specificity* and *Accuracy* are sometimes used in context with seizure detection, however, the commonly enormous imbalance between the number of seizure samples and non-seizure samples limits their expressiveness. More significant values are provided by *Cohen's Kappa* or the *fdr*.

Classification precision is always assessed through the number of true and false detections. The definition of those values can vary according to the underlying problem. The area for true detections could be restricted to the marked seizure period, or be relaxed to a wider range including an additional pre-ictal and/or post-ictal period. When counting false detections either each wrong sample adds up or consecutive false detections are counted as one as long as they lie within a certain time window.

1.4.3. State of the Art

For a seizure detection system design the following topics are of main interest:

- *Artifact treatment*
- *Feature selection*
- *Classification method*

The following sections will provide detailed information about how other studies have dealt with those topics. Furthermore, the concept of a seizure prediction system is presented.

1.4.3.1. Artifact Treatment

The used signals are often contaminated with all sorts of artifacts including electrooculographic (EOG) and electromyographic events. Various approaches are available to cope with these signal disturbances [66].

Ignoring: Artifacts with little influence can be ignored. This is often done with EOG artifacts, although some studies state their possible similarity to seizure activity. In [56] false detections have mainly been due to chewing, short rhythmic bursts and rapid eye blinking.

Rejecting: Rejection should only be used in severe cases, when artifacts distort the signal beyond repair and no valuable information can be extracted from the signal. Possible situations are signal overflows or electrode flat lines caused by strong muscular artifacts or electrode failures.

Removing: Several different removing techniques can be found in literature. Their goal is to identify and eliminate artifact influence. Regression techniques or blind source separation (cf. [67]) as well as adaptive filtering methods (cf. [33]) are used for EOG artifacts. Power line interference is usually removed using a notch filter. EMG artifacts can be reduced by lowpass filtering. A total elimination of the EMG through filtering is not possible, however, as the spectra of EEG and EMG are overlapped.

Learning: Machine learning algorithms like Artificial Neural Networks (ANN) or Support Vector Machines (SVM) are capable of learning the patterns of certain artifacts. Signals contaminated by artifacts are presented during the training phase. If similar samples occur during the testing phase, they are more likely to be classified correctly.

1.4.3.2. Features Selection

Many different feature combinations have been proposed for seizure detection in the last few years. In this section some of the existing publications are presented. The studies are analyzed separately depending whether invasive (ECoG), non-invasive (EEG), or a combination of both signal types have been used for evaluation.

ECoG Signals

Line-length has been identified as a good feature to separate ictal events from inter-ictal events by [24]. This feature is sensitive to changes in frequency as well as changes in amplitude of the signal. Besides, computation is cheap and easy. *Line-length* is again used by Chua et al. [18] in combination with standard *Gotman features* (cf. Section 1.4.1), and *rectified zero crossings*. *Rectified zero crossing* is sensible to positive as well as negative changes in the baseline frequency. Chua et al. observed 15 patients providing 529 h of data and 63 seizures. Together with a *quadratic discriminant analysis* the described feature combination results in a sensitivity of 78 % and an fdr of 0.18/h.

EEG Signals

Shoeb [60] used frequency features and an SVM for automatic on-line seizure detection. Shoeb examined 844 h from 23 patients containing 163 seizures. His results show an early detection, a high sensitivity ($\sim 96\,\%$) and a median fdr of about 0.08/h. Because of these promising results, a similar approach is chosen for this thesis. More information about the used features will be provided in Chapter 2.

In [37] only left temporal lobe seizures were observed. Four electrodes near to the diagnosed focus were used for each patient. The electrode positions were chosen individually for all patients. *Autoregressive (AR) parameters* that describe frequency, spectral power and rhythmicity were used as features. They were calculated with the *Burg maximum entropy AR method* [14]. A single threshold was used for classification. 1624 h of data containing 83 seizures from 10 patients was evaluated. With this approach 91.6 % of all seizures were detected and an fdr of 0.27/h was reached.

An on-line attempt was performed by Webber et al. [68] who used information about *amplitude*, *slope*, *curvature*, *rhythmicity*, and *frequency* of the signal. Together with an artificial neural network (ANN) they reached a sensitivity of 76 % and an fdr of 1/h.

Another on-line detection system was suggested by Meier et al. [46]. A number of different features were used: *continuous wavelet transform* to capture rhythmical behavior in different frequency bands, *mean sliding variance* to detect signal power changes, *mean cross correlation* to find changes in synchrony, *zero crossings* to get information about the dominant frequency, and *Savitzky-Golay* filter. The latter was used to get the mean signal power which is also a sign for ictal activity. The features were ranked and related to data from a delayed background window for normalization. A seven class SVM was used for classification, which allowed the differentiation of some common ictal patterns. Data from 57 patients containing 91 seizures within 1400 h of recording were analyzed. Sensitivity amounted to about 96 %. A mean delay of 1.6 s and an fdr of 0.5/h were reached.

Standard *Gotman features* (cf. Section 1.4.1) were used together with the *dominant frequency*, the *average power around the dominant frequency*, and *information of the seizure location* by Qu and Gotman [55]. Their system worked on-line and they reached a sensitivity of 100 % with a modified nearest neighbor classifier. Mean detection delay was about 9 s and an average fdr of 0.02/h was acchieved. The observed data amounted to about 300 h and contained 47 seizures from 12 different patients.

Saab and Gotman [56] used *wavelet transform* and a Baysian classifier. Prior probabilities were extracted from training data. For each testing sample the probability of being a seizure sample was calculated. If the probability was high enough a seizure had been detected. The

algorithm was designed for on-line use and worked patient unspecific. Therefore, a lower sensitivity and fdr was reached. 360 h of data, including 69 seizures in 16 patients were analyzed. The sensitivity amounted to 77.9 % and a median delay of 9.8 s was reported. An fdr of 0.86/h was achieved.

Van Putten et al. [65] considered temporal lobe seizures for their study only. For the detection task they compared a number of different features: *phase synchronization*, *mean amplitude*, *minima* and *maxima*, *zero crossing*, *Omega complexity*, and *brain symmetry*. *Phase synchronization* was analyzed as epileptic seizures tend to behave in a synchronized manner and therefore might show a fixed phase difference between various brain areas. *Mean amplitude* relies on increased activity during seizures. The number of *minima* and *maxima* as well as the number of *zero crossings* was used as they capture frequency behavior. *Omega Complexity* was tested because seizure activity is thought to change the complexity of the observed signal. The spectrum of brain activity usually appears quite synchronized between the two hemispheres. During focal ictal events this synchronization level decreases. Therefore, the *brain symmetry index* had been calculated. Van Putten et al. identified the *brain symmetry index* as the best feature for detecting unilateral seizure activity. Bilateral activity was identified best by the number of *minima* and *maxima*. Altogether sensitivities between 77 % and 97 % and an fdr of about 1/h were achieved.

McSharry et al. [45] compared linear features with their own developed *nonlinear technique*. Linear features included the *signal variance*, the *power spectrum*, and the *autocorrelation function* of the signal. Results showed that variance delivers the same sensitivity as the nonlinear approach while being easier to compute. On the other hand less false detections and a reduced detection delay were stated using the nonlinear feature.

Combination of EEG and ECoG Signals

A small number of datasets containing EEG recordings of epileptic seizures is freely available on-line. A list of these sources can be found in Appendix A. One of the datasets contains both EEG data and ECoG data [9]. Due to the fact that a number of publications are based on this combined dataset the similarity between EEG and ECoG features seems to be sufficient. The described dataset had been used by [64] in combination with time-frequency features. These features were computed using a smoothed pseudo-Wigner-Ville distribution [7]. The used features basically extracted information of the signal's spectrogram. Depending on the used parameters an accuracy of up to 100 % was reached in this study. The comparability of this result to other studies is very limited, however. The dataset only provides segmented data of a length of 23.6 s per segment. This segment is either classified as seizure or not.

Furthermore, in some cases seizure free scalp EEG from healthy persons was compared to ictal ECoG.

Kannathal et al. [36] used the same dataset. They applied different entropy measures in time as well as frequency domain for seizure detection. The study concluded that ictal events show less entropy compared to inter-ictal events.

ECG

For seizure detection a promising feature of the ECG signal seems to be the *Heart Hate Variability (HRV)* as well as the *R-R Interval (RRI)* [41]. The RRI measures the distance of two consecutive R waves of the ECG. Therefore, the R waves need to be detected first. This is illustrated in Figure 1.5. Shoeb [60] used a combination of the mean heart rate and the heart rate change within a certain time window together with EEG frequency features for a small subset of his data. Results show that the additional usage of the ECG decreases the number of false detections and partly also decreases the detection delay.

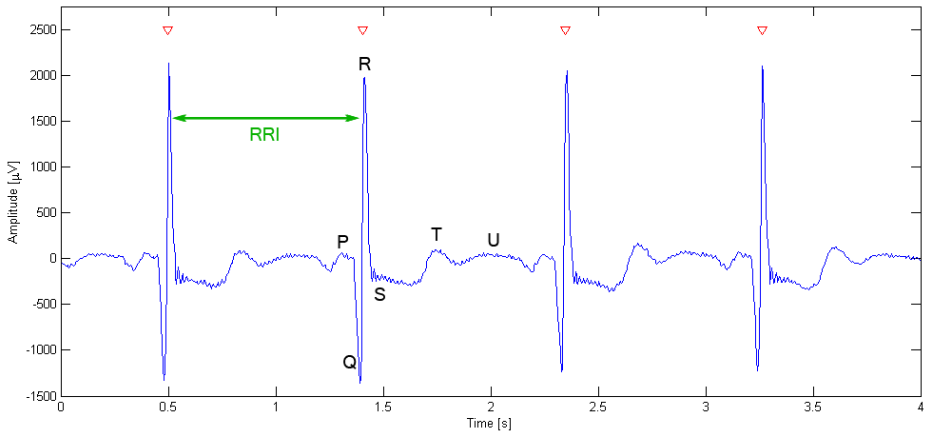

Figure 1.5.: Exemplary snippet of an ECG to illustrate the R-R Interval. Red triangles point at detected R waves. The RRI denotes the temporal distance between to consecutive R waves. The letters P to U describe structural landmarks of a single ECG complex.

1.4.3.3. Classification Methods

In the previous section a number of different classification methods have already been mentioned. In this section the methods that are most often used in seizure detection are shortly described. These methods utilize simple thresholding techniques which do not need any training and the implementation of a classifier which has to be trained before use:

Association Rules: In [66] the approach of manually defining thresholds to distinguish between ictal and inter-ictal patterns is summed up under the term "association rules". This technique does not need a training phase. Class features are inspected and thresholds are set where differences are visible. Therefore, only features with obvious inter-class differences can be used. When using multiple features the definition of appropriate thresholds might become very difficult.

Discriminant Functions: For this method the classes are assumed to be normally distributed in feature space. The goal of the discriminant function is to maximize the distance between the class means, while minimizing the intraclass (co)variances [13]. Several different types of discriminant functions have been used for seizure detection. In [52] Linear Discriminant Analysis (LDA), Quadratic Discriminant Analysis (QDA), and Mahalanobis Discriminant Analysis (MDA) have been compared to each other. Best results have been achieved by LDA in their study. Compared to SVMs, LDAs are more sensitive to the number of used features. The use of too many features may therefore result in overfitting.

Artificial Neural Networks (ANN): ANNs are based on the structure of the human brain. A network usually consists of a number of input neurons, intermediate neurons (hidden neurons) and output neurons. This architecture makes it relatively easy to deal with multiple classes, because each existing class only needs to be assigned to a distinct output neuron. Each neuron takes an input and calculates an output with its "activation function". Both, linear and nonlinear activation functions can be implemented. Connections between neurons are weighted during a training phase to map the training input to the correct output class.

Different neural network architectures, including feed-forward networks [64, 68] and self-organizing maps (SOM) [27] have already been tried in seizure detection. The easy application to multi-class problems enables a detector to learn and distinguish common artifacts or special brain wave patterns like alpha activation from typical seizure activity. On the other hand ANNs do not cope well with unbalanced data. Every training sample influences the model's weights and therefore equal amounts of training data for each class are needed to guarantee balanced performance ([35] cited in [68]).

Support Vector Machines (SVM): SVMs have originally been developed for two-class classification problems. They are trained with a number of feature vectors that represent the two different classes. Their goal is then to find a separating hyperplane in an n-dimensional feature space. This hyperplane is located in a way that a maximum margin is obtained between the two competitive classes. It is called the "optimal separating hyperplane".

Feature vectors of each class located nearest to this hyperplane are called support vectors. Figure 1.6 (a) shows an example for the optimal separating hyperplane in a linearly separable two-dimensional feature space [6].

Unlike ANNs the SVMs always end up with the same solution when being trained with the same data. It also does not get stuck in local minima.

SVMs can be divided into hard-margin and soft-margin SVMs. Hard-margin SVMs do not allow any misclassification on the training data. The separating hyperplane is placed in the middle of the outermost samples of the different classes (cf. Figure 1.6 (a)). Soft-margin SVMs on the other hand allow a certain amount of misclassified samples. Figure 1.6 (b) shows the separating hyperplane determined by a soft-margin SVM.

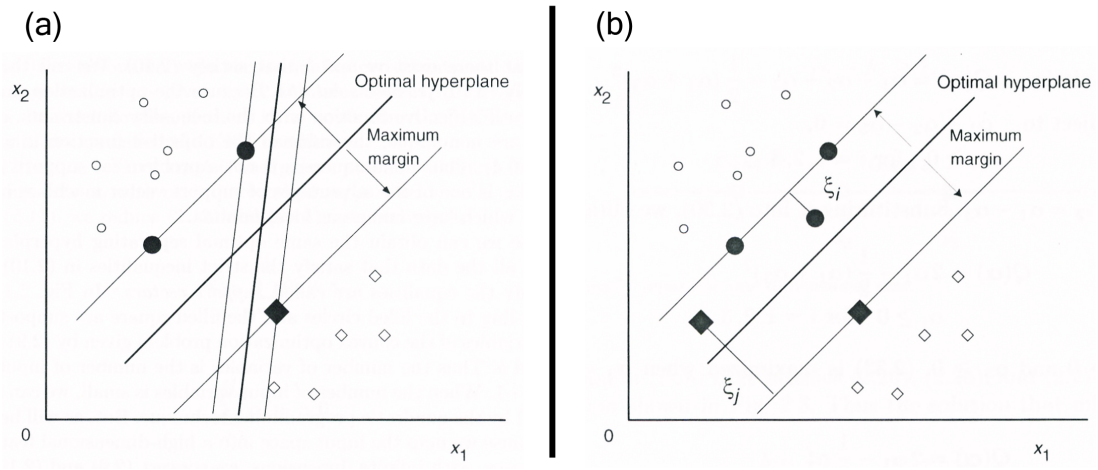

Figure 1.6.: Optimal separating hyperplane for a two class problem in a two dimensional feature space. Support vectors are emphasized. Adapted from [6].
(a) Linearly separable classification problem. A non optimal hyperplane is indicated as well. (b) A soft-margin SVM calculates a trade off between maximal margin and minimal classification error.

The soft-margin SVM searches for the solution of the following optimization problem:

$$\min_{\mathbf{w},b,\boldsymbol{\xi}} \ \frac{1}{2}\mathbf{w}^{\mathrm{T}}\mathbf{w} + C\sum_{i=1}^{l}\xi_i \tag{1.9}$$

$$\text{subject to } \mathrm{y}_i\left(\mathbf{w}^{\mathrm{T}}\phi\left(\mathbf{x}_i\right) + b\right) \geq \ 1 - \xi_i, \tag{1.10}$$

$$\mathrm{K}\left(\mathbf{x}_i, \mathbf{x}_j\right) \equiv \phi\left(\mathbf{x}_i\right)^{\mathrm{T}}\phi\left(\mathbf{x}_j\right) \tag{1.11}$$

where : $\mathbf{x}_i$ . . . input training sample — $\mathbf{w}$ . . . weight vector
y_i . . . input class label — b . . . bias term
$\mathrm{K}\left(\mathbf{x}_i, \mathbf{x}_j\right)$ . . . kernel function — C . . . margin parameter
$\phi\left(\mathbf{x}_i\right)$ . . . nonlinear vector function — ξ_i . . . slack variable (≥ 0)
l . . . number of training samples

Training samples $\mathbf{x}_i$ together with their corresponding class labels y_i serve as input to the SVM. Parameter $C > 0$ is called the margin parameter which "determines the trade-off between the maximization of the margin and the minimization of the classification error." [6]. Depending on the nature of the observed problem SVMs can integrate different kernels in their kernel function $\mathrm{K}\left(\mathbf{x}_i, \mathbf{x}_j\right)$. For linearly separable data a linear kernel is used. An application of a linear kernel can be seen in Figure 1.6. For more complex input data other kernels, like polynomial kernels or radial basis function (RBF) kernels can be applied [6, 17].

Equation 1.12 shows the mathematical description of a RBF-kernel ($\mathrm{K}_{\mathrm{RBF}}$). Parameter $\gamma > 0$ is responsible for the radius of the kernels that are centered at the support vectors $\mathbf{x}_i$. $\mathbf{x}_j$ are the sample input vectors.

$$\mathrm{K}_{\mathrm{RBF}}\left(\mathbf{x}_i, \mathbf{x}_j\right) \ = \ \exp^{-\gamma\left\|\mathbf{x}_i - \mathbf{x}_j\right\|^2} \tag{1.12}$$

SVMs have originally been developed for two class problems [13]. However, they are also capable of solving multi-class problems. As mentioned earlier, Meier et al. [46] have used a multi-class SVM to differentiate between several seizure morphologies.

Relevance Vector Machines (RVM): RVM is a concept that is quite similar to SVM. In contrast, it is a probabilistic classification method. The resulting model is usually sparser than in the SVM case and therefore faster testing is possible. The generalization ability is comparable or even better and no hyper parameters need to be adjusted. On

the downside training time is likely to take longer for RVM [13, 69]. RVM has also been used in seizure detection already [32].

1.4.3.4. Concept of Seizure Prediction Systems

Seizure prediction is a related topic to seizure detection. Instead of detecting a seizure at onset, the detection should occur at some point in time preceding the seizure onset. At Graz University of Technology, Hieden [34] has used ECoG data for a seizure prediction system. Features are derived from an autoregressive model and three different classifiers (Linear Discriminant Analysis, Support Vector Machine, and Mahalanobis Distance Analysis) are compared. Instead of class separation in ictal and inter-ictal class as usually done in detection systems, pre-ictal events are discriminated from all other events. The only exceptions are ictal events which are left out completely. The results of the study show a sensitivity slightly better than random. However a lot of false alarms and a large prediction time window are mentioned as problematic.

1.5. Motivation & Goal

1.5.1. Why Real-Time Seizure Detection?

As mentioned earlier epilepsy is a widespread chronic disease. Epileptic seizures often occur without warning and therefore involve the risk of injury or death. Patients could hurt themselves when falling to the ground or while twitching. But even if the posture is retained during the seizure, dangers may arise in certain situations as responsiveness might be impaired. Examples for such situations are car driving and a number of sporting activities like swimming, mountaineering or biking. Patients with epilepsy might be excluded from these activities completely or they need to take special precautions. Day trips to scarcely visited places without company may be problematic as well, as nobody has information about the whereabouts and physical condition of the person. All these restrictions cause a reduction of the quality of life for the patients. In severe cases persons with frequent seizures might withdraw from social life completely because of their handicap [40].

For people suffering from epilepsy it would be beneficial to reduce the uncertainty of when epileptic events occur. Reliable seizure detection straight at onset would help to reduce the risk of injury and allow the patients to take part in activities they usually cannot do.

The idea behind this thesis is to use the detection algorithm together with a specially designed EEG-cap (smaXcap). This cap is being designed in the course of the “Product Innovation

Program (PIP)" of Graz University of Technology. Some details about the development of the cap can be found in [61]. Depending on the achieved accuracy and latency of the detection, the user should be enabled to participate in activities that would otherwise be too risky. A future goal will be to reduce detection delay even further and even try to predict seizures before onset. This would enlarge the possible fields of application for the cap even more.

1.5.2. Possible Applications

1.5.2.1. Warning System

The detection can basically occur in three different situations:

1. The patients are still conscious at the time the seizure is detected.
2. The patients are not conscious any more, but their posture is still contained.
3. The patients have already fallen to the ground.

When patients are still conscious at the time, the seizure is detected safety precautions like sitting or lying down, putting away harmful objects, etc. could be applied by themselves.

In the other cases, the patients have to rely on outside help. Surrounding people can be alarmed acoustically to provide immediate help if needed. In addition relatives and/or friends can be informed automatically (possibly including GPS data) to take appropriate actions. Furthermore, harmful electrical objects could be switched off straight at detection.

1.5.2.2. Monitoring System

Another possible use of early detection involves epilepsy monitoring. Automatic detection of seizures would be a great assistance for medical staff, as the process of filtering long-term EEG records is very time consuming. Furthermore, for a better location of the epileptic focus it is important that straight after seizure onset some tests are performed by the medical staff. In practice this means nonstop monitoring of the patient. The risk of "missing" a seizure especially at night, when the observer might be inadvertently could be reduced. If an alarm is set out when a seizure is detected, the chances for accurate testing would be improved.

Another possibility to locate a focus more precisely is the use of perfusion tracers and Single Photon Emission Computed Tomography (SPECT). Cerebral blood flow is captured at the moment of injection. As blood flow is increased in brain regions with epileptic activity conclusions about epileptic foci can be drawn. To get an accurate picture, however, the

injection needs to be applied straight at seizure onset. Otherwise false regions might be detected as the seizure tends to spread to different brain areas [51]. Automatic detection could be used to accelerate the injection process by either informing medical staff earlier or even by automatically triggered injection [60].

At the moment epileptic patients need to undergo long-term EEG monitoring with drug deprivation at hospitals in order to locate epileptic foci. The application of an EEG cap at home could deliver additional information. A few minutes of EEG could be stored continuously and, in case of an alarm, be read out and analyzed by professionals.

1.5.2.3. Relieve Symptoms

There might be the possibility to influence the course of a seizure. If so, treatment could be started automatically at detection. The only quite common intervention after seizure onset found in literature is the administration of anticonvulsant drugs during status epilepticus. However, it is stated that this application is combined with great risks because depending on different symptoms different medication might be needed [63].

2. Methods

2.1. Overview

The seizure detection system used in this thesis is based on the approach that Shoeb proposed in his PhD thesis [60]. The automatic detection system relies on two different signals: EEG and ECG. The frequent appearance of tachycardia during or even before ictal events especially in temporal lobe epilepsy (cf. Section 1.3.2) is one pillar of the system. Therefore, the R-R-Interval (RRI) of the ECG is analyzed. The other part of the system exploits rhythmic behavior in the EEG often observed during seizures. The EEG signal is divided into 3-Hz wide frequency bands in the interval of 0.5 to 24.5 Hz. This range has been used by [60] with reference to Gotman et al. [31] who state that most rhythmical ictal patterns have a frequency lower than 25 Hz while at the same time EMG artifacts are reasonably reduced when using this range.

Figure 2.1 shows the basic concept of the proposed system. First, the most severe artifacts of the input signal are rejected. After that the signal is sampled into 2-s segments with one second overlap and the EEG and ECG features are computed. Therefore, preprocessing steps like EEG channel selection, EEG signal derivation, and filtering are applied. The previously defined features are then extracted from the preprocessed data and put together to a feature vector. This feature vector is then fed to the SVM. During the training phase an additional class vector is needed to tell the SVM how to classify certain inputs. After that a testing phase follows where the classification output of the SVM is calculated and post processed. Post processing allows to define an additional detection criterion in order to improve the classification results. If this predefined detection criterion is satisfied an alarm is triggered. A true alarm has been raised if a seizure is ongoing at that very moment or if seizure onset occurs within the next 30 s. In all other cases the alarm has to be classified as false.

The evaluation of the alarms is performed differently, depending whether the exact seizure period is known or unknown beforehand. For unknown data, as in real-time applications, the correctness of a triggered alarm can only be validated after waiting for 30 s. Whenever additional alarms occur during this period, the time window has to be reset to 30 s.

For known data, it is possible to immediately classify an alarm as false or correct, because the exact seizure period is already determined. This scenario is true for the results of this thesis. Some simplifications and restraints are applied for evaluation:

- Each seizure can only be detected once.
- A detection delay is calculated using the first detection within the seizure period.
- If a seizure is first detected after more than 60 s from onset this detection is ignored.
- False detections are grouped together if they occur within 30 s of each other.

These restraints have been chosen because for the detection task it does not matter whether a seizure is detected once or more often. Furthermore, a detection with small or negative delay is requested, therefore detection delays of more than 60 s are handled as if the seizure had been missed. The grouping of false detections is chosen because in real-time application, the patient would have to wait for 30 s each time an alarm is triggered before being able to validate this alarm.

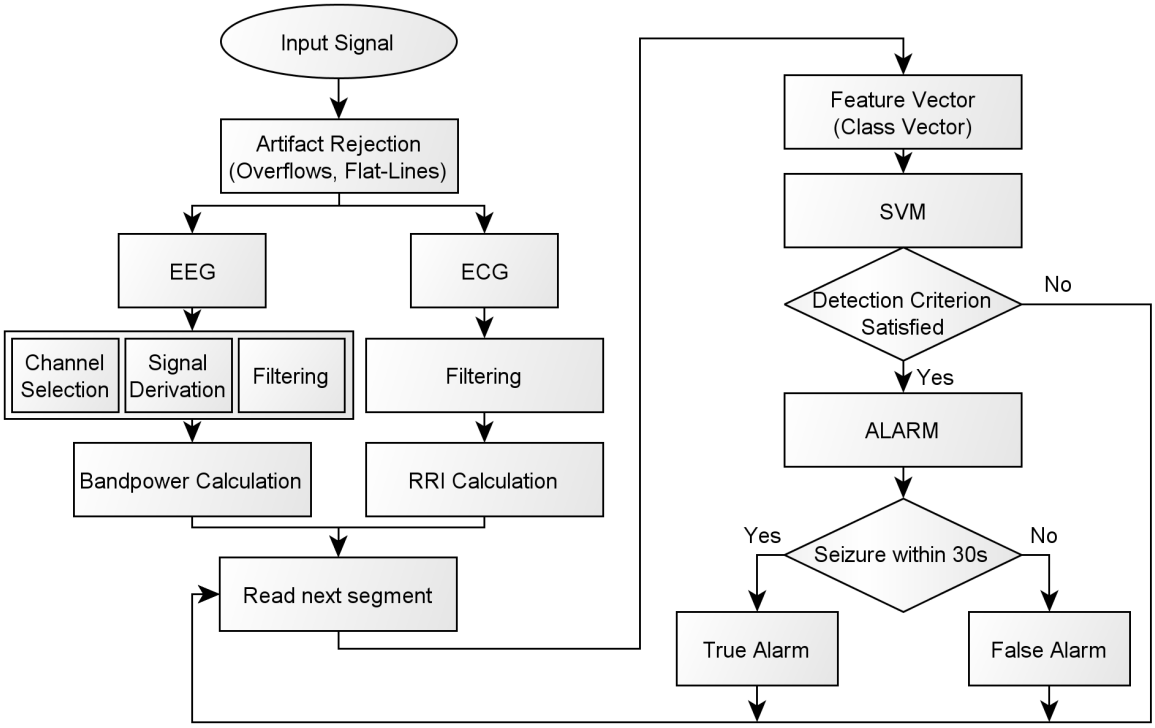

Figure 2.1.: Schematic representation of the used detection algorithm.

2.2. Data

The EEG and ECG data used in this thesis have been recorded and provided by the "University Hospital for Neurology" in Graz [3]. The data have been collected during long-term EEG monitoring preceding surgical interventions. Seizure onset and duration have been marked by professional staff. Only patients suffering from temporal lobe epilepsy are used in this thesis.

The dataset contains both seizures originating from the left and from the right hemisphere of the brain, respectively. Differing seizure onset locations sometimes even occur within one and the same patient. Despite having a focal onset, seizures taken for this study sometimes have become secondarily generalized.

Altogether data from 21 patients, 8 male and 13 female, was observed. Their age ranged from 15 to 70 years with mean 37.9 ($\pm$ 14.1) years. Pediatric data is rejected as the human EEG changes during growing up (cf. [48]) and therefore joint observations are difficult. A total of about 310 hours of recorded EEG containing 61 seizures were studied.

Seizure durations vary between 9 s and more than 5 min. The median duration is 75 s. Very short seizures are sometimes the result of reintroduced anti epileptic drugs.

The length of recorded data and the number of seizures varies strongly among all patients. In Table 2.1 all patient specific information is summarized.

Table 2.1.: Information about the number of seizures a patient has experienced during monitoring. Also the cumulated recording time for each patient as well as gender and age is stated.
* One seizure recording is rejected due to artifact contamination.

Patient No.	No. of Seizures	Recording Time [h]	Sex	Age [a]	Patient No.	No. of Seizures	Recording Time [h]	Sex	Age [a]
1	3	0.70	f	70	12	6	0.92	f	38
2	1	2.03	m	33	13	7*	1.43	m	44
3	3	2.68	f	23	14	3	20.45	f	40
4	1	0.65	f	40	15	2	17.15	f	42
5	3	0.68	f	35	16	4	46.55	m	21
6	3	1.58	f	25	17	2	22.47	f	70
7	1	0.22	m	15	18	2	43.07	f	46
8	1	0.20	m	45	19	3	21.05	f	47
9	1	0.15	f	32	20	3	67.17	m	40
10	1	0.12	m	19	21	10	62.72	m	35
11	1	1.37	f	36					

2.2.1. Equipment

At the epilepsy monitoring center of the "University Hospital for Neurology" in Graz the amplifier "alpha-trace digitalEEG TC-32" from "B.E.S.T. medical systems" [1] is used. A high-pass filter with $f_g = 0.3\,\text{Hz}$ and a low-pass filter with $f_g = 70\,\text{Hz}$ is implemented. A notch filter is activated to reduce power line interference. The amplifier provides 32 channels. The analog measuring range is located between $\pm 819.2\,\mu\text{V}$ for EEG data and between $\pm 2048.0\,\mu\text{V}$ for ECG data. A 12-bit analog-digital converter digitizes the signal and the data is sent to the workstation via optical fiber at a sample rate of $f_s = 256\,\text{Hz}$.

For the long-term measurement gold cup electrodes are used. They are adhered onto the skin with collodion and gauze. Additionally a conductive gel is applied.

2.2.2. Electrode-Positions & Setup

Up to 31 EEG electrodes plus one ECG electrode are applied for long-term monitoring. Figure 2.2 shows the principal setup for the measurement. The setup is based on the international 10-20 system. In addition a so-called "basal ring" is used. This ring includes the electrodes AF7/AF8, F11/F12, FT9/FT10 and TP9/TP10 marked red in the Figure. The 29

EEG electrodes delineated in Figure 2.2 plus electrodes for ground, reference and ECG are used for each patient. For some patients two sphenoidal electrodes or two electrodes for EOG measurement are used in addition.

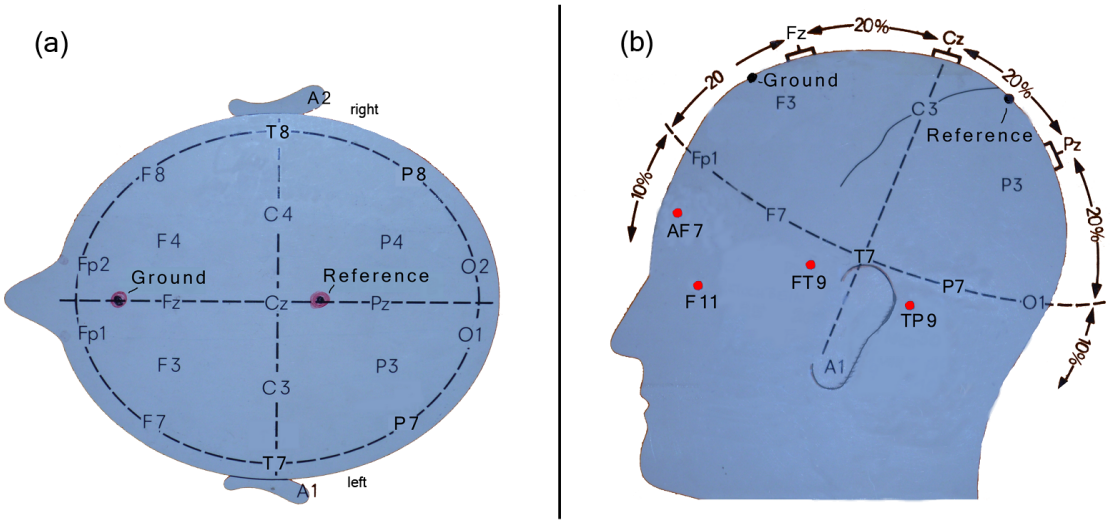

Figure 2.2.: Electrode setup for long-term monitoring based on the international 10-20 system. Adapted picture from University Hospital for Neurology, Graz.
(a) View from above: Ground electrode is situated on the forehead in front of Fz. Reference electrode is placed in between Cz and Pz. (b) Lateral view: Illustration of the 10-20 system. Basal ring electrodes are marked with red dots. Location information: AF7/AF8 - above eyebrows, F11/F12 on cheekbone, FT9/FT10 anterior to ear, TP9/TP10 posterior to ear.

Impedance values for all electrodes are kept below 5 kΩ when preparing the patient for measurement. The impedance is only measured once, when applying the electrodes.

The EEG signal is derived monopolarly. The reference electrode is positioned between *Cz* and *Pz*. The ground electrode is placed on the forehead, in front of *Fz*. (cf. Figure 2.2)

Figure 2.3 shows a patient prepared for long-term monitoring with mounted gold electrodes.

2.3. Signal Processing

The monitoring data is available in two different file formats: Alpha-Trace (.alp) and European Data Format (.edf). Files containing multiple hour recordings are split roughly into one hour partitions. All analyzing and signal processing is done using Matlab® (Mathworks Inc., Natwick, USA, http://www.mathworks.com/) in combination with the BioSig-Toolbox [57]

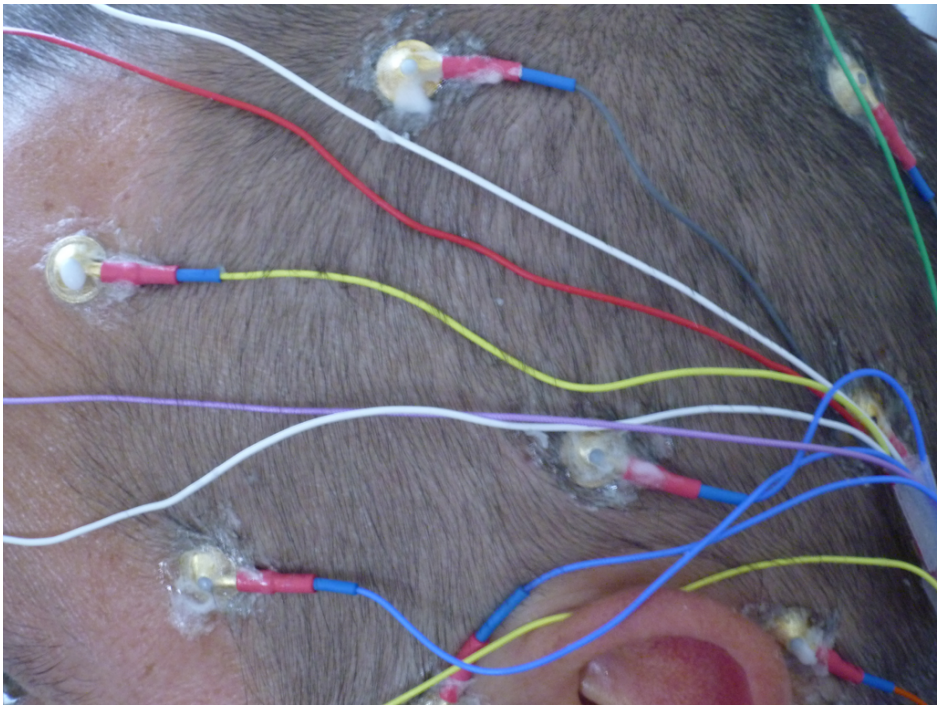

Figure 2.3.: Picture of a patient with applied gold electrodes for long-term monitoring.

which is available under the GNU General Public License (GPL). LIBSVM [17] for Matlab® is employed for all SVM related calculations.

2.3.1. Preprocessing

As a first step the recording is inspected for artifacts that render the signal useless. These include signal overflows and flat lines. Whenever signal overflows occur, the corresponding sequence including half a second before and after the overflow are rejected. This additional section is chosen because overflows are usually due to strong muscular artifacts that might also render the signal useless shortly before and/or after the overflow detection. Flat lines due to electrode failure do not contain applicable information as well. Therefore, these artifacts are also detected and excluded. No filtering is applied to smoothen the edges before and after rejected segments as this will not be done during on-line testing.

For on-line testing, the previously described artifacts need to be detected and classification has to be paused when contaminated data is delivered. This means classification results are only evaluated while the input data complies with certain quality criteria. Additionally

in future applications a warning could be presented to prompt the patient to examine the electrodes in case the signal does not recover autonomously after a short period.

As a next step a signal derivation is performed on the adjusted data. Both, bipolar derivation and monopolar derivation with common average reference (CAR) are used for further calculations. The following equations show how to calculate these derivations. N denotes the total number of electrodes used.

$$\mathrm{Bipolar_{ij}} = \mathrm{Electrode_i} - \mathrm{Electrode_j} \tag{2.1}$$

$$\mathrm{CAR_i} = \mathrm{Electrode_i} - \frac{1}{N}\sum_{\mathrm{j}=1}^{\mathrm{N}} \mathrm{Electrode_j} \tag{2.2}$$

In order to reduce the data amount only a selection of electrode positions is used for further processing. Figure 2.4 illustrates the electrodes chosen for the different derivations.

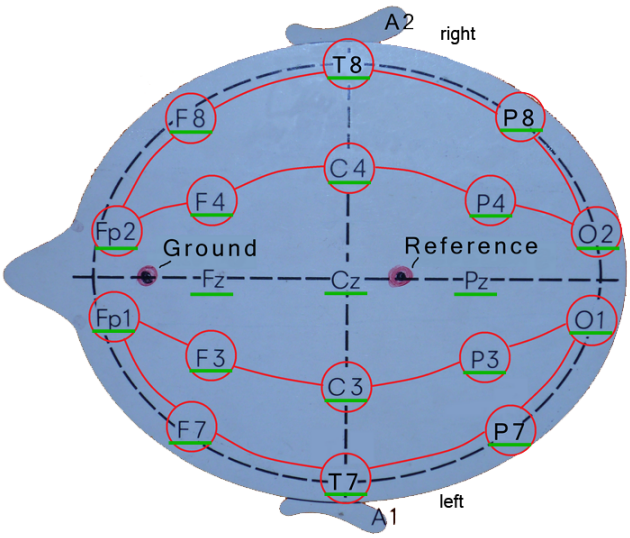

Figure 2.4.: Used EEG electrodes for detection. Red circles identify electrodes used for bipolar derivation. Red lines indicate which pairs of electrodes are related to each other. Green lines show the electrodes used for CAR derivation. Adapted picture from University Hospital for Neurology, Graz.

As a next preprocessing step the input data is digitally filtered. A notch filter is applied to further suppress 50 Hz power line interference. The ECG channel is additionally lowpass filtered with $\mathrm{f_g} = 30\,\mathrm{Hz}$. For both applications 4^{th} order Butterworth filters are used.

2.3.2. Feature Extraction

As stated in Section 2.1 both ECG and EEG features are extracted for classification.

2.3.2.1. ECG

Two second segments of the ECG are inspected. A new segment starts every second, therefore the data shows a one second overlap. For each period the median R-R Interval (RRI) is calculated. This *median* might have to be interchanged by the *mean* of the RRI for on-line use, as median filtering is computationally far more expensive than mean filtering. For the calculation of the RRI, the functions *qrsdetect()* and *berger()* from the BioSig-Toolbox [57] have been used.

As basic heart rate may differ from day to day, depending on certain factors like stress level or physical exhaustion the RRI related to its recent values rather than the absolute RRI is examined. This $\mathrm{RRI}_{\mathrm{ratio}}$ is calculated using the median value of a 10 s wide moving background window which ends 25 s in front of the actually calculated segment. Figure 2.5 illustrates the calculation of the $\mathrm{RRI}_{\mathrm{ratio}}$.

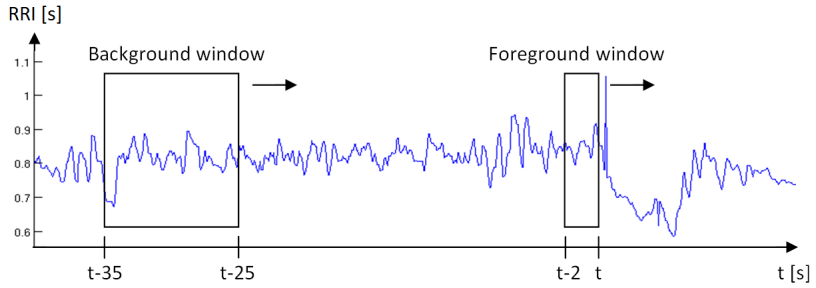

Figure 2.5.: Calculation scheme for $\mathrm{RRI}_{\mathrm{ratio}}$. The median of the foreground window and the background window is calculated and put into relation. $\left(\mathrm{RRI}_{\mathrm{ratio}} = \frac{\mathrm{median}_{\mathrm{fg}}}{\mathrm{median}_{\mathrm{bg}}}\right)$ Both windows are shifted one second to the right in every step.

An example for seizure related tachycardia is presented in Figure 2.6. Both, $\mathrm{RRI}_{\mathrm{absolute}}$ and $\mathrm{RRI}_{\mathrm{ratio}}$ are illustrated. The vertical red lines indicate the start and the end of the seizure.

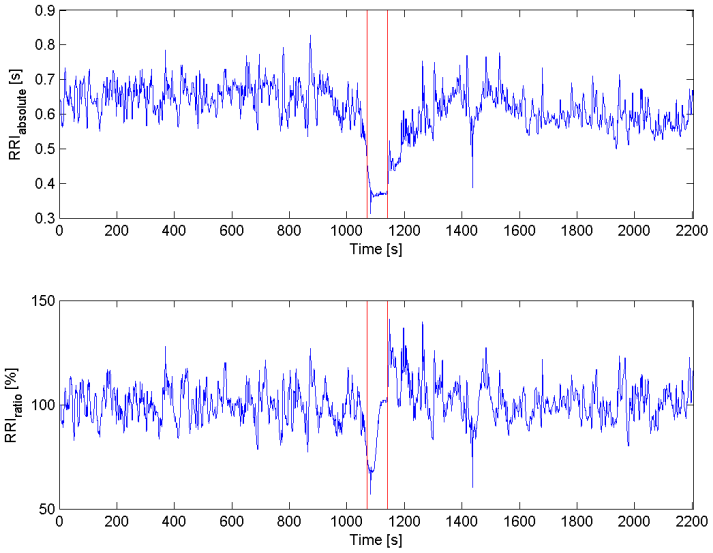

Figure 2.6.: $RRI_{absolute}$ and RRI_{ratio} for a data sequence containing a seizure. Red lines indicate the seizure period. $RRI_{absolute}$ decreases during the seizure which indicates an increased heart rate. RRI_{ratio} shows a similar behavior, however, the comparison of the actual RRI with the RRI of past periods should make this feature more robust as basic heart rate might be changing during the day.

2.3.2.2. EEG

For each considered EEG channel eight consecutive 3-Hz wide frequency bands between 0.5 Hz and 24.5 Hz are extracted. The frequency bands are obtained using 4^{th} order Butterworth filters. The filtered data is segmented in two second blocks analogous to the ECG feature and the mean logarithmic band power *logBP* is calculated for each segment.

$$\log\mathrm{BP}\,(\mathrm{j}) = \log\left(\frac{1}{\mathrm{N}}\sum_{\mathrm{i}=1}^{\mathrm{N}}\mathbf{x}^2_{\mathrm{bp\,filtered}}\,(\mathrm{i})\right) \tag{2.3}$$

where : $\mathbf{x}_{\mathrm{bp\,filtered}}$ . . . bandpass filtered input signal

i, j . . . time index

N . . . size of calculation window (sample rate $\times$ seconds)

Figure 2.7 shows the spectrum of a data sequence containing a seizure. For this image the signal is bandpass filtered between 0.5 and 24.5 Hz. The redder the area, the higher the power within a certain frequency band. The example represents a pattern repeatedly found in the data: The power in the whole spectrum is increased during the seizure. Furthermore, a narrow strongly increased band can be found between 5 and 10 Hz. The increased band power first starts at a frequency of about 10 Hz and gradually slows down to 5 Hz on seizure

progression.

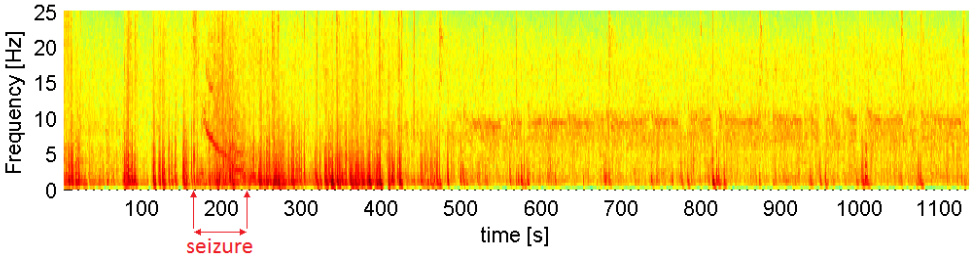

Figure 2.7.: Spectrum of a data sequence containing a seizure. Green and yellow areas in the spectrum indicate little power. Regions with increased power appear red.

The logarithmic band power plots corresponding to the spectrum shown in Figure 2.7 are illustrated in Figure 2.8. The bandwidth between 0.5 and 24.5 Hz is divided into eight 3-Hz bands. The seizure interval is marked by vertical red lines. Increased logarithmic band power during the seizure occurs mostly between 3.5 and 18.5 Hz.

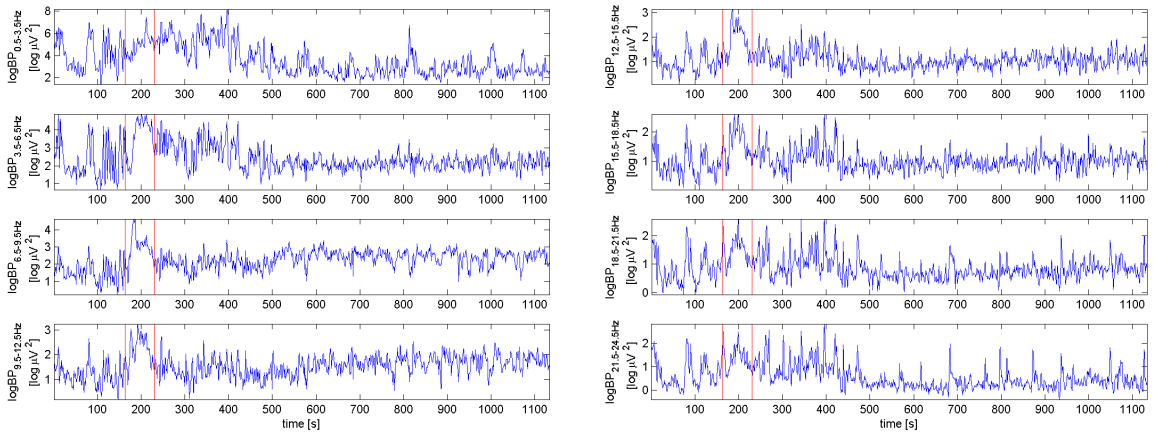

Figure 2.8.: Logarithmic band power of a data sequence containing a seizure. The seizure interval is marked by vertical red lines.

In addition to the EEG and ECG features chosen for this thesis a number of other features have been tested on their capacity to differentiate between ictal and inter-ictal states. These additional features can be viewed in Appendix B.

2.3.2.3. Feature Vector & Class Vector

As a next step, the calculated EEG and ECG features are put together in a single feature vector for each observed two second period. Additionally Shoeb [60] has used a special technique to capture temporal developments of the data. Not only the features for a two second segment are presented to the SVM at each step, but also the features of the two preceding non-overlapping segments. This thesis implements the same approach. The number of features at any point in time is computed as follows:

$$\#\,\text{Features} = (\text{Channels} \times \text{Bands} + \text{RRI}) \times \text{Consecutive Segments}$$

In Figure 2.9 the exact design of the feature vector is illustrated.

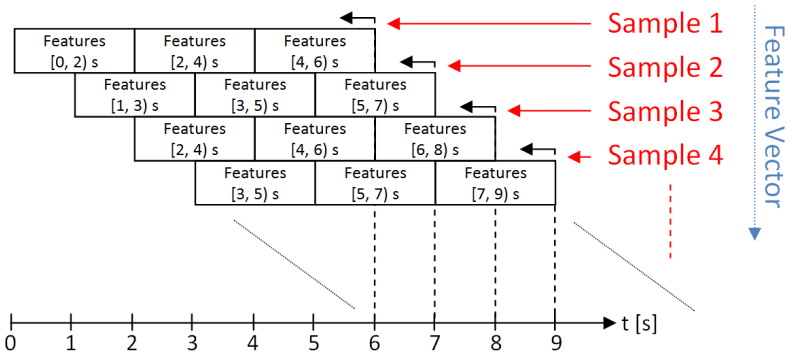

Figure 2.9.: Structure of the feature vector. Altogether one column of the feature vector is now using information from 6 s of the input signal.

For the training of the classifier a class vector is needed as well. This vector provides information whether a feature sample belongs to the ictal class or to the inter-ictal class. For training, only the first 20 samples after the seizure onset are classified as ictal class. More precisely, the first ictal sample includes data starting already 4 s ahead of the seizure onset, as this sample already includes first features from within the ictal period which might carry useful information. If the seizure is not finished after these 20 samples, the remaining samples are rejected. This means they are not assigned to either of the two classes. Also all samples preceding onset 30 s and less are rejected. All remaining samples belong to the inter-ictal class. For short seizures that do not provide 20 ictal samples only samples within the seizure period are used.

The previous restrictions are made for the following reasons: Seizure morphology tends to change in the course of an ictal event. The algorithm should detect seizures close to the onset, therefore only morphologies occurring at onset are evaluated. The choice has fallen on 20 ictal samples because on the one hand, the number should not be too large in order

to capture seizure onset conditions only. On the other hand enough ictal samples should be available for training and testing the SVM. Furthermore, Shoeb [60] has achieved best results with this setting.

The unclassified area preceding the seizure onset is chosen, as there might be pre-ictal changes similar to the changes at seizure onset which would allow an earlier detection. An example of this would be seizure related tachycardia that sometimes starts ahead of the seizure (cf. Section 1.3.2).

The whole structure of the class vector is illustrated in Figure 2.10. Green rectangles show ictal samples, blue rectangles show inter-ictal samples. The red shaded regions show areas that deliver no training input for classification.

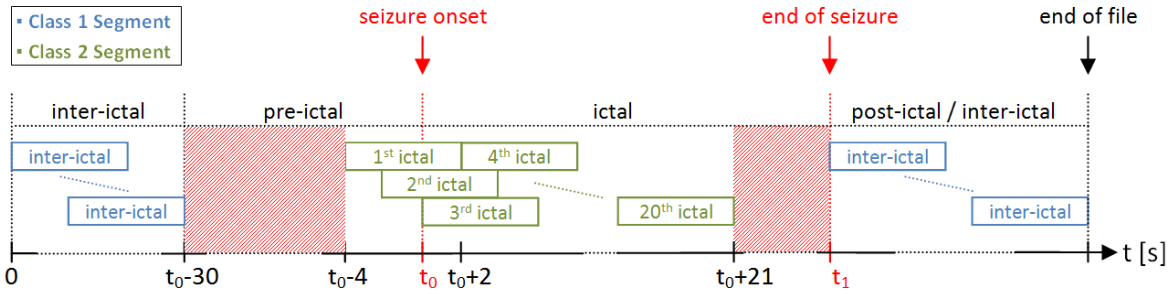

Figure 2.10.: Structure of the class vector. Green rectangles show ictal samples, blue rectangles show inter-ictal samples. The red shaded regions show areas that deliver no training input for classification. t_0 marks the seizure onset and t_1 marks the end of the seizure.

The previously defined feature and class vector are generated for each data partition containing roughly one hour of data in the off-line approach. The partitions do not contain exactly one hour of recording for the following reasons:

- splitting leaves a remainder
- parts of data need to be rejected due to artifacts after splitting
- seizures are near the splitting region, therefore, the region has to be relocated
- partitions are too small to be considered for splitting

Each partition either contains a single seizure or it provides seizure free recordings.

2.3.3. Classification

So far, classification has only been performed and evaluated off-line. Two different classification approaches have been examined:

- Patient independent classification (all patients are evaluated together)
- Patient dependent classification (each patient is evaluated individually)

The *patient independent classification* approach provides enough data (feature and class vectors) to perform a cross validation. Therefore, the data are divided into training, validation and test set. For cross validation, two different data pools are arranged: data from partitions containing seizures and data from partitions containing inter-ictal recordings. 10% of both pools are then randomly selected for each testing iteration. With the remaining data ten different training and validation pairs are defined and evaluated. Again 10% of both pools are randomly chosen for the validation set while the rest is used for training.

The classifier with the best results on the validation set is then applied to the test set. For a 10-fold cross validation usually every data should be tested in 10 different combinations meaning the 10-fold repetition of the previously described procedure. Computation amount for classification has been too large, however, so each data has only been tested once. The used validation scheme is illustrated in Figure 2.11.

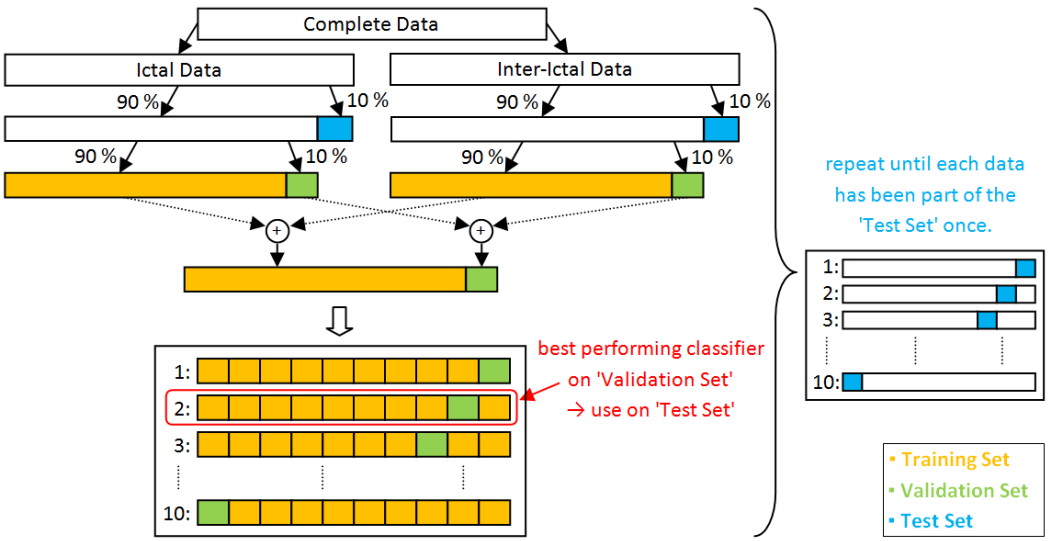

Figure 2.11.: Cross validation scheme for patient independent classification. Ictal and inter-ictal data is separated into training, validation and test sets. For each test set 10 different training and validation set combinations are calculated. The classifier delivering the best results is then used on the test set.

For the *patient dependent classification* approach less data is available. Especially the amount of data from seizures is small with some patients as described in Table 2.1 in Section 2.2. Patients that only experienced one seizure during recording are rejected completely from this approach. The reduced data material only allows a leave-one-out cross validation. Data from a partition either containing a seizure or inter-ictal data is used for testing. All other data of the same person is applied for training. This process is performed for data from all partitions of each person. The according validation scheme can be seen in Figure 2.12.

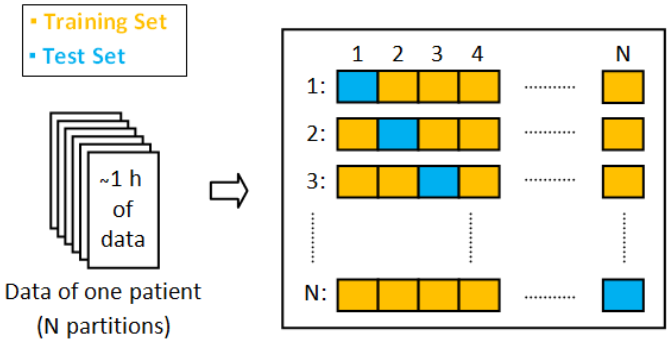

Figure 2.12.: Leave-one-out validation scheme for patient dependent classification. Data of one patient is divided in more or less one hour partitions. All but one partitions are used to train a classifier which is then applied to the left out partition. This process is repeated for all partitions.

2.3.3.1. Setup of Support Vector Machine (SVM)

In a first step, the training data is normalized to zero mean and unit variance. This is done separately for each patient, even in the patient independent approach. The normalized data is then handed on to the SVM. The normalization parameters are stored, because testing data needs to be normalized according to the training data. In the patient independent approach it can happen, that some persons do not contribute data in the training process and therefore no normalization parameters are available for them. In these cases, average values of the parameters are applied to calculate appropriately normalized data during the testing phase.

Next, an appropriate kernel for the SVM needs to be chosen. As a nonlinear decision boundary is suspected, an SVM with radial basis function (RBF) kernels is used for classification. This choice is also made because Shoeb has obtained good results with a RBF-SVM [60]. As mentioned earlier RBF-SVMs offer the two parameters C (margin parameter) and γ (kernel radius) for adjusting. A grid search is applied to find the best values for these parameters.

Both parameters $\mathbf{C}$ and $\boldsymbol{\gamma}$ are chosen to be exponentially growing. $\mathbf{C} = 2^{-5}, 2^{-3}, 2^{-1}, ..., 2^{15}$ and $\boldsymbol{\gamma} = 2^{-15}, 2^{-13}, 2^{-11}, ..., 2^{3}$. Cohen's kappa is used as quality criteria.

2.3.4. Post Processing

The capability to detect seizures is measured by a specially adapted quality criteria. The usually used measures defined in Section 1.4.2 are adapted, to better suit the underlying problem. The most important property of the algorithm is to detect a seizure as early as possible. Therefore, multiple detections within a single seizure period do not improve the accuracy of the algorithm. Furthermore, if a seizure is first detected with a delay of more than 60 s this detection is handled as too late and therefore ignored. Also false detections are grouped together if they occur in a certain time window. All these requirements lead to the following modifications:

True Positives: Only one true positive per seizure can be achieved.

False Positives: False detections that occur within 30 s to each other are counted as one.

Delay: The real time of the seizure onset is subtracted from the time of detection.

Figure 2.13 illustrates how the SVM output is handled. Figure 2.14 shows an exemplary output of the SVM and information about the applied post-processing steps.

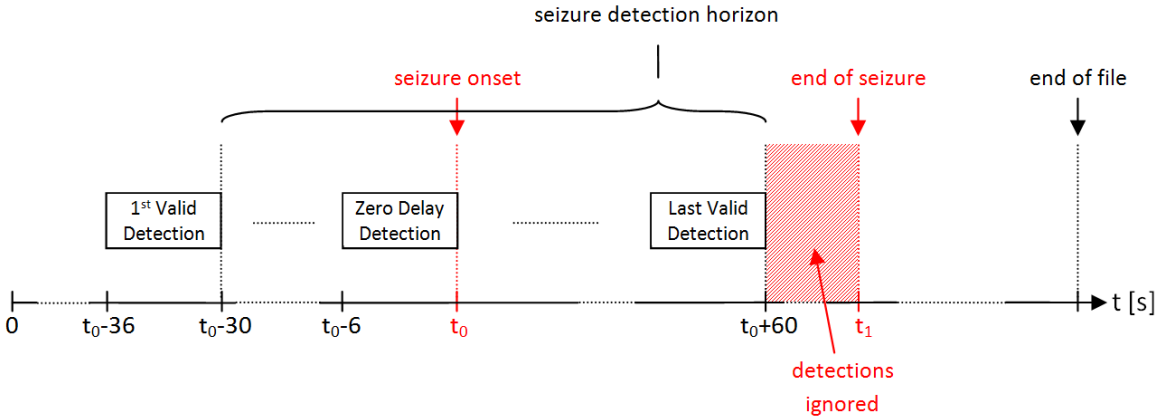

Figure 2.13.: A seizure is truly detected, whenever the SVM classifies a segment as ictal within the seizure detection horizon. Detections are valid between 30 s ahead of and 60 s past seizure onset. The calculation of the detection delay relies only on the first valid detection.

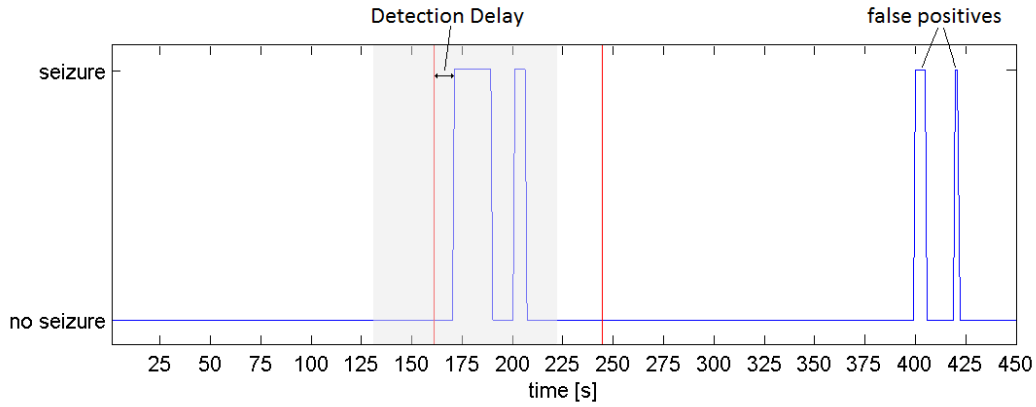

Figure 2.14.: Post-processing of SVM output. Red vertical lines indicate the seizure period. The gray shaded region indicates the area where detections are counted as true. The first detection within the gray shaded region is used to calculate the detection delay. Detections outside the gray region, but within the red vertical lines are neither counted as true nor as false. At the right hand of the plot some false classifications are visible. As there are less than 30 s between each two false classifications all of them are grouped together and counted as a single false detection.

2.3.4.1. Adjustment of Detection Criterion

Additionally, it is evaluated whether detection results could be improved by demanding $k \in \mathbb{N}$ consecutive segments to be classified as ictal by the SVM before a detection is declared.

2.4. Input Variations

2.4.1. Channel Selection

It is investigated whether the number of used electrodes can be restricted further while retaining a high detection rate and a low number of false positives. This would be beneficial in two ways:

- Computational cost reduces for less channels both in training and in testing.
- An EEG cap for detection is easier to construct and apply. Also the error-proneness of the cap is reduced.

The channel reduction attempt is based on the bipolar derivation method starting with 16 bipolar channels illustrated in Figure 2.4 (Section 2.3.1). To find the best channel combinations an exhaustive search would have to be performed. However, a complete exhaustive search allowing all possible sub-combinations of these 16 channels cannot be computed within reasonable time. Therefore, a reduced search is performed, where the number of used bipolar channels is fixed to six. Those six channels are further assigned to be symmetrically arranged on either hemisphere which then results in only 56 possible combinations.

The electrodes that are involved in the best channel selection are subsequently used in the reduced CAR approach as well.

2.4.2. Feature Adaptation

2.4.2.1. Feature Reduction

A first attempt to reduce the number of features is undertaken in combinations with the CAR approach. Instead of the 8 equally broad frequency bands some of the bands are grouped together. The reduction results in the following three bands: 0.5 to 3.5 Hz, 3.5 to 18.5 Hz, and 18.5 to 24.5 Hz. For further information refer to Chapter 3.

For the reduced settings computation time decreases, therefore, additional calculations like a new selection of parameters C and γ and the patient independent approach for the CAR derived data can be performed.

2.4.2.2. RRI Adaptation

The time delay of the background window used for the $\mathrm{RRI}_{\mathrm{ratio}}$ calculation (cf. Figure 2.5 in Section 2.3.2) is modified. The distance between foreground and background window is varied between 5 and 105 s. Due to computational expense this adaptation is only performed for the reduced feature set, given previously.

2.5. Evaluation Table

Most evaluation is performed using the design shown in Table 2.2.

Table 2.2.: Default table design.

Patient No.	No. of Seizures	Recording Time [h]	Missed Seizures	Mean Detection Delay [s]	False Detections	fdr [1/h]
pat_i	$seiz_i$	$time_i$	$missed_i$	$meanDD_i$	fd_i	fdr_i
⋮	⋮	⋮	⋮	⋮	⋮	⋮
	$\sum$	$\sum$	$\sum$	**total meanDD**	$\sum$	**total fdr**

The *Patient Number*, the *Number of Seizures* and the *Recording Time* correspond to the data given in Chapter 2. Column *Missed Seizures* shows how many seizures of a certain person have not been detected. The *Mean Detection Delay* can range between $-30\,\mathrm{s}$ and $+60\,\mathrm{s}$ as this time horizon has been specified for correct detections (cf. Chapter 2). If a seizure is missed, it is excluded from the calculation of the *Mean Detection Delay*. If all seizures of a patient are missed, there are no values to calculate a detection delay. Therefore, *N/A* is filled into the table. The column *False Detections* shows how many false detections occurred for the patient. The *fdr* relates the number of false detections to the recording time of the patient which can be found in Table 2.1 in Chapter 2.

The last row of the table shows overall results. The *Number of Seizures*, the *Missed Seizures*, and the *False Detections* are simply summed up. The *total meanDD* and the *total fdr* have to be calculated separately. To calculate the *total meanDD* the mean of every single detection delay rather than the already calculated mean delays of each patient are used. Again only the number of detected seizures is taken into account. The *total fdr* relates the sum of the false detections to the total recording time of all patients.

3. Results

3.1. General Settings

3.1.1. SVM Parameter Selection

As mentioned in Chapter 2, parameters C and γ are determined using a grid search. Only patients number 1 to 13 (cf. Table 2.1 in Section 2.2) are considered for the parameter search because no other data has been available at the time this choice has been made. Retesting with more data has been postponed as computation is costly. Tests are conducted in a leave one out fashion and all patients are considered together ($\Rightarrow$ patient independent). The grid search is performed for the bipolar approach and all 16 bipolar channels marked in Figure 2.4 (Section 2.3.1) are used. Cohen's Kappa is used as quality criteria. Figure 3.1 shows the averaged results of this search on logarithmic scales. Red lines denote higher values, blue lines denote lower values. The grid search showed best results for parameter values $\mathbf{C} = 2^3$ and $\boldsymbol{\gamma} = 2^{-9}$. Therefore further calculations apply these values.

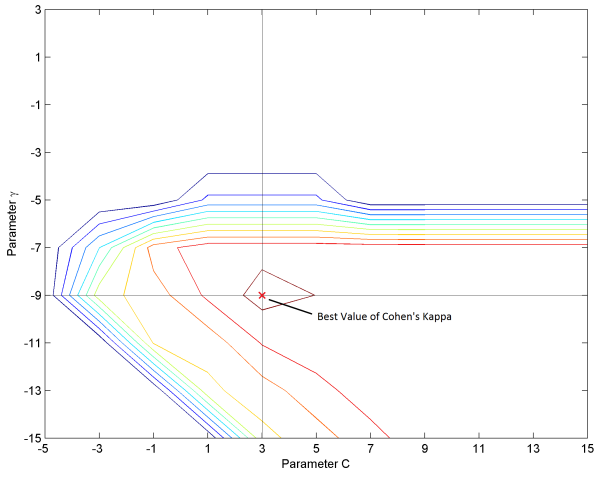

Figure 3.1.: Grid search results for parameters $\mathrm{C} = 2^{-5}, 2^{-3}, ..., 2^{15}$ and $\gamma = 2^{-15}, 2^{-13}, ..., 2^3$ on logarithmic scales. Values for Cohen's Kappa are illustrated. Red lines indicate higher values, blue lines lower values.

3.1.2. Best Channel Selection

The results of the exhaustive search for 6 symmetric bipolar channels are illustrated in Figure 3.2. Again only patients number 1 to 13 have been used with leave one out testing. Measured by the number of missed seizures and the number of false detections, channel combination number 23 shows the best results. Figure 3.3 shows the channel setup of this combination.

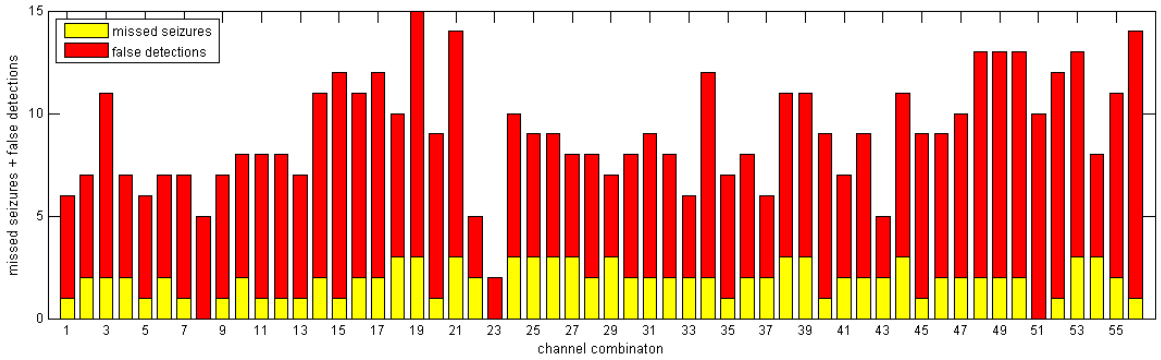

Figure 3.2.: Number of missed seizures and false detections for different channel combinations. Combination number 23 delivers the best result.

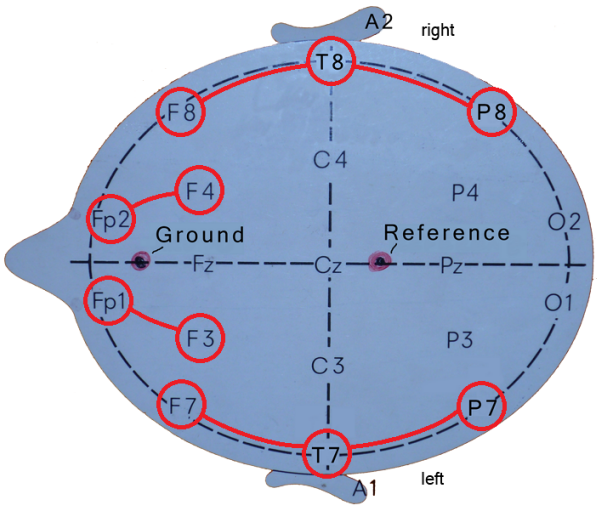

Figure 3.3.: Channel combination number 23 using F7–T7, T7–P7 and FP1–F3 on the left hemisphere and F8–T8, T8–P8 and FP2–F4 on the right hemisphere delivers the best results. Therefore, it is used for further calculations. The chosen electrodes are marked in red.

3.1.3. Adjustment of Detection Criterion

The evaluation results have been optimized by varying the demanded duration of seizure activity. Parameter $k \in \mathbb{N}$ indicates how many consecutive ictal classifications by the SVM are needed to trigger an alarm. Figure 3.4 shows the influence of delayed detection with an example data period.

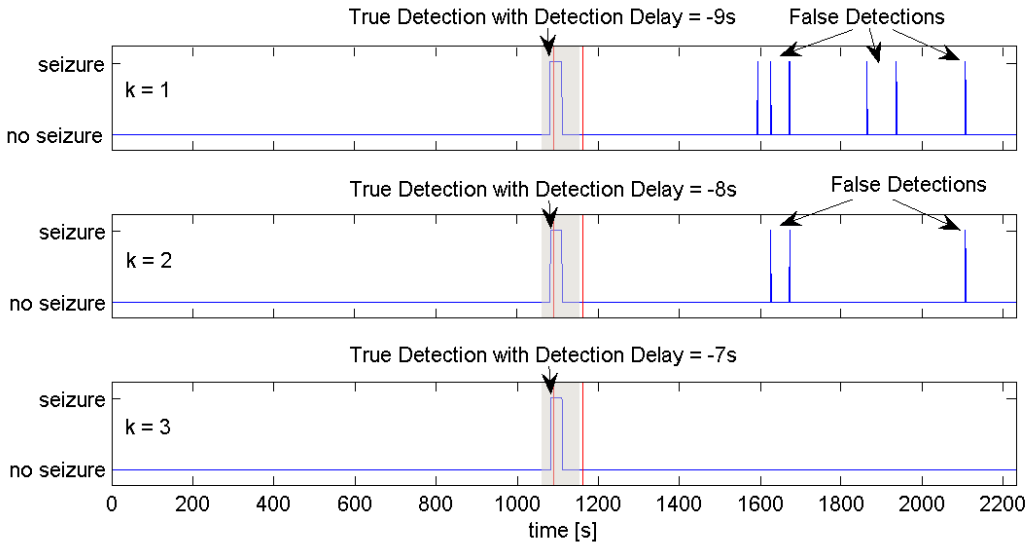

Figure 3.4.: Delayed detection. Detections are only counted if the SVM classifies k consecutive samples as ictal. Red vertical lines show the seizure period. The gray shaded box shows the horizon for true detections. For larger k on the one hand the number of false detections decreases, on the other hand the detection delay increases.

3.2. Instance of Temporal Lobe Seizure

Figure 3.5 shows the onset of a temporal lobe seizure. The seizure starts in the right hemisphere.

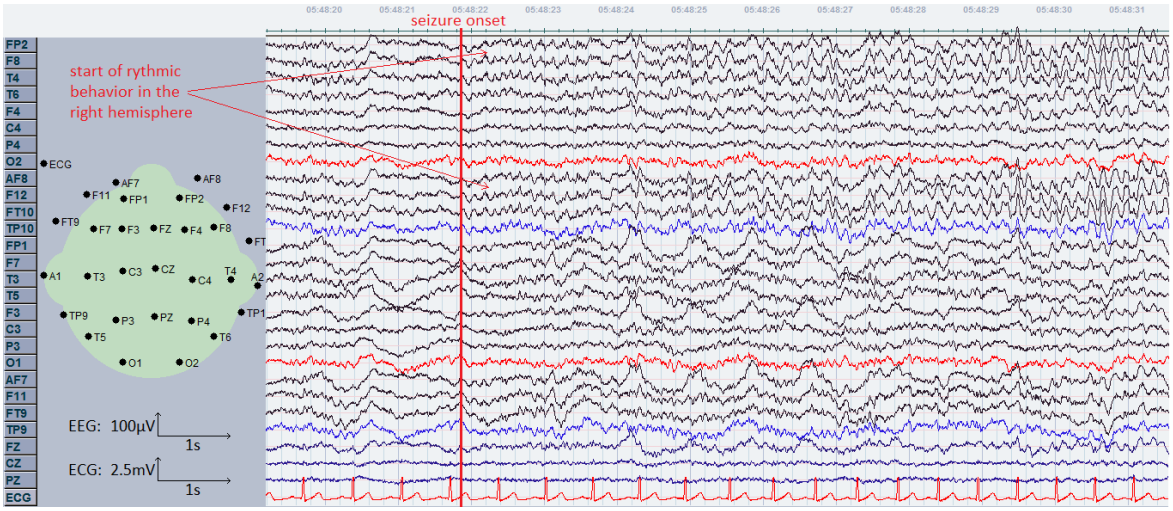

Figure 3.5.: Onset of a temporal lobe seizure that starts in the right hemisphere. The rhythmic behavior with a frequency of about 8 Hz starts in the right hemisphere (electrode positions with *even* numbers). In the time course the amplitude of the rhythmic oscillations increases while the frequency decreases slightly. When examining the ECG, a decrease of the RRI is visible. Picture generated using the software alphaView (B.E.S.T. Medical Systems, Vienna, http://www.alpha-trace.at/)

3.3. Patient Dependent Evaluation

In the patient dependent evaluation only persons that experienced more than 1 seizure are observed. Evaluation is performed individually for each patient by leave one out cross validation on all its one hour data partitions.

3.3.1. Basic Setup

3.3.1.1. CAR Derivation (19 Channels)

As a first attempt all 19 channels marked in Figure 2.4 (Section 2.3.1) are used for detection. Table 3.1 shows the results for the patient dependent approach using 19 CAR channels. Detections are triggered at the first sample classified as ictal by the SVM (k=*1*). After a mean detection delay of 2.7 s 48 of the 54 seizures ($\Rightarrow$ Sensitivity = 88.89%) are detected. The missed seizures of patient number 15 are due to insufficient data. Both seizures only last for 7 and 14 s, respectively. Therefore, they provide too little training samples. When rejecting

patient number 15 the result increases to 48 of 52 seizures (⇒ Sensitivity = 92.31%). An fdr of about 0.013/h is achieved in both cases.

Table 3.1.: Summarized results for the patient dependent evaluation using 19 CAR derived channels.
* Insufficient data.

Patient No.	No. of Seizures	Recording Time [h]	Missed Seizures	Mean Detection Delay [s]	False Detections	fdr [1/h]
1	3	0.70	0	4.3	0	0
3	3	2.68	0	8.0	0	0
5	3	0.68	0	4.0	0	0
6	3	1.58	0	-1.7	0	0
12	6	0.92	0	-8.0	0	0
13	7	1.43	0	4.0	0	0
14	3	20.45	0	5.7	1	0.05
15*	2	17.15	2	N/A	0	0
16	4	46.55	0	7.8	0	0
17	2	22.47	0	2.0	0	0
18	2	43.07	0	8.5	0	0
19	3	21.05	0	11.0	0	0
20	3	67.17	3	N/A	0	0
21	10	62.72	1	0.4	3	0.048
	54	**308.62**	**6**	**2.7 ±9.9**	**4**	**0.013**

3.3.1.2. Bipolar Derivation (6 Channels)

Table 3.2 shows the results for the patient dependent approach using the 6 bipolar channels highlighted in Figure 3.3. Detections are only triggered if the SVM classifies three consecutive samples as ictal (*k=3*). Altogether 46 of the 54 seizures (⇒ Sensitivity = 85.19%) are detected within a mean delay of 6.6 s. 15 false detections are triggered leading to an average fdr of 0.049/h. As stated earlier patient number 15 should be excluded from calculations. This improves the result to 46 of 52 detected seizures (⇒ Sensitivity = 88.46%).

Table 3.2.: Summarized results for the patient dependent evaluation using six bipolar derived channels.
* Insufficient data.

Patient No.	No. of Seizures	Recording Time [h]	Missed Seizures	Mean Detection Delay [s]	False Detections	fdr [1/h]
1	3	0.70	0	-1.7	1	1.43
3	3	2.68	0	9.3	9	3.35
5	3	0.68	0	7.7	0	0
6	3	1.58	0	2.7	0	0
12	6	0.92	0	-0.5	0	0
13	7	1.43	0	15.4	2	1.34
14	3	20.45	0	18.0	0	0
15*	2	17.15	2	N/A	0	0
16	4	46.55	0	11.0	0	0
17	2	22.47	0	4.0	0	0
18	2	43.07	0	10.0	0	0
19	3	21.05	3	N/A	0	0
20	3	67.17	3	N/A	0	0
21	10	62.72	0	1.8	3	0.048
	54	**308.62**	**8**	**6.6 ±12.3**	**15**	**0.049**

3.3.1.3. CAR Derivation (10 Channels)

Table 3.3 shows the results for the patient dependent approach using 10 CAR channels. These channels refer to the same electrode positions as being used in the bipolar approach before. Detections are again triggered if the SVM classifies three consecutive samples as ictal (*k=3*).

Altogether 48 of the 54 seizures are detected (⇒ Sensitivity = 88.89%). 14 false detections are triggered leading to an average fdr of 0.045/h. When rejecting patient number 15, 48 of the 52 seizures are detected (⇒ Sensitivity = 92.31%).

Table 3.3.: Summarized results for the patient dependent evaluation using 10 CAR derived channels.
* Insufficient data.

Patient No.	No. of Seizures	Recording Time [h]	Missed Seizures	Mean Detection Delay [s]	False Detections	fdr [1/h]
1	3	0.70	0	1.0	0	0
3	3	2.68	0	9.0	9	3.35
5	3	0.68	0	-2.7	0	0
6	3	1.58	0	0.3	0	0
12	6	0.92	0	-4.8	0	0
13	7	1.43	0	6.0	0	0
14	3	20.45	0	9.7	1	0.05
15*	2	17.15	2	N/A	0	0
16	4	46.55	1	10.0	2	0.12
17	2	22.47	0	4.0	0	0
18	2	43.07	0	9.0	0	0
19	3	21.05	1	13.5	0	0
20	3	67.17	2	28.0	1	0.015
21	10	62.72	0	4.5	1	0.016
	54	**308.62**	**6**	**4.7 ±10.7**	**14**	**0.045**

3.3.2. Influence of ECG

In Table 3.4 the results for different RRI modes: *no RRI*, the absolute RRI (RRI_{abs}), and the RRI related to its recent values (RRI_{ratio}) are summarized. Results are posted for the CAR evaluation with 19 channels (CAR_{19}) and with 10 channels (CAR_{10}) as well as for the bipolar evaluation with 6 channels ($Bipolar_6$).

Table 3.4.: Summarized results for different RRI modes. Results for CAR derivation with 19 channels and with 10 channels as well as for bipolar derivation with 6 channels are given.

Derivation Method	Mode	Sensitivity [%]	Mean Detection Delay [s]	False Detections	False Detection Rate (fdr) [1/h]
CAR_{19}	no RRI	87.04	2.6 ±9.8	12	0.039
	RRI_{abs}	87.04	3.0 ±9.5	10	0.032
	RRI_{ratio}	88.89	2.7 ±9.9	4	0.013
$Bipolar_6$	no RRI	81.48	8.4 ±12.7	21	0.068
	RRI_{abs}	83.33	7.8 ±13.0	17	0.055
	RRI_{ratio}	85.19	6.6 ±12.3	15	0.049
CAR_{10}	no RRI	88.89	5.8 ±10.6	20	0.065
	RRI_{abs}	88.89	6.0 ±10.2	19	0.061
	RRI_{ratio}	88.89	4.7 ±10.7	14	0.045

Classification using RRI_{abs} or no RRI results in a higher number of false detections than classification using RRI_{ratio}. Furthermore in CAR_{19} and $Bipolar_6$ less seizures are missed when using RRI_{ratio}. Detection delays are similar for the different RRI modes, however, RRI_{ratio} is again delivering slightly better results than the other modes.

3.3.3. Detection Delay

Figure 3.6 shows the percentage of detected seizures in relation to the detection delay. Results from the different derivation methods CAR_{19}, $Bipolar_6$, and CAR_{10} are plotted. Patient number 15 is excluded from this observation for reasons described earlier. About 30% of the tested seizures are detected before their real onset. Results after 5 s and after 10 s are highlighted. The percentage of detected seizures after 30 s is marked in red.

3.3.4. Feature Adaptation

The feature adaptations are only performed for the CAR derivation reduced to 10 channels. CAR has been chosen as it has reached superior results to the bipolar derivation in previous testing. The reduced 10 channel setup has been favored over the 19 channel setup although mean detection delays are slightly higher and the number of false detections is also increased. This approach is justified as the goal of the adaptation is a slimmer model that is easier to implement.

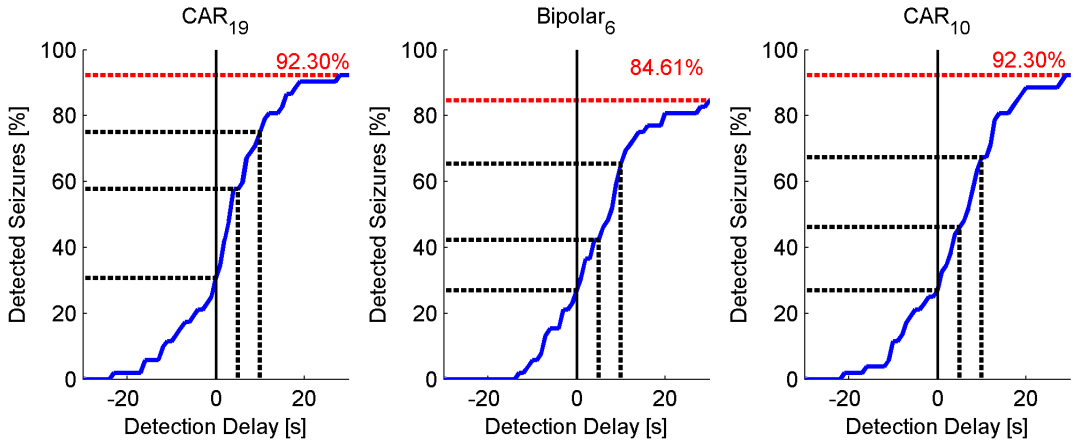

Figure 3.6.: Percentage of detected seizures in relation to the detection delay. (Patient dependent approach.)

3.3.4.1. Feature Reduction

After visual inspection of the 8 frequency bands used in the basic setup logarithmic band power appeared to be especially increased during seizures for the sub bands between 3.5 and 18.5 Hz. Therefore, these sub bands have been grouped together to one feature. As a result a reduction to three frequency bands (0.5–3.5 Hz, 3.5–18.5 Hz, and 18.5–24.5 Hz) has been performed. Parameters C and γ of the SVM have been re-evaluated and changed to $C = 2^5$ and $\gamma = 2^{-7}$. Detections are triggered only if three consecutive samples are classified as ictal by the SVM (*k=3*). The results for this approach can be seen in Table 3.5.

3.3.4.2. RRI Adaptation

When varying the time delay of the background reference window for $\mathrm{RRI}_{\mathrm{ratio}}$ calculation the results can even be improved further. Table 3.6 shows the results for time delays between 5 and 105 s. The best result is highlighted. Compared to the results in Table 3.5 where a background window delay of 25 s has been used the results could be further improved by choosing a background window delay of 35 s. An additional seizure of patient number 19 is then detected. Therefore the sensitivity is increased to 90.74% or even 94.23% when excluding patient number 15. Also false detections are reduced by one with this setting while the mean detection delay is slightly increased to 4.7 s.

Table 3.5.: Summarized results for the patient dependent evaluation using CAR_{10} with a reduced feature set.
* Insufficient data.

Patient No.	No. of Seizures	Recording Time [h]	Missed Seizures	Mean Detection Delay [s]	False Detections	fdr [1/h]
1	3	0.70	0	-3.3	0	0
3	3	2.68	0	1.3	0	0
5	3	0.68	0	-1.7	0	0
6	3	1.58	0	0.7	0	0
12	6	0.92	0	-5.3	0	0
13	7	1.43	0	7.4	0	0
14	3	20.45	0	8.3	1	0.05
15*	2	17.15	2	N/A	1	0.06
16	4	46.55	1	8.3	1	0.02
17	2	22.47	0	4.0	0	0
18	2	43.07	0	5.0	0	0
19	3	21.05	1	27.5	0	0
20	3	67.17	2	28.0	1	0.01
21	10	62.72	0	5.2	4	0.06
	54	**308.62**	**6**	**4.5 ±12.1**	**8**	**0.026**

Table 3.6.: Results for varied delay windows for the calculation of RRI_{ratio}. Delays range from 5 to 105 s. The patient dependent approach using 10 CAR derived channels and a reduced feature set is taken for evaluation.

Background window delay [s]	Detected seizures	False detections	Mean detection delay [s]
5	48	15	5.7 ±10.0
15	46	11	3.7 ±10.2
25	48	8	4.5 ±12.1
35	**49**	**7**	**4.7 ±12.0**
45	49	7	4.8 ±12.0
55	49	8	4.1 ±11.0
65	49	10	5.0 ±10.2
75	48	9	5.1 ±10.4
85	47	9	5.0 ±10.5
95	47	10	4.7 ±10.7
105	47	10	5.0 ±10.7

3.4. Patient Independent Evaluation

For the patient independent approach an alteration of 10-fold cross validation has been used to ensure statistical significance (cf. Section 2.3.3). Due to computational cost only the bipolar derivation with 6 channels and the CAR derivation with 10 channels and a reduced feature set have been evaluated. Also the influence of the ECG has not been evaluated for the patient independent approach.

3.4.1. Basic Setup

3.4.1.1. Bipolar Derivation (6 Channels)

Table 3.7 shows the results of the patient independent evaluation. EEG features are taken from six bipolar channels. Detections are triggered if two consecutive samples are classified as ictal by the SVM (k=*2*). Altogether 41 of 61 seizures have been detected ($\Rightarrow$ Sensitivity = 67.21%) within a mean delay of 14.0 s. 5 false positive detections result in an average fdr of 0.016/h.

3.4.1.2. CAR Derivation (10 Channels)

Table 3.8 shows the results of the patient independent evaluation using ten CAR derived channels. Detections are again triggered if the SVM classifies two consecutive samples as ictal (k=*2*). In total, 55 of 61 seizures have been detected ($\Rightarrow$ Sensitivity = 90.16%) within a mean delay of 9.7 s. 6 false positive detections result in an average fdr of 0.019/h.

3.4.2. Detection Delay

Figure 3.7 shows the percentage of detected seizures in relation to the detection delay. Again, patient number 15 is excluded from this observation. Results after 5 s and after 10 s are highlighted. The percentage of detected seizures after 60 s is marked in red.

3.4.3. Feature Adaptation

Again, the feature adaptation is only performed for the CAR_{10} derived data. The changed SVM parameters $C = 2^5$ and $\gamma = 2^{-7}$ are used. RRI adaptation has not been calculated due to computational cost.

Table 3.7.: Summarized results for the patient independent evaluation using six bipolar derived channels.
* Insufficient data.

Patient No.	No. of Seizures	Recording Time [h]	Missed Seizures	Mean Detection Delay [s]	False Detections	fdr [1/h]
1	3	0.70	1	9.5	0	0
2	1	2.03	1	N/A	0	0
3	3	2.68	0	9.3	3	1.12
4	1	0.65	1	N/A	0	0
5	3	0.68	0	22.3	0	0
6	3	1.58	0	8.3	0	0
7	1	0.22	1	N/A	0	0
8	1	0.20	1	N/A	0	0
9	1	0.15	0	9.0	0	0
10	1	0.12	1	N/A	0	0
11	1	1.37	0	20.0	0	0
12	6	0.92	1	5.2	0	0
13	7	1.43	0	19.7	0	0
14	3	20.45	3	N/A	0	0
15*	2	17.15	2	N/A	1	0.05
16	4	46.55	1	11.0	0	0
17	2	22.47	0	8.5	0	0
18	2	43.07	0	18.0	0	0
19	3	21.05	2	33	1	0.05
20	3	67.17	3	N/A	0	0
21	10	62.72	2	15.4	0	0
	61	**313.36**	**20**	**14.0 ±10.2**	**5**	**0.016**

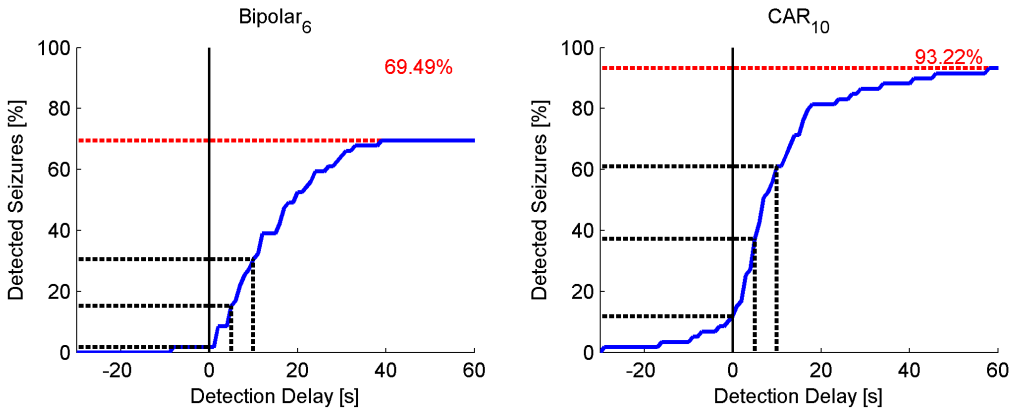

Figure 3.7.: Percentage of detected seizures in relation to the detection delay. (Patient independent approach.)

Table 3.8.: Summarized results for the patient independent evaluation using CAR_{10}.
* Insufficient data.

Patient No.	No. of Seizures	Recording Time [h]	Missed Seizures	Mean Detection Delay [s]	False Detections	fdr [1/h]
1	3	0.70	0	12.3	0	0
2	1	2.03	0	41.0	0	0
3	3	2.68	0	12.3	0	0
4	1	0.65	0	5.0	0	0
5	3	0.68	0	-3.7	0	0
6	3	1.58	0	0.3	0	0
7	1	0.22	0	46.0	0	0
8	1	0.20	1	N/A	0	0
9	1	0.15	0	8.0	0	0
10	1	0.12	0	58.0	1	8.33
11	1	1.37	0	13.0	0	0
12	6	0.92	0	3.3	0	0
13	7	1.43	0	8.7	0	0
14	3	20.45	0	8.3	0	0
15*	2	17.15	2	N/A	0	0
16	4	46.55	1	9.0	0	0
17	2	22.47	0	4.0	3	0.13
18	2	43.07	0	8.0	0	0
19	3	21.05	0	10.0	0	0
20	3	67.17	2	24.0	2	0.03
21	10	62.72	0	8.8	0	0
	61	**313.36**	**6**	**9.7 ±13.8**	**6**	**0.019**

3.4.3.1. Feature Reduction

The same feature reduction as in the patient dependent approach has been used. The eight frequency bands are merged to three bands (0.5–3.5 Hz, 3.5–18.5 Hz, and 18.5–24.5 Hz). Results for this approach are listed in Table 3.9. 53 of the 61 seizures ($\Rightarrow$ Sensitivity = 86.89%) are detected within a mean detection delay of 7.1 s. 6 false positive detections occurred which result in an *fdr* of about 0.019/h.

Table 3.9.: Summarized results for the patient independent evaluation using CAR_{10} and a reduced feature set.
* Insufficient data.

Patient No.	No. of Seizures	Recording Time [h]	Missed Seizures	Mean Detection Delay [s]	False Detections	fdr [1/h]
1	3	0.70	0	8.3	0	0
2	1	2.03	0	16.0	0	0
3	3	2.68	0	9.7	0	0
4	1	0.65	0	8.0	0	0
5	3	0.68	0	-1.7	0	0
6	3	1.58	0	7.3	0	0
7	1	0.22	1	N/A	0	0
8	1	0.20	1	N/A	0	0
9	1	0.15	0	13.0	0	0
10	1	0.12	1	N/A	0	0
11	1	1.37	0	13.0	0	0
12	6	0.92	0	4.2	0	0
13	7	1.43	0	13.1	0	0
14	3	20.45	0	8.7	0	0
15*	2	17.15	2	N/A	0	0
16	4	46.55	1	8.3	0	0
17	2	22.47	0	14.0	2	0.09
18	2	43.07	0	7.5	0	0
19	3	21.05	0	15.7	1	0.05
20	3	67.17	2	27.0	3	0.04
21	10	62.72	0	7.4	0	0
	61	**313.36**	**8**	**9.1 ±10.7**	**6**	**0.019**

3.5. Summary of Results

Table 3.10 shows the total results for different derivation methods (CAR, Bipolar) as well as different channel numbers (6, 10, 19) and feature settings (3bp, 8bp). Both patient dependent (d) and independent (i) results are stated.

Table 3.10.: Summary of evaluation results. 3bp (8bp) .. 3 (8) logarithmic band power features per channel; d (i) .. patient dependent (independent) evaluation.

Mode	No. of Seizures	Recording Time [h]	Missed Seizures	Mean Detection Delay [s]	False Detections	fdr [1/h]
$CAR_{19}^{8bp,d}$	54	308.62	6	2.7 ±9.9	4	0.013
$Bipolar_{6}^{8bp,d}$	54	308.62	8	6.6 ±12.3	15	0.049
$CAR_{10}^{8bp,d}$	54	308.62	6	4.7 ±10.7	14	0.045
$CAR_{10}^{3bp,d}$	54	308.62	6	4.5 ±12.1	8	0.026
$Bipolar_{6}^{8bp,i}$	61	313.36	20	14.0 ±10.2	5	0.016
$CAR_{10}^{8bp,i}$	61	313.36	6	9.7 ±13.8	6	0.019
$CAR_{10}^{3bp,i}$	61	313.36	8	9.1 ±10.7	6	0.019

4. Discussion/Outlook

4.1. Discussion

In this thesis, it has been evaluated whether temporal lobe seizures can be detected from a subset of EEG and ECG electrodes within a reasonable time. As a first step, some general remarks on the data, results, and other selected topics will be made. The achieved results will then be compared to state of the art results. Furthermore, considerations about classification and general information for future on-line application will be stated.

4.1.1. General Remarks

4.1.1.1. Data

One of the eight seizures recorded for patient number 13 has been totally contaminated by artifacts and, therefore, has been rejected.

The seizure provided by patient number 10 constitutes an exception to the restriction to temporal lobe seizures. This patient experienced a generalized seizure onset. Classification of this seizure is attempted regardlessly to see whether detection of generalized seizures might be possible as well.

4.1.1.2. Influence of the Number of Electrodes

The numbers of used EEG electrodes have been varied for different evaluations (10 electrodes for Bipolar_6 as well as CAR_{10} and 19 electrodes for CAR_{19}). When using more channels for detection, the risk of losing seizure data due to artifact contamination increases, as overflows or flat lines occurring in any channel lead to rejection of the values of all channels for the respective period. For the CAR_{19} electrode selection only two seconds of a seizure of patient number 21 remain for classification. Therefore, this seizure has been missed.

On the other hand, a higher number of electrodes seems to provide a more robust classifier. The number of false detections is far less than in all other approaches. Therefore, no additional detection criterion is needed. A detection is already counted at the first sample classified as ictal by the SVM. This again improves the detection delay.

4.1.1.3. Best Channel Combination

When searching for the best channel combination of bipolar channels center and "basal ring" electrodes have been excluded beforehand. These restrictions have been chosen, for the following reasons:

- Center electrodes have been rejected, because focal epileptic activity should be better detectable in one or the other hemisphere.
- Electrodes near to the ears and eyes have been rejected, because these positions are more vulnerable to EMG/EOG artifacts.
- Another reason for the chosen selection is the better comparability to Shoeb's data [60] who had no "basal ring" recordings.

4.1.1.4. Results

The results achieved by CAR_{10} with 3 frequency bands are superior to the ones using CAR_{10} with all 8 frequency bands. The number of false detections as well as the detection delay is improved. This could be signaling overfitting for the approach using features from 8 frequency bands.

The large number of false detections of patient number 3 in most patient dependent approaches are due to insufficient data. False detections are caused by chewing artifacts. Patient number 3 provides less than three hours of recording. Within the data three seizures are stored. Only one segment is contaminated by chewing artifacts. These false detections could possibly be prevented by using more training data. It could be beneficial to demand data with chewing artifacts in the training set.

4.1.1.5. Patient Dependent versus Patient Independent

The patient independent approach uses a lot more data than the patient dependent approach. Therefore, the training of the SVM takes much longer, which makes calculations impracticable to a certain extent. A complete 10-fold cross-validation has not been performed due to this

problem. All data has only been evaluated once instead of 10 times as usually done in 10-fold cross-validation. Therefore, the results of this section might lack statistical power.

The received results indicate that the used derivation method has substantial influence on the overall performance. Bipolar derivation leads to worse results than the CAR method. Too large distances between the different electrodes might be the reason for this. By applying a patient independent approach, even seizures from persons that experienced only a single seizure have been detected. The detection delays in some of those cases are high, however. Nevertheless, this indicates that at least for some seizures the inter-patient variations are negligible and that a few universally valid properties might exist. Another improvement realized by the patient independent approach is the decrease of false positive detections in patient number 3.

A possible conclusion might be to use a patient independent approach as long as not enough data is available for a specific patient, while simultaneously collecting more data. As soon as a certain amount of data is reached, a change to a patient dependent approach can be performed. This transition could also happen gradually, constantly increasing the patient dependent data proportion as new measurements arrive.

4.1.2. Comparison to State of the Art

As already stated earlier a comparison between different detection systems is not entirely easy. Nevertheless, some conclusions can be drawn. Altogether it is a very challenging task to match any of the proposed results in literature. First of all the results have to be compared to Shoeb's study [60] as the system is based on his approach. Shoeb reached a sensitivity of 96% with patient dependent classification. This high value has not been reached in this thesis. Depending whether patient number 15 is excluded or not, sensitivities of up to 91% or 94% are achieved. As far as the fdr is concerned, this study delivers better results than Shoeb's. A mean fdr of about 0.134/h is compared with false detection rates of 0.016/h to 0.049/h in this thesis. 91% of the detected seizures which account for about 87% of all seizures are detected within 10 s from onset in Shoeb's work. The same amount of seizure detections is only reached after about 18 s in this thesis (cf. Figure 3.6 in Section 3.3.3).

The better detection delay and sensitivity in Shoeb's study might be due to the greater amount of available training data both, inter-ictal and ictal. On the other hand no restriction to temporal lobe seizures has been made in his research. There is no information about the composition of seizure types within his data, therefore, no conclusions can be drawn whether the task has been made more difficult or even easier. In principle allowing different seizure types is more likely to negatively influence the classification accuracy. But also the opposite

could be the case: other seizure types than temporal lobe seizures could produce a larger inter-class difference between ictal and inter-ictal data and, therefore, could be easier to detect (e.g. tonic-clonic seizures).

Compared with the studies [37, 65] which also specialized only on temporal lobe seizures, similar sensitivity rates are reached while false detection rates are lower in this thesis. Khamis et al. observed 1624 h of data containing 83 seizures from 10 patients. They detected 91.57% of all seizures while producing about 0.27 false detections per hour. Van Putten et al. evaluated long-term EEG recordings from 16 patients. They extracted 2.5 h of each recording and observed at least one seizure per person. They reached a sensitivity of about 77 - 97% combined with a fdr of about 1/h.

A better fdr has been reached in this thesis. The adaptation of the number of consecutive ictal detections that is needed to trigger an alarm has helped to improve this rate. Additionally, the aggregation of consecutive false positives (within 30 s) has reduced the false detections even further.

4.1.3. Why SVM?

Epileptic seizure detection seems to be a complex task. More accurate results might be possible when using many different features. Therefore, the feature set suggested by [60] has been chosen for this study together with ECG features. For this large number of features some of the classification methods described in Section 1.4.3.3 are inapplicable. Discriminant analysis tends to *overfit* when trained with too many features. This leads to bad generalization and, therefore, bad testing results. Also the approach to choose thresholds is too difficult for a large combination of features. RVM has been tried in contrast to SVM as sparser models should be produced by RVM. Unfortunately the RVM did not finish the training of a single classifier within several days when using the complete feature set. Therefore, this method has been rejected. Furthermore, the data provided for this task is very unbalanced, meaning that there is much more inter-ictal data than ictal one. ANNs are ruled out as well, as they cannot handle this unbalanced data well. In contrast SVMs are capable to deal with these conditions. Furthermore, SVM has been used in some seizure detection publications so far and has proven to be able to achieve reasonable results [60, 46].

4.1.4. Hospital Data versus Home Data

All data used so far has been recorded during hospital stay. Patients have not even left their bed during monitoring. Therefore, future investigations need to evaluate the influence of

physical activity. All detection systems described in literature work with "hospital data". Therefore, the effect of many typical daily activities (e.g. walking up/walking down the stairs) on false detections is unknown.

Especially the influence of a more varying RRI has to be tested. Also the size as well as the delay of the background window for RRI_{ratio} calculation should be investigated further. Also the approach to use multiple ECG features as proposed in [60] could lead to better results.

4.1.5. Testing Inconsistencies

The data material has steadily increased in the course of this thesis. At the beginning, when some decisions have already been made the available data might not have been representative enough for the whole data. The ratio between recorded ictal and inter-ictal data is varying too much between all patients. For example, data of patient number 12 contains 6 seizures in 55 minutes of recording whereas data of patient number 20 contains 3 seizures in more than 67 h of recording. This ratio might, however, influence the choice of the RBF-SVM parameters C and γ and also the optimal channel combination. Therefore, it might be useful to re-evaluate the parameters and channel combinations with more homogeneous data.

A new evaluation of SVM parameters and channels might also be beneficial as in the course of this project, the quality measures for the detection system have been changed. The rules whether a sample counts as falsely detected or not have been adapted. For the parameter grid search Cohen's kappa is used to identify the best constellation. After that detection rules have been softened allowing pre-ictal alarms. Also an attempt to reduce false positives by triggering alarms only after a number of consecutive detections has been applied.

Testing modalities have also changed, as a result of the growing data supply during this thesis. The first tests that have been needed to determine the SVM parameters as well as the choice of a smaller channel combination have been conducted patient independent in a leave-one-out fashion. After more data has arrived this method has been unpracticable, therefore, a change to patient dependent leave-one-out testing has occurred.

4.1.6. Dataset Design

The needs the dataset has to fulfill only crystallized during the thesis and, therefore, supplied data does not match the ideal criteria. For further investigations it would be helpful to build a homogeneous dataset that complies with the following restrictions:

- Only data recorded while the patient is awake should be used. The algorithm should work in combination with the specially designed EEG-cap mentioned in Section 1.5.1. As a primary step this cap is going to be used only when awake, therefore, good or bad behavior on data recorded while sleeping only distorts the real quality of the detection system.
- More detailed information about the epileptic focus and whether secondarily generalization occurred (including the moment of generalization) would be helpful as well. Especially information about the focus could be exploited to choose the best electrode positions for detection dependent for each patient. On the other hand a better localization of the focus could also be a task for the EEG cap. Still some prior knowledge would be beneficial in this case, as the number of electrodes used with the cap is restricted.
- For every patient within the dataset at least 3 or 4 seizures have to be recorded.
- The duration of inter-ictal recording should be adjusted as well. Each patient should provide roughly the same amount of data. Inter-ictal data should be provided in a to some extent natural ratio to ictal data. In contrast, recordings of patient number 1 to patient number 13 used in this thesis only include seizure periods with a few minutes of inter-ictal data before and after the seizures.
- Maybe some typical artifacts known to produce false detections, like chewing, blinking and certain movement artifacts, should be produced deliberately during inter-ictal recording to provide better training data for the SVM.

4.1.7. Considerations for On-line Testing

The memory requirements for on-line detection are analyzed with regard to the bipolar derivation approach restricted to 6 channels. The SVM has to be trained off-line first. The trained SVM uses about 1000 support vectors on average. A single sample vector consists of 147 features in *double* precision:

$$\rightarrow (6\,\text{Channels} \times 8\,\text{Bands} + 1\,\text{ECG Feature}) \times 3\,\text{Time Segments} = 147\,\text{Features}$$

Therefore, to store the support vectors about $1000 \cdot 147 \cdot 8\,\text{Bytes} \approx 1\,\text{MB}$ of memory is needed. For classification, the support vectors need to be multiplied with each observed sample vector. This doubles the storage amount.

Every second 49 features - the logarithmic band power for 48 data segments and the $\text{RRI}_{\text{ratio}}$ - need to be computed. $6 \cdot 49$ feature values need to be stored in shifting registers. Furthermore,

it would be useful to provide additional memory that can be used for the storage of the most recent data. Every time a seizure occurs, this data could be kept for further analysis. Thus better information about the seizure focus as well as additional data for retraining the SVM can be achieved.

4.2. Future Work

A future goal is to lead the detection system to market maturity. Therefore, a number of tasks need to be performed:

Excessive testing: More data has to be evaluated to check whether the generalization abilities of the classifier are sufficient.

Feature alteration: The search for adequate features has to be repeated with a larger and more balanced dataset as described in Section 4.1.6. Also the reduction of features as proposed in Section 2.4.2 needs to be investigated further.

Other classifier: If the number of used features can be reduced massively, other classifiers, possibly RVM, might lead to a sparser model and, therefore, to quicker and easier on-line implementation.

On-line testing: The algorithm should be tested in an on-line scenario to see if estimated detection delays and false detection rates are stable.

Patient specific electrode positions: The electrodes used for detection could be selected patient specific with the help of medical staff. This might improve the detection accuracy of the system. Also electrode positions divergent from the 10-20 system could be used.

Reduction of detection delay: Further efforts have to be made to decrease the detection delay. The goal has to be a detection preceding the real seizure onset.

A. Freely Available Epilepsy Data On-line

The following links contain epilepsy data freely available on the internet:

- http://www.cs.tut.fi/ gomezher/projects/eeg/databases.htm
  - Signal: EEG →21 scalp electrodes, ECG
  - Patients: 21 persons; focal epilepsy
  - Number of seizures: one seizure each
  - Recorded length: about 11 hours each
- https://epilepsy.uni-freiburg.de/freiburg-seizure-prediction-project/ eeg-database
  - Signal: invasive EEG →6 electrodes
  - Patients: Two persons; male; 35 years; suffering from mesial temporal lobe epilepsy
  - Number of seizures: 2 to 5 seizures per person
  - Recorded length: at least 24 hours each
- http://www.physionet.org/pn6/chbmit/
  - Signal: EEG →23 or more scalp electrodes
  - Patients: 22 persons; 5 males, ages 3-22; and 17 females, ages 1.5-19
  - Number of seizures: 198 seizures altogether
  - Recorded length: about 1000 hours altogether
- http://epileptologie-bonn.de/cms/ front_content.php?idcat=193&lang&lang=3&changelang=3
  - 5 different sets with 100 single channel recordings each
    2 sets from healthy persons; scalp EEG
    3 sets from patients; intra-cranial EEG

  - Recorded length: $5 \times 100 \times 23.6$ seconds

Another source is going to be on-line in the next view years:

- http://www.epilepsiae.eu/project_outputs/european_database_on_epilepsy

In total this database will contain continuous long-term recordings of 275 patients; 225 scalp recordings and 50 intra-cranial recordings.

B. Additionally Investigated Features

The following features have already been used in seizure detection systems [24, 46, 52, 65] as well as in epilepsy diagnosis [11, 16]. The following features appeared to be inferior to those features used within this thesis. Consequent testing with additional data might however lead to different conclusions. Therefore, equations for all additionally calculated but rejected features are listed next.

Line Length (LL): Changes in frequency and amplitude can be observed by calculating the line length proposed by [24].

$$\mathrm{LL}\,(\mathrm{j}) \;=\; \frac{1}{\mathrm{N}} \sum_{\mathrm{i}=1}^{\mathrm{N}} \left|\mathbf{x}\,(\mathrm{i}-1) - \mathbf{x}\,(\mathrm{i})\right| \tag{B.1}$$

$\mathbf{x}$ . . . EEG input signal

i, j . . . time index

N . . . size of calculation window (sample rate $\times$ seconds)

Nonlinear Energy (η): To identify nonlinear signal alterations, a formula is described in [52].

$$\eta\,(\mathrm{j}) \;=\; \frac{1}{\mathrm{N}} \sum_{\mathrm{i}=1}^{\mathrm{N}} \left[\mathbf{x}^2\,(\mathrm{i}) \;-\; \mathbf{x}\,(\mathrm{i}+1) \cdot \mathbf{x}\,(\mathrm{i}-1)\right] \tag{B.2}$$

$\mathbf{x}$ . . . EEG input signal

i, j . . . time index

N . . . size of calculation window (sample rate $\times$ seconds)

Variance (σ^2): Changes in variance during seizures are described in a number of studies (cf. [45]). The energy of the signal carries the same information as the variance. Therefore, the following simplified equation can be used:

$$\sigma^2\,(\mathrm{j}) \;=\; \frac{1}{\mathrm{N}} \sum_{\mathrm{i}=1}^{\mathrm{N}} \mathbf{x}^2\,(\mathrm{i}) \tag{B.3}$$

$\mathbf{x}$ . . . EEG input signal

i, j . . . time index

N . . . size of calculation window (sample rate $\times$ seconds)

Mean Cross Correlation ($\overline{\mathrm{CC}}$): This feature determines the pairwise similarity of electrode measurements. It is preferably used for the detection of generalized seizures, where large brain areas are synchronized [46].

$$\overline{\mathrm{CC}}\,(\mathrm{j}) \;=\; \frac{2}{\mathrm{N}\,(\mathrm{N}-1)} \sum_{\mathrm{i}}^{\mathrm{N}} \sum_{\mathrm{j}\neq\mathrm{i}}^{\mathrm{N}} \mathbf{x}\,(\mathrm{i})\,\mathbf{x}\,(\mathrm{j}) \tag{B.4}$$

$\mathbf{x}$ . . . EEG input signal

i, j . . . time index

N . . . size of calculation window (sample rate $\times$ seconds)

Number of Minima and Maxima (minmax): This feature indirectly analyzes the frequency of the signal [65].

$$\mathrm{minmax}\,(\mathrm{j}) \;=\; \frac{1}{\mathrm{N}} \sum_{\mathrm{i}=1}^{\mathrm{N}} \left(|\mathbf{x}(\mathrm{i}) - \mathbf{x}(\mathrm{i}-1)| \;<\; \epsilon\right) \longrightarrow \epsilon \;=\; 0.01 \tag{B.5}$$

$\mathbf{x}$ . . . EEG input signal

i, j . . . time index

N . . . size of calculation window (sample rate $\times$ seconds)

ϵ . . . permitted tolerance for extreme value calculation

Mean Amplitude ($\overline{\mathbf{Amp}}$): Amplitude is often increased during seizures [65]. This is measured by the following equation.

$$\overline{\mathrm{Amp}}\,(\mathrm{j}) \;=\; \frac{1}{\mathrm{N}} \cdot \sum_{\mathrm{i}=1}^{\mathrm{N}} \mathbf{x}\,(\mathrm{i}) \tag{B.6}$$

$\mathbf{x}$ . . . EEG input signal

i, j . . . time index

N . . . size of calculation window (sample rate $\times$ seconds)

Hjorth Parameters: Hjorth parameters have been used in a few studies for epilepsy diagnosis already. Both initial diagnosis using inter-ictal EEG and seizure lateralization have been examined [11, 16]. The three parameters describe the signals *activity (h_0)*, *mobility (h_1)*, and *complexity (h_2)*.

$$h_0 \;=\; m_0 \mathrel{\widehat{=}} \sigma^2 \qquad\qquad h_1 \;=\; \sqrt{\frac{m_2}{m_0}} \qquad\qquad h_2 \;=\; \sqrt{\frac{m_4}{m_2} - \frac{m_2}{m_0}} \tag{B.7}$$

m_0 . . . variance of the EEG signal

m_2 . . . variance of the first derivative of the EEG signal

m_4 . . . variance of the second derivative of the EEG signal

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