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Miikka Ermes

Methods for the Classification of Biosignals Applied to the Detection of Epileptiform Waveforms and to the Recognition of Physical Activity

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Miikka Ermes

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Miikka Ermes. Methods for the Classification of Biosignals Applied to the Detection of Epileptiform Waveforms and to the Recognition of Physical Activity [Menetelmiä biosignaalien luokitteluun sovellettuna epileptiformisten aaltojen havaitsemiseen ja fyysisen aktiviteetin tunnistamiseen]. Espoo 2009. VTT Publications 707. 77 p. + app. 69 p.

Keywords biosignals, classification, EEG, accelerometers, activity recognition

Abstract

Biosignals are such signals that quantify the physiological processes of a living organism. Classification of biosignals aims at inferring the physiological condition of the organism based on the biosignals obtained from it. In this thesis, the classifications of two biosignals originating from the human body are studied in detail: the electroencephalogram (EEG) and acceleration signals recorded from body-worn sensors (body accelerometry).

EEG quantifies the electrical activity of the brain. In this thesis, EEG recorded in hospital operating room and intensive care unit environments is classified to detect epileptiform brain activity which is a potentially brain-damaging phenomenon. Wavelet subband entropy of EEG is shown to be statistically associated with epileptiform activity both in operating room patients under sevoflurane-induced anesthesia and in intensive care unit patients resuscitated after cardiac arrest. The results support the hypothesis that epileptiform activity can be continuously monitored in both clinical settings.

Body accelerometry quantifies the movements of the human body with body-worn sensors. In this thesis, body accelerometry is classified for activity recognition purposes, i.e. the purpose is to detect the type of physical activity of the subject from the body acceleration signals. State-of-the-art offline classification results are obtained in two studies. In addition, conversion of the presented offline activity classification algorithms to an online version is demonstrated. The results confirm that multiple classes of daily physical activities and sports can be reliably recognized with body accelerometry.

Miikka Ermes. Methods for the Classification of Biosignals Applied to the Detection of Epileptiform Waveforms and to the Recognition of Physical Activity [Menetelmiä biosignaalien luokitteluun sovellettuna epileptiformisten aaltojen havaitsemiseen ja fyysisen aktiviteetin tunnistamiseen]. Espoo 2009. VTT Publications 707. 77 s. + liitt. 69 s.

Avainsanat biosignals, classification, EEG, accelerometers, activity recognition

Tiivistelmä

Biosignaalit kuvaavat elävien organismien fysiologisia prosesseja. Biosignaalien luokittelun tavoitteena on päätellä organismin fysiologinen tila siitä kerättyjen biosignaalien avulla. Tässä väitöskirjassa tutkitaan kahden ihmisruumiista kerätyn biosignaalin luokittelua: aivosähkökäyrän (EEG:n) ja puettavista antureista kerätyn kiihtyvyyssignaalin.

EEG mittaa aivojen sähköistä aktiivisuutta. Tässä väitöskirjassa sairaalan leikkaussalissa ja teho-osastolla kerättyä EEG-signaalia luokitellaan epileptiformisen aivotoiminnan tunnistamiseksi, joka on mahdollisesti aivoja vaurioittava ilmiö. EEG-signaalista lasketun wavelet-hajotelman kaistan entropian osoitetaan olevan tilastollisesti riippuvainen epileptiformisesta aivotoiminnasta sekä leikkauspotilailla sevofluraanianestesiassa että sydänpysähdyksestä elvytetyillä tehohoitopotilailla. Tulokset tukevat olettamusta, että epileptiformista toimintaa voidaan tarkkailla molemmissa kliinisissä ympäristöissä.

Vartalon kiihtyvyysmittaukset puettavilla antureilla tuottavat biosignaaleja, jotka kuvaavat vartalon liikettä. Tässä väitöskirjassa näitä signaaleja luokitellaan, jotta henkilön fyysisen aktiviteetin tyyppi pystyttäisiin määrittelemään. Tieteellistä huippua edustavia luokittelutuloksia saavutetaan kahdessa tutkimuksessa. Lisäksi testattujen menetelmien soveltamista reaaliaikaiseen aktiviteetin tunnistamiseen havainnollistetaan. Tulokset vahvistavat, että monia päivittäisiä fyysisen aktiviteetin muotoja voidaan luotettavasti tunnistaa puettavista kiihtyvyysantureista saatavista signaaleista.

Preface

The research presented in this thesis was carried out during 2004–2008 at VTT Technical Research Centre of Finland, Tampere, Finland. The opportunity to work with such talented, and most importantly kind, people in our research center has been a priviledge. So, thank you all!

My instructor at VTT, Docent Mark van Gils, has had an enormous effect on the fact that this thesis saw the daylight. He has always found the time to guide me regardless of being busyer than ever.

Docent Ilkka Korhonen has had a major impact on many important decisions in my early career. He has actively guided the whole process leading to this point and the many inspiring discussions with him have steered my thoughts probably more than even I can see.

My supervisor, Docent Alpo Värri, has looked after my studies since I began to write my MSc thesis. His active suggestions especially regarding the post-graduate courses significantly helped me along the way.

I was fortunate to start my career as a research scientist in a project led by Mr. Juha Pärkkä, MSc, as I found myself in a middle of a well-organized study that was destined to produce state of the art results regardless of my interference. Also since then, Mr. Pärkkä has been the driving force of our research on activity recognition. He has co-authored all the publications of this thesis concerning activity recognition.

Mr. Mika Särkelä, PhD, from GE Healthcare has been a long-time collaborator in our research related to EEG. By working with him, I have learned the most that I know about the abnormalities of EEG. He has also been a co-author in all of the EEG-related publications of this thesis. I thank him and the rest of the team led by Ms. Hanna Viertiö-Oja, PhD, for the fruitful co-operation.

The analysis of biosignals is a cross-disciplinary research field and the collaboration with many clinicians has been essential. I sincerely thank Dr.

Johanna Wennervirta, MD, and Dr. Anne Vakkuri, MD, PhD, for the possibility to participate in analysing clinical data collected with great discipline.

I thank the pre-examiners of my thesis, Professors Pasi Karjalainen and Anna Bianchi, for their useful comments. I completely agreed with their suggestions which significantly improved the quality of this thesis by making it more concise and understandable.

I am grateful to the VTT technology managers Mr. Jukka Perälä, and Mr. Markus Tallgren for their supportive attitude towards my PhD studies and the writing process.

I would like to thank Professor Niilo Saranummi for helping me to obtain the required permissions to reproduce the articles included in this thesis.

The financial support from Instrumentarium Science Foundation is gratefully acknowledged.

Tampere, March 2009

Miikka Ermes

Contents

Appendices of this publication are not included in the PDF version. Please order the printed version to get the complete publication (http://www.vtt.fi/publications/index.jsp).

List of publications

The thesis is based on the following original publications which are referred to in the text as **E1**–**E4** for the publications considering EEG research, and as **A1**–**A3** for the publications considering activity recognition research. The publications are reproduced here with kind permissions from the publishers.

E1: **Ermes, M.**, Särkelä, M., van Gils, M., Vakkuri, A., Yli-Hankala, A. & Jäntti, V. 2006. Method for the Automatic Detection of Epileptiform Waveforms in Sevoflurane-Induced Anesthesia EEG. Proceedings of the 28th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. Pp. 6343–6346.

E2: Särkelä, M., **Ermes, M.**, van Gils, M., Yli-Hankala, A., Jäntti, V. & Vakkuri, A. 2007. Quantification of Epileptiform Electroencephalographic Activity During Sevoflurane Mask Induction. Anesthesiology, Vol. 107, No. 6, pp. 928–938.

E3: **Ermes, M.**, Särkelä, M., van Gils, M., Wennervirta, J., Vakkuri, A. & Salmi, T. 2007. Prediction of Poor Outcome Using Detector of Epileptiform EEG in ICU Patients Resuscitated After Cardiac Arrest. Proceedings of the 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. Pp. 3056–3059.

E4: Wennervirta, J., **Ermes, M.**, Tiainen, M., Salmi, T., Hynninen, M., Särkelä, M., Hynynen, M., Stenman, U., Viertiö-Oja, H., Saastamoinen, K., Pettilä, V. & Vakkuri, A. Hypothermia-Treated Cardiac Arrest Patients with Good Neurological Outcome Differ Early in Quantitative Variables of EEG Suppression and Epileptiform Activity. Critical Care Medicine. Accepted for publication.

A1: Pärkkä, J., **Ermes, M.**, Korpipää, P., Mäntyjärvi, J., Peltola, J. & Korhonen, I. 2006. Activity Classification Using Realistic Data From Wearable Sensors. IEEE Transactions on Information Technology in Biomedicine, Vol. 10, No. 1, pp. 119–128.

A2: **Ermes, M.**, Pärkkä, J., Mäntyjärvi, J. & Korhonen, I. 2008. Detection of Daily Activities and Sports with Wearable Sensors in Controlled and Uncontrolled Conditions. IEEE Transactions on Information Technology in Biomedicine, Vol. 12, No. 1, pp. 20–26.

A3: **Ermes, M.**, Pärkkä, J. & Cluitmans, L. 2008. Advancing from Offline to Online Activity Recognition with Wearable Sensors. Proceedings of the 30th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. Pp. 4451–4454.

Author's contribution

The following describes the author's contribution to the individual publications of the thesis:

E1: The author has performed the EEG preprocessing and feature extraction. He has assisted in developing the classification model. He has had the main responsibility in writing the publication.

E2: The author computed most of the EEG signal features presented in the study. He has contributed to the publication by writing parts of it.

E3: The author has had the main responsibility in all signal processing tasks of the publication. He has also had the main responsibility in writing the publication.

E4: The author is responsible for all signal processing of EEG presented in publication. He has also performed the statistical tests presented in the publication. He has had the main responsibility in writing the chapters concerning statistical methods and EEG analysis in the publication.

A1: The author has had the main responsibility in the signal preprocessing, feature extraction, and classification procedures of the publication. He has taken part in writing the publication.

A2: The author has had the main responsibility in signal preprocessing, feature extraction, and classification procedures of the publication. He has had the main responsibility in writing the publication.

A3: The author has been involved in adjusting the classification and feature extraction algorithms for the online environment but he has not made the actual implementation. The author has had the main responsibility in writing the publication.

Publication **E2** has been recently considered also in the doctoral dissertation of Dr. Mika Särkelä [Särkelä 2008]. However, the contributions of Dr. Särkelä and the author to the publication are distinct from each other. Dr. Särkelä has established the structure of the study and participated in the performance evaluation.

Symbols and abbreviations

Abbreviations

3D	Three dimensional
ANN	Artificial neural network
BIS	Bispectral index
CWT	Continuous wavelet transform
DC	Direct current
DOA	Depth of anesthesia
EEG	Electroencephalogram
ECG	Electrocardiogram
FWT	Fast wavelet transform
HMM	Hidden Markov model
ICU	Intensive care unit
IDEEA	Intelligent device for energy expenditure and activity
MA	Moving average
NLEO	Nonlinear energy operator
OR	Operating room
PDA	Personal digital assistant
PED	Periodic epileptiform discharge
PSD	Power spectral density function
SE	Status epilepticus
STFT	Short-term Fourier transform
WSE	Wavelet sub band entropy

Variables, functions, and transforms

$a_j(k)$	Approximation coefficients of wavelet decomposition level j
$\hat{c}_j(k)$	Normalised version of either detail or approximation coefficients of wavelet decomposition level j
$c_j(k)$	Either detail or approximation coefficients of wavelet decomposition level j
$d_j(k)$	Detail coefficients of wavelet decomposition level j
f	Frequency
$H(\bullet)$	Entropy
$I(\bullet)$	Gini inpurity
i, j, k	General index variables
N	Number of elements
n_i	Node i in decision tree
$P(\bullet)$	Power spectral density function
$p(\bullet)$	Probability of incidence
s	Scaling variable in wavelet transform
$S(\bullet)$	Spectral entropy
t	Time
u	Translation variable in wavelet transform
$W\{\bullet\}$	Wavelet transform
$\boldsymbol{X}$	Random variable
$X(f)$	Signal in frequency domain
$x(n)$	Signal in discrete time domain
$x(t)$	Signal in continuous time domain
$\Psi(u,s)$	Wavelet atom

1. Introduction

Living organisms are composed of different functional systems. In the human body there exist, for example, the nervous system, the cardiovascular system, the musculosceletal system, the digestive system, and the immune system. These systems employ physiological processes such as blood circulation and breathing in the case of cardiovascular system.

Biosignals are signals that quantify the physiological processes. They can be measured as physical quantities such as temperature or pressure, electrical quantities such as currents and voltages and biochemical quantities such as concentrations.

The clinical need for the monitoring of biosignals arises from the fact that diseases and dysfunctions in the biological processes cause changes that usually degrade their performance. Such changes lead to pathological processes – rise in the body temperature during an infection as an example.

Also nonpathological changes in the status of the body can cause changes in the physiological processes. For example, physical strain increases the heart rate and blood pressure whereas talking causes irregularities in the breathing rhythm. The nonclinical biosignal monitoring solutions, such as fitness monitors, concentrate on such nonpathological changes in the biosignals.

1.1 General outline of the thesis

This thesis contains publications from the author's research during years 2004–2008 on two biosignal-based research subjects: detection of epileptiform waveforms (publications **E1**–**E4**) and recognition of physical activity (publications **A1**–**A3**). In both research subjects, the purpose has been to utilize signal processing methods to detect certain states, i.e. classes, in the time sequences of biosignals. In all of the publications, similar signal processing approach has been utilized.

First the obtained biosignal recordings have been divided into short segments. The signal in each segment has been considered stationary and features have been calculated from the signal in each segment. Then the obtained features have been used to assign classes for the segments either by automatic classification algorithms or by rules based on a priori knowledge. The rest of this chapter presents an introduction to the research subjects.

Detection of epileptiform waveforms

The studies on the detection of epileptiform waveforms presented in this thesis are based on quantitative analysis of the electroencephalogram (EEG). Epileptiform EEG activity is similar to that encountered in patients with epilepsy, but it may also occur in patients without diagnosed epilepsy. Continued epileptiform activity may result in brain damage and thus it should be avoided. Aside from patients suffering from epilepsy, epileptiform activity has been reported to occur during operating room (OR) anesthesia and during intensive care unit (ICU) treatment.

Anesthesia is described as a drug-induced loss of consciousness during which a patient is not arousable. Sevoflurane is among the drugs most commonly used to induce anesthesia. Its patient safety has been questioned as it has been reported to induce epileptiform EEG activity and epileptic symptoms such as convulsions. The avoidance of epileptiform activity and the related symptoms are the motivation for the studies of EEG during sevoflurane anesthesia in publications **E1** and **E2**.

In publication **E1**, the EEG registered from 60 subjects during sevoflurane anesthesia is studied. The different EEG waveforms, including epileptiform activity, were annotated by a clinical expert and a classification algorithm was developed to recognize the annotated waveforms. In publication **E2**, the connection between the inconsistent readings of BIS, the most popular commercially available depth-of-anesthesia index, and epileptiform EEG activity during sevoflurane anesthesia was established with the same study population as in publication **E1**. In addition, a novel EEG feature, wavelet subband entropy, was shown to indicate the occurrence epileptiform activity and the resulting falsely high BIS readings.

While the epileptiform activity during sevoflurane anesthesia is reversible and will disappear once the anesthesia is discontinued, the epileptiform activity encountered in ICU patients may not be reversible and may indicate poor patient

outcome. The epileptiform activity in ICU patients can be caused by a variety of reasons, such as ischemic brain damage and brain tumour. Because of their critical condition and heavy medication, patients in the ICU are often unresponsive and the traditional tests of neuronal recovery based on patient's responses to certain stimuli, cannot be applied. This typically long-lasting unclear situation is difficult for the next of kin and it may also lead to suboptimal use of the limited ICU resources. These are the motivations for the EEG-based prediction of outcome presented in publications **E3** and **E4**.

Publication **E3** presents the results of predicting the outcome of 20 ICU patients with a wavelet subband entropy algorithm developed originally in publications **E1** and **E2** for the detection of epileptiform activity. In publication **E4**, wavelet subband entropy, other quantitative EEG features, and conventional biochemical markers were examined to find out their associations with the patient outcome in a study of 30 ICU patients.

Recognition of physical activity

The recognition of physical activity presented in this thesis is primarily based on signals from body-worn acceleration sensors. The purpose of the activity recognition is to motivate people to perform more and a larger variety of physical exercise by giving them feedback about their daily share of activities. Activity counters, such as pedometers are simple examples of monitors of physical activity. However, activity counters are typically only able to monitor the duration of activity and not its type. There are at least six physiological aspects affected by physical activity: body shape, bone strength, muscular strength, skeletal flexibility, motor fitness, and metabolic fitness. In order to evaluate the overall effect of different activities on these aspects, more sophisticated information about the performed activities than that available by simple activity counters is needed. Wearable monitoring with activity recognition solutions could provide the required sophisticated information about the daily share of different activities and their benefits and thus promote a larger variety of physical exercise. This is the motivation of the studies reported in publications **A1**–**A3**.

In publication **A1**, activity data were collected from 16 subjects while they performed predefined tasks under supervision. A supervisor made notes about the true activity of the subjects. The recorded data were later analysed offline. Features were extracted and classification results for the detection of the different activities of the recordings were obtained. For publication **A2**, a new

data collection was performed that contained data from 12 subjects. The major part of the recordings was made without supervision. That is, the subjects were instructed to make their own notes about their activities. Similar offline analysis as in publication **A1** was performed. In publication **A3**, the results of converting the existing offline analysis methods into an online activity classification system are presented. The performance of the system was evaluated with 3 subjects.

This thesis is organized as follows: Chapter 2 describes the signal processing concepts most important for the understanding of the thesis. Also the two biosignals considered in the publications, EEG and body accelerometry, are considered. Chapter 3 summarises the objectives of the publications. In Chapter 4, the outlines of the publications are briefly described. Chapter 5 presents the results of the publications. In Chapter 6, the implications of the results are discussed, and Chapter 7 draws the final conclusions on the results.

2. Background and review of literature

Before the classification of obtained biosignals can take place, two signal processing steps are typically needed: 1) signal preprocessing; and 2) feature extraction. In the preprocessing step, the signals are prepared for further processing. This step may include, for example, filtering out unnecessary frequencies, artefact rejection, signal resampling and scaling, and signal transformations. Feature extraction is often the most crucial step in a successful biosignal algorithm. Here the expert knowledge on the signal properties is utilized in extracting such features from the signals which are dependent on those attributes of the subject that need to be recognized. The methods used in feature extraction are highly dependent on the signal processing problem at hand. However, they can often be divided into those obtained directly from the time domain signal and those obtained from the frequency domain transforms of the signal. In the following classification step, algorithms are trained to assign correct classes to the data based on the input features. Classification algorithms are usually not dependent on any particular problem and the same algorithms can be utilized in a variety of different research fields.

This chapter presents the essential biosignal processing methods needed for the understanding of the studies included in this thesis:

- Wavelet decomposition, a signal preprocessing step applied in publications **E1**–**E4**.
- Wavelet entropy, a feature extraction step applied in publications **E1**–**E4**
- Spectral entropy, a feature extraction step applied in publications **A1**–**A3** and **E4**.
- Decision tree, a classification step applied in publications **A1**–**A3** and **E1**.

Also the analyses of the two most important biosignals considered in this thesis are described and the state of the art in the related literature is reviewed:

- Analysis of electroencephalogram (publications **E1**–**E4**).
- Analysis of body accelerometry (publications **A1**–**A3**).

2.1 Wavelet transform and decomposition

A traditional tool for the analysis of the frequency content of biosignals is the Fourier transform. However, the problem with the Fourier transform is that it provides poor time resolution, i.e., it does not describe the location of the frequency components in time. To improve the time resolution of Fourier transform, a windowed version called short-term Fourier transform (STFT) is often used in biomedical signal processing. In STFT, the signal is divided into segments and the Fourier transform is applied to each segment thus enabling a more accurate description of the time of occurrence of different frequency domain phenomena. However, the cost is that the frequency resolution of the transform will be less accurate. Based on Heisenberg's uncertainty principle, there is always a trade-off between the accuracies of the time resolution and frequency resolution. The wavelet transform is an analysis tool which can specify the time and frequency resolutions optimally for a given application domain. The wavelet transform W of a signal $x(t)$ is defined as a correlation between the signal and a wavelet atom Ψ:

$$W\{x(t)\} = \int_{-\infty}^{\infty} x(t) \frac{1}{\sqrt{s}} \psi\left(\frac{t-u}{s}\right) dt \tag{1}$$

where s is the scaling variable and u is the translation variable of the wavelet. These two variables of the wavelet transform govern the frequency and time localization of the wavelet atom. There are different wavelets that can be used and each of them has its distinct properties. Their common factor is that they all have their energy localized both in frequency and time domains. The Daubechies wavelets [Daubechies 1992] are among the most widely used ones for biomedical signal processing and they were also used in publications **E1**–**E4**.

In digital signal processing, signals are discrete and the Equation 1 cannot be applied there. However, a wavelet transform can also be defined for discrete signals and in digital signal processing it is commonly implemented as Fast

Wavelet Transform (FWT) first presented by Mallat [Mallat 1989]. Mallat noticed that only a limited number of scalings and translations was needed for wavelet decomposition with perfect reconstruction property. The FWT algorithm proceeds by filtering the signal *x(t)* into lowpass and highpass signals with a conjugate mirror filter pair *Lo_D* and *Hi_D*. Lowpass and highpass signals are downsampled by a factor of 2 to produce the output vectors of the decomposition step: detail coefficients d_1 and approximation coefficients a_1. The process of an individual decomposition step is depicted in Figure 1.

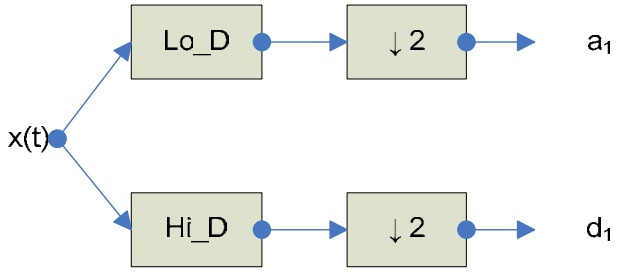

Figure 1. The first decomposition scale of the Fast Wavelet Transform (FWT). The signal x(t) is decomposed into highpass and lowpass signals with a conjugate mirror filter pair Lo_D and Hi_D. The outputs of the filters are decimated by a factor of 2 to obtain the detail coefficients d_1 and approximation coefficients a_1.

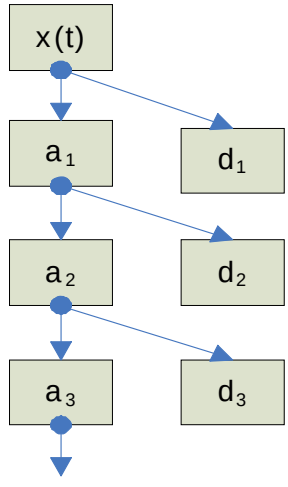

Figure 2. The decomposition scheme of FWT. The original signal x(t) is decomposed into approximation coefficients (a_1) and detail coefficients (d_1). a_1 are then decomposed further as if they were the original signal. This process can be continued until the resulting a_x is a single value.

The properties of the conjugate mirror filter pair are designed so that a perfect reconstruction of the original signal can be obtained from d_1 and a_1. To continue the decomposition, a_1 can be further decomposed similarly as it were the original signal. This process can be continued until the resulting a_j is a single value which cannot be decomposed further. The FWT decomposition tree with three decomposition steps is depicted in Figure 2.

The perfect reconstruction property of the FWT decomposition implies that all the information in the original signal is preserved in the decomposition coefficients. This is illustrated schematically in Figure 3 showing how the amplitude responses of the different decomposition scales fill the whole spectrum in the case of FWT with three decomposition steps.

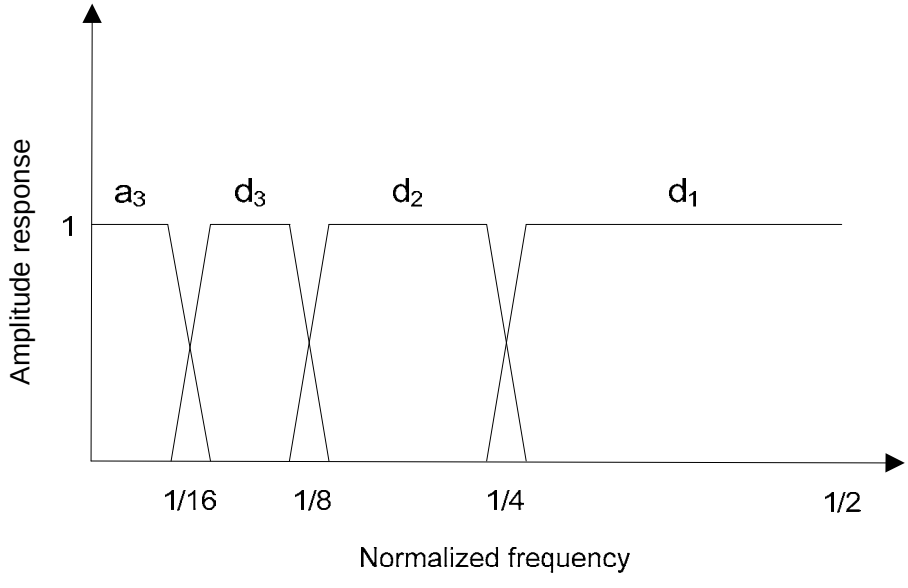

Figure 3. Schematic presentation of the amplitude responses of the FWT decomposition scales in the case of 3-level decomposition. Sampling frequency of the original signal is 1.

2.2 Wavelet entropy

Entropy is originally a thermodynamic concept which quantifies the disorder in a system. Influenced by this concept, Shannon defined in 1948 his information theoretic concept of entropy H of a random variable X as

$$H(X) = -\sum_{i=1}^{N} p(x_i) \log_2 p(x_i), \tag{2}$$

where x_i is a state of the variable, N is the number of the possible states and $p(x_i)$ is the probability of the state x_i in the process [Shannon 1948]. Since then, different versions of the entropy concept for digital signal processing have been introduced.

For wavelets, the entropy principle has been applied in different ways. A common way in EEG signal processing has been to calculate wavelet entropy H from the relative powers of wavelet decomposition details at different scales as:

$$H = -\sum_{j=1}^{\infty} \left(\frac{\sum_{k=1}^{N_j} \left| d_j(k) \right|^2}{\sum_{j=1}^{\infty} \sum_{k=1}^{N_j} \left| d_j(k) \right|^2} \right) \log_2 \left(\frac{\sum_{k=1}^{N_j} \left| d_j(k) \right|^2}{\sum_{j=1}^{\infty} \sum_{k=1}^{N_j} \left| d_j(k) \right|^2} \right) \tag{3}$$

where $d_j(k)$ is a detail coefficient of a decomposition scale j, and N_j is the number of detail coefficients in the time window for a particular scale [Al-Nashash et al. 2003, Al-Nashash & Thakor 2005, Rosso et al. 2001, Quiroga et al. 2001]. Equation 3 considers the wavelet decomposition scales as states of the system and calculates the entropy based on the distribution of the signal power over the decomposition scales.

In publications **E1**–**E4**, wavelet subband entropy (WSE) is defined for a decomposition scale j as

$$WSE_j = -\frac{\sum_{i=1}^{N_j} \hat{c}_j(i) \cdot \log \hat{c}_j(i)}{\log N_j}, \tag{4}$$

where N_j is the number of wavelet decomposition coefficients (either detail or approximation coefficients) for the given decomposition level j, and $\hat{c}$ represent the normalized versions of the original coefficients c:

$$\hat{c}_j(i) = \frac{c_j(i)^2}{\sum_{k=1}^{N_j} c_j(k)^2}. \quad (5)$$

It should be noted that the WSE defined in Equations 4 and 5 is strictly speaking not related to the original entropy concept as it does not operate on the probability distributions of the wavelet coefficients. Thus it does not describe the information content of the EEG signal. Instead, it provides a nonlinear transformation of the decomposition coefficients of a certain decomposition level into a scale [0, 1], which describes the variation in the energy distribution of the wavelet coefficients in the time window. Specifically, WSE of a single impulse on a flat background is 0 whereas WSE of a constant DC signal is 1. This is a desired property as sharp spikes, which cause rapid changes in the power of the EEG signal, are a common feature of the epileptiform activity. Figure 4 illustrates the performance of WSE with 5-second EEG samples with and without epileptiform activity. The more uneven energy distribution in the EEG sample with epileptiform activity results in a lower WSE value.

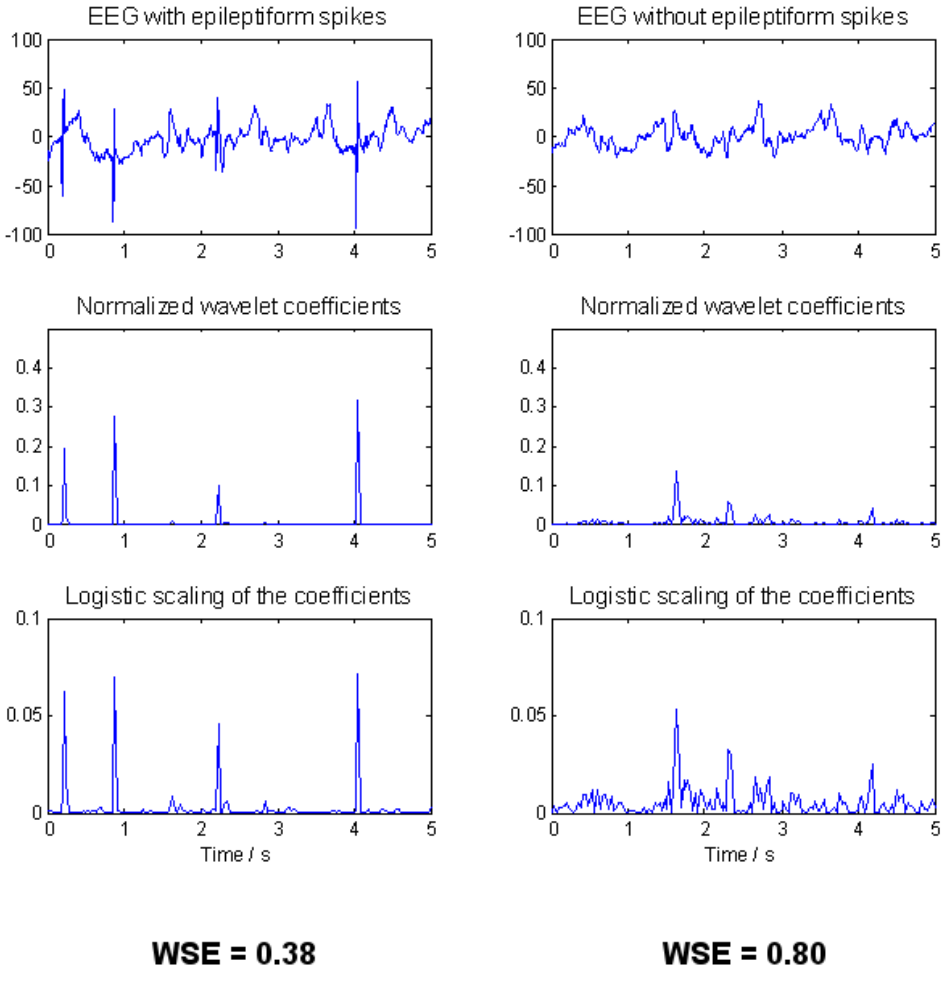

Figure 4. Illustration of the WSE algorithm. In the first row, two 5-second EEG samples are presented one with epileptiform activity and the other without epileptiform activity. The second row presents for both samples the normalized wavelet detail coefficients of the decomposition scale roughly corresponding to frequency band 16–32 Hz. The coefficients are normalized as indicated in Equation 5. The third row shows the normalized detail coefficients after the logistic scaling of Equation 4 before the final summation. The WSE values in the last row are obtained by the summation of the coefficients with the logistic scaling.

2.3 Spectral entropy

Spectral entropy is another form of applied entropy concept which was originally developed in optical signal processing in the 70's [Frieden 1972, Gordon & Herman 1971, Johnson & Shore 1984]. Since then, spectral entropy has been successfully applied in many fields of biomedical engineering including depth of anesthesia monitoring [Viertiö-Oja et al. 2004] and activity recognition [Bao & Intille 2004, Lester et al. 2006]. Although originally defined as the Fourier transform of the autocorrelation function, a simple estimate of power spectral density (PSD) function *P(f)* can be obtained from the squared absolute value of the discrete Fourier transform *X(f)* of a discrete signal *x(n)* as:

$$P(f) = \frac{1}{N} X(f) X^*(f) = \frac{1}{N} \left| X(f) \right|^2, \tag{6}$$

where N is the number of frequency coefficients in *X(f)*. Based on this definition of the PSD, spectral entropy *S* for a frequency band *[f1, f2]* is defined in publications **A2** and **A3** as

$$S(f_1, f_2) = \frac{-\sum_{f_i=f_1}^{f_2} P(f_i) \log(P(f_i))}{\log(N_{f_1,f_2})}, \tag{7}$$

where $p(f_i)$ represents the PSD value of the frequency component f_i. The PSD values are normalized so that their sum in the band *[f1, f2]* is one. $N_{f1, f2}$ is the number of frequency components in the corresponding band in PSD. In spectral entropy, the PSD is considered a probability distribution and its frequency components are considered states of the system.

2.4 Decision tree classifiers

Decision trees are classification and decision support tools which are characterized by their easy understandability, possibility to add expert knowledge, and intuitive graphical presentation [Breiman 1984].

Decision tree learning algorithms are popular in data mining and machine learning. In Figure 5, the basic concepts and structure of decision trees are presented.

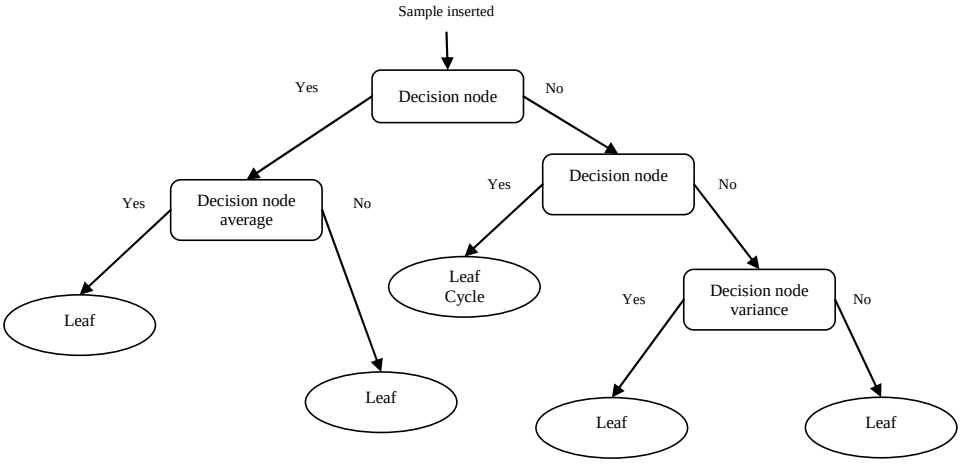

Figure 5. An exemplary structure of a binary decision tree. A classification result for a data sample input to the tree is defined outputs to sequential questions (e.g. comparison to a threshold) made in the decision nodes. The leaves represent the different classification results

The end nodes (leaves) of the tree represent the classification output classes and the decision nodes (branches) resemble the decisions that are made in order to reach the end node.

Classification decision trees are utilised in publications **A1**, **A2**, and **A3**. Decision trees can also be considered as descriptive tools for calculating conditional probabilities as done in publication **E1**.

The decision tree learning is an iterative task. The initial input data set is divided into subsets based on some criterion. These subsets are then further divided until the proper class division is reached. The most common version of decision trees is a binary tree where the initial set is always divided into two subsets in each decision.

The main question in classification decision tree learning is how to optimally divide the initial set into the subsets. The purpose of the commonly used division algorithms is to divide the original set into subsets which are as “pure” as possible. The purity can be characterized in many different ways. In publications **A1** and **A2**, The Gini impurity index has been utilized [Breiman 1984]. The iteration of a splitting algorithm finds a split that causes a maximal decrease in the impurity of the system (as compared to the impurity of the earlier node). The Gini impurity $I(n)$ for a node n is measured as

$$I(n) = \sum_{i \neq j} p(i \mid n)\, p(j \mid n), \tag{8}$$

where $p(i|n)$ and $p(j|n)$ are the conditional probabilities of the output states i and j of the node n. The best split threshold s_k using a feature vector x_k is the one maximizing the decrease in the impurity $\Delta I(s_k, N)$ of the system:

$$\Delta I(s_k, N) = I(N) - p_L I(N_L) - p_R I(N_R), \tag{9}$$

where the subscripts L and R refer to the left and right subnodes. The probabilities of p_L and p_R are given by

$$p_L = \frac{p(n_L)}{p(n)}, p_R = \frac{p(n_R)}{p(n)}. \tag{10}$$

Once the optimal split and the resulting decrease of impurity are found for a feature vector x_k, the same procedure is repeated for all features and only the one producing the largest decrease of impurity is used for this split.

Also a stopping criterion needs to be introduced to govern the splitting and growth of the tree. Naturally, the splitting can be stopped when the nodes are completely pure, i.e. all the samples in the node represent the same class, or alternatively when the node has identical feature values for each output class which does not allow for further splitting. However, this might lead to an overfitted classifier. Especially in biomedical signal processing, the data consist of desired information and additionally measurement noise, artefacts and intrasubject and intersubject variances in the measured features. The purpose of the classifier is to learn the desired information and not the undesired ones. To stop the splitting before overfitting can occur, several methods have been suggested:

1. Introducing a maximum depth of the tree. The depth is measured by the amount of sequential decisions in the tree (the height of the tree).
2. Introducing a minimum node size, meaning the amount of measurements arriving to a node must be larger than this size to allow further splitting.

3. Introducing a minimum child node size, meaning the amount of measurements in the subnodes resulting from a split must be larger than this size to allow the split to occur.
4. Introducing a minimum decrease of purity, meaning that the decrease of purity resulting from the split must be higher than this value to allow for the split to occur.

In addition to these stopping rules, there are effective post hoc rules for pruning the obtained tree to an optimal size. In publications **A1** and **A2**, a post hoc pruning of the tree was utilized. For this purpose, a crossvalidation procedure was used. The training data set was divided into 10 subsets with approximately equal sizes. In each crossvalidation cycle, 9 subsets were used for fitting the tree and the remaining subset was then tested with the obtained tree. The misclassifications of all 10 crossvalidation cycles were pooled together to obtain total misclassification cost for each pruning level of the tree. The smallest tree which had a misclassification cost within one standard error from the original, unpruned, tree was then chosen for the final result.

Decision tree learning with the Gini impurity index is a completely automatic process. However, a decision tree can also be built either completely or partly with the help of expert knowledge. In publications **A1**–**A3** and **E1**, there are decision tree structures that have been completely built based on expert knowledge. The possibility to easily embed *a priori* knowledge in the classifier was also the main motivation for the use of decision tree classifiers. In publications **A1**–**A3**, the structure of the decision tree was first designed based on expert knowledge. Then the features used in each decision node and the decision thresholds were manually adjusted based on the statistics of the data in the node. Specifically, the thresholds were selected so that they maximized the classification accuracy with the training data.

In publication **E1**, the decision tree scheme was used for the characterization of a conditional probability model. In that model, first the structure of the tree was designed based on expert knowledge about the problem. Then, logistic regression classifiers combining nonlinearly information from multiple features were assigned for each decision node of the tree. A logistic regression classifier with a sigmoid output provides an output between 0 and 1. These outputs were then considered as probabilities. For each sample to be classified, its probability of belonging to a particular class was calculated for all end nodes (leaves) n_i of the tree using the chain rule of conditional probabilities:

$$p(n_i) = p(n_i \cap n_{i-1} \cap \cdots \cap n_1) = p(n_i | n_{i-1} \cap \cdots \cap n_1) p(n_{i-1} | n_{i-2} \cap \cdots \cap n_1) \cdots p(n_2 | n_1) \cdot p(n_1), \quad (11)$$

where $p(n_i)$ represents the probability of arriving to a leaf node n_i and n_{i-1} … n_1 are the nodes through which the path leads to the node n_i. This approach is visualized in Figure 6 in the case of two decisions leading to the leaf node. In this approach, the conditional probability $p(n_i)$ was calculated for every end node and the end node with the highest probability was chosen to be the output of the classifier for the particular input sample.

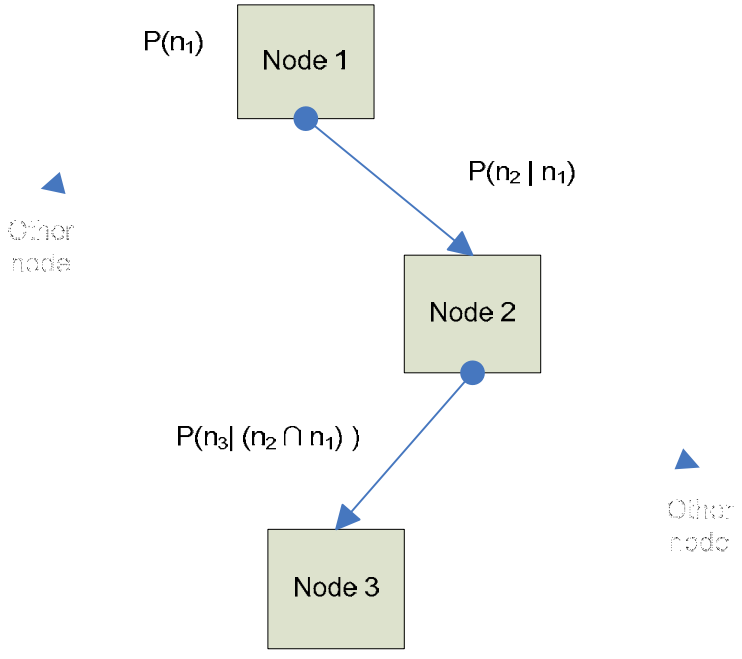

Figure 6. Visualization of the conditional probability model with a decision tree.

The utilization of a tree-structured classifier in publication **E1** was motivated by the ability to easily adjust the classification accuracies of individual classes and intuitively understand the concequences of the adjustments. For example, adjusting the nonlinear regression classifier of a particular node only affects the classification results of the classes that are considered in the latter nodes.

Improving the sensitivity of a particular detection decreases the classification accuracy of the latter nodes as more of the samples truly belonging to the classes detected in these latter nodes are wrongly assigned to the earlier class because of the adjusted threshold. However, the classification results of the classes that were detected earlier in the tree stay the same.

2.5 Analysis of the electroencephalogram

The electroencephalogram (EEG) is a biosignal representing the electrical activity of the brain. Specifically, it mostly represents the electrical activity of the outer layer of the brain, the cortex. EEG is measured as a potential difference (voltage) between two electrodes placed on the scalp. The potential in the measurement area under each electrode is defined by the extent of cortical activity beneath the electrode location. It is estimated that it requires approximately 5 cm^2 area of activation on the cortex for a visible activation on the EEG [Partanen & Cheour 2006]. An area of this size corresponds to an activation of 10000–100000 neurons simultaneously. The electrodes are most commonly placed on the scalp following the 10–20 system recommended by the International Federation of Societies for Electroencephalography and Clinical Neurophysiology [Klem et al. 1999, Jasper 1958]. The 10–20 system specifies the electrode locations by defining relative distances between anatomical landmarks: nasion, inion, and mastoids. This way, the EEG recordings from different subjects are made comparable. EEG signal, when compared to other bioelectric signals, is characterized by its low amplitude which is typically in the order of 100 μV. EEG does not have the same cyclostationary structure that some other biosignals (e.g. ECG) have. Healthy EEG in awake subjects can be modelled as a stochastic process [Stam et al. 1999]. Pathological phenomena such as epileptic seizures can introduce nonlinearities in the EEG [Pijn et al. 1991, Burioka et al. 2005, Ferri et al. 2001]. EEG has also been characterized as a nearly random signal with chaotic properties [Pijn et al. 1991]. Four channels of simultaneously recorded EEG from a healthy subject are shown in Figure 7.

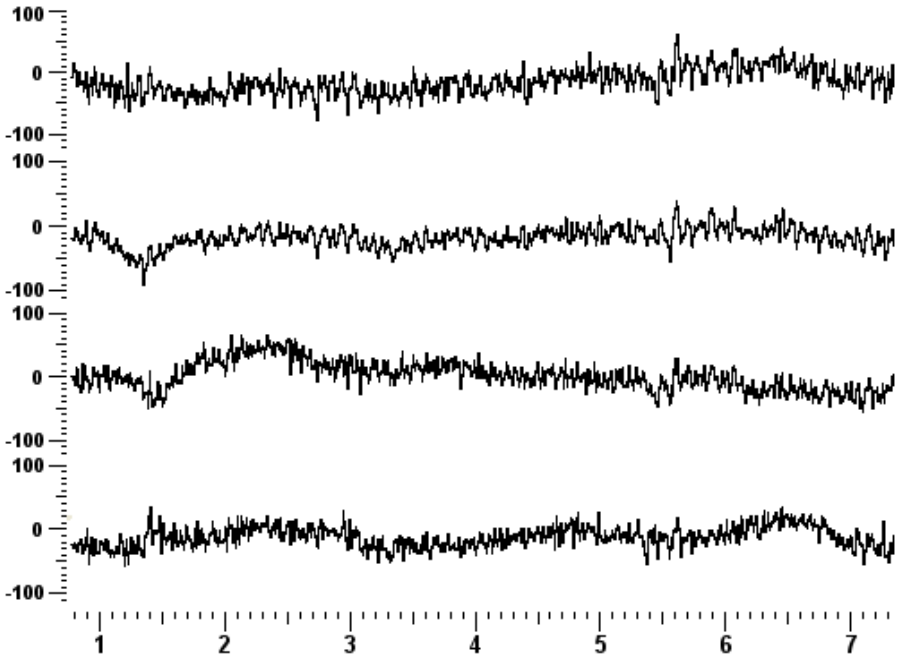

Figure 7. Four simultaneously recorded channels of healthy EEG. The horizontal axis is time in seconds. The vertical axes are μV. The sampling frequency is 128 Hz.

The clinical use of EEG is mostly based on qualitative analysis performed by a clinical specialist, a neurophysiologist. When the content of EEG is quantitatively described, the description is traditionally based on the dominance of certain frequency bands in the signal: Delta band below 4 Hz; Theta band from 4 to 8 Hz; Alpha bands from 8 to 13 Hz; and Beta band above 13 Hz [Partanen & Cheour 2006, Fisch & Spehlmann 1991]. These rhythms are assumed to reflect the internal processes of the brain as different rhythms are observed under different situations. Factors affecting EEG frequency content include vigilance level, aging, diseases and medications.

Whereas qualitative analysis by clinical experts describes the EEG characteristics as words, quantitative analysis describes them as numbers. Quantitative EEG analyses are practically always performed by computer programs with digital signal processing. The sampling frequencies used in quantitative EEG processing are recommended to be more than 200 Hz [Nuwer et al. 1998] as the information content of EEG is traditionally assumed to reside approximately between 0.5 Hz and 100 Hz, although definitions vary slightly

[Partanen & Cheour 2006, Sanei & Chambers 2007]. There is also increasing interest to analyse frequencies outside this band [Vanhatalo et al. 2004, Vanhatalo et al. 2005, Bragin et al. 2002] -largely due to the improvements in the measurement technology enabling the acquisition of very low and very high frequencies.

2.5.1 Epileptiform EEG and seizures and their monitoring

Epilepsy is a a disease of the brain caused by spontaneous, intermittent and abnormal electric burst activity in the brain [Partanen & Cheour 2006]. Epileptiform EEG activity refers to waveforms which resemble those encountered in patients with epilepsy. However, subjects having temporarily epileptiform EEG do not necessarily have epilepsy. An epileptic seizure lasting more than 30 minutes is called status epilepticus (SE) – a persistent state of epileptic seizure. SE is a life-threathening condition as the mortality rate of SE patients within 30 days after the end of the seizure is on average 20% [DeLorenzo et al. 1995, Eriksson & Koivikko 1997]. An example of epileptiform EEG is presented in Figure 8.

The automatic detection of epileptic characteristics is arguably the most studied research topic of clinical quantitative EEG. The first algorithms were suggested in the 70's [Gotman & Gloor 1976, Babb et al. 1974, Ives et al. 1974]. Since then, the topic has been under constant interest mainly because of the unsatisfactory reliability of the presented methods for clinical use. The constantly increasing computation power of microprocessors is enabling the research and utilization of more complex algorithms for the detection of epileptic seizures.

Traditionally, the detection algorithms for epileptiform activity have been classified to be either mimetic (copying the rationale of a human expert), linear predictive (using signal processing techniques to distinguish transients from ongoing background activity) or template based (find events that match previously selected spikes) [Wilson & Emerson 2002]. However, this division is not applicable anymore since many recent algorithms combine multiple approaches and cannot be classified to these categories.

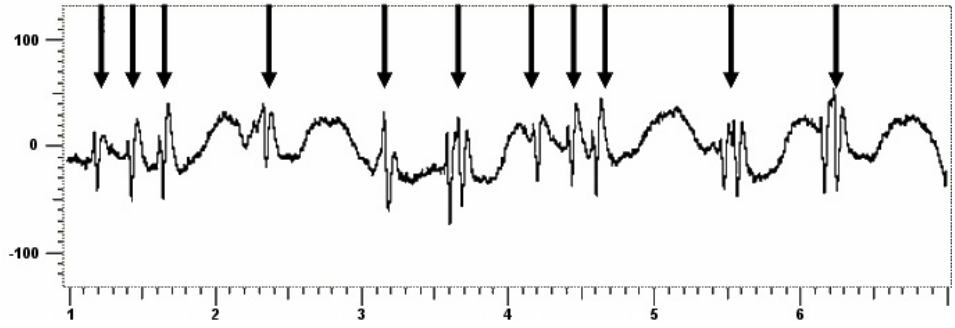

Figure 8. An example of epileptiform EEG. The epileptiform spikes in the sample are indicated by the arrows. The vertical axis represents the EEG amplitude in μV. The horizontal axis is time in seconds. The sampling frequency is 500 Hz.

Many of the algorithms for the detection of epileptiform activity are in practice designed to detect the epileptiform spikes in EEG. EEG spike in general is a triangular transient distinguishable from the rest of the EEG activity, often described as 'background activity' [Gloor 1975]. The estimation of the background activity is a fundamental first step in many of the detection algorithms for epileptiform EEG as the exact amplitude of an epileptiform spikes is usually less important than its amplitude relative to the background activity [Gotman 1982].

In the approach of Gotman and Gloor [Gotman & Gloor 1976], the background activity was defined as the average amplitude of the half-waves from the 5 seconds preceeding a potential spike. In the revised algorithm of Gotman [Gotman 1982] the background was defined similarly but the time window of calculation was from 28 seconds before the potential spike until 12 seconds after the spike. Guedes de Oliveira et al. [Guedes de Oliveira et al. 1983] used the standard deviation of the amplitude of the EEG and its first and second derivatives for the definition of background EEG level. Wilson et al. [Wilson et al. 1999] defined the background from the previous 5 seconds of EEG from curvatures and angles.

When considering the EEG feature extraction for the detection of epileptiform activity, there are two prominent categories of presented features: those based on half-wave decomposition and those based on wavelet transforms.

The half-wave approach was first used by Gotman and Gloor [Gotman & Gloor 1976]. In their work, the EEG signal is decomposed into halfwaves, which are lines connecting two consecutive extrema (minimum and maximum, or vice versa) of the EEG signal. These halfwaves generate waves that are then further

processed to extract features of relative amplitude, pseudoduration, relative sharpness and the duration of a third half-wave to describe a spike. The features are then normalised by dividing them by their corresponding background activity values. Other features extracted from the halfwave representation include, e.g., standard deviation of the halfwaves and their first and second derivates [Guedes de Oliveira et al. 1983], curvatures and angles [Wilson et al. 1999], and coefficient of variation [Saab & Gotman 2005, Khan & Gotman 2003].

In the recent publications on epileptiform EEG recognition, the interest has been shifted to the utilization of wavelet transforms. The use of wavelets may seem intuitive as many of them resemble epileptic spikes and the convolution of them with the EEG signal should be expected to produce good 'template matching' results.

Khan et al. [Khan & Gotman 2003] presented a partly wavelet-based method for seizure detection on intracranial EEG. 5-level wavelet decomposition was performed for the 100 Hz EEG signals. The features extracted from the detail coefficients included: 1) Energy as measured from the sum of the squared detail coefficients and normalized so that the sum of the energies from all decomposition levels equals one; 2) Coefficient of variation calculated by first applying the half-wave decomposition by Gotman [Gotman 1982]. The coefficient of variation was then obtained by dividing the variance of the amplitudes of the half-waves with the squared average of the amplitudes of the half-waves; 3) Relative amplitude, as defined by the mean of the half-wave amplitudes in the segment divided by the average amplitude from a time window from 35 to 20 seconds before the segment.

Saab and Gotman [Saab & Gotman 2005] applied a 5-level wavelet transform for 2 second epochs of 100 Hz EEG although coefficients only from scales 3–5 were utilized in features calculation. The features extracted from the detail coefficients were similar to those obtained by Khan and Gotman [Khan & Gotman 2003]. Bayesian rules were used in the classification procedure.

Goelz and co-workers apply continuous wavelet transform (CWT) to obtain a highly detailed time-frequency presentation of EEG which is also translation-invariant [Goelz et al. 2000]. This is achieved by using complex wavelets. They also consider the use of matching pursuit algorithm [Mallat & Zhang 1993] in the search for an optimal wavelet presentation of an EEG signal.

Osorio and colleagues [Osorio et al. 1998] used Daubechies 4 wavelet as a bandpass filter whose output was utilized when changes in the EEG patterns were detected.

Besides half-wave and wavelet approaches, also other methods have been recently presented for the feature extraction of epileptiform activity. The Reveal algorithm by Wilson [Wilson et al. 2004] uses Gabor atoms instead to obtain a time-frequency presentation of the EEG for seizure detection. In the work by Navakatikyan and colleagues [Navakatikyan et al. 2006] a seizure detection algorithm is presented for neonates which calculates a moving average (MA) and then finds the intersection points of the MA output and the EEG signal and calculates features based on the intersections.

2.5.2 EEG activity during anesthesia and its monitoring

The EEG of healthy subjects in full awareness contains desynchronized, low voltage, high frequency patterns (alpha and beta waves) [Rampil 1998]. Depression of consciousness, caused by sleep, illness, or anesthesia, in general slows down the EEG rhythms as the synchrony of the neurons on the cortex is increased.

General anesthesia is described as a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. Anesthesia is mostly used in hospitals during surgical operations. Anesthetic drugs also depress many other physiological processes than just brain activity. Cessation of heart beating and breathing are among the risks associated with a too deep anesthesia. These are among the reasons for developing methods for the assessment of adequacy of anesthesia. The most straightforward way for the assessment has been to estimate the drug dosage in the body. However, it has been shown that EEG patterns can provide a better objective estimate on the adequacy of anesthesia than direct estimation from the drug dosage [Hoffman 1995, Schwilden et al. 1995] as there seems to be large patient-to-patient differences in the body sensitivities to anesthetic drugs.

The drugs used to induce anesthesia can be divided into intravenous (i.v.) drugs and volatile drugs (inhaled anesthetics). The EEG effects of drugs belonging to these groups are mostly similar, although each family of drugs has its own characteristic effects on the EEG. The most common changes in EEG in the order of increasing concentrations of anesthetics are: 1) Initial shift of the EEG power to higher bands (especially beta band); 2) Shift of the EEG power from higher to lower bands (delta and theta); 3) Alternating periods of slow EEG activity and EEG suppression 4) Complete EEG suppression. The EEG features of inhalational anaesthetics are generally less dramatic than with i.v. anaesthetics. All of these changes are reversible when the anesthesia is discontinued. The

complexity of this sequence of changes is a challenge for the EEG signal processing in anesthesia. [Binnie 2003]

Sevoflurane is an ultra-short-acting volatile anesthetic. Hemodynamic stability, fast onset and offset, and lack of respiratory irritation are some of its most important assets. Since its introduction to clinical practice in 1990, it has begun to replace many older anesthetic drugs in use. However, its use has also raised concern as it has been reported to generate epileptiform EEG activity [Woodforth et al. 1997, Vakkuri et al. 2001, Vakkuri et al. 2000, Yli-Hankala et al. 1999, Jääskeläinen et al. 2003]. The appearance of the epileptiform activity during sevoflurane anesthesia has been considered an alarming finding [Vakkuri et al. 2001, Hilty & Drummond 2000, Schultz et al. 2001] as also external epileptic symptoms similar to seizures have been reported [Yli-Hankala et al. 1999, Hilty & Drummond 2000, Adachi et al. 1992]. Prolonged epileptiform activity during anesthesia may result in ischemic brain damage the same way as the regular epileptic seizure and thus it should be avoided.

Total EEG power was the first EEG-based feature used in controlling the depth of anesthesia [Bickford 1950]. The traditional frequency band approach was also considered for the monitoring of depth of anesthesia but it was soon observed that the frequency band variables were not suitable features for the purpose because of the complexity of EEG waveform changes during deepening anesthesia and differences in the waveforms when different anesthetic drugs are used. Since then, more sophisticated EEG features for the monitoring of depth-of-anesthesia (DOA) have been investigated.

Bispectral Index (BIS) is the best-known index of DOA. The algorithm is proprietary and has not been completely published, although the main concept has been revealed [Rampil 1998]. The algorithm has been developed with exploratory data analysis meaning that a large data library was collected, a large number of features were extracted and the most important features correlating with the depth of anesthesia were identified and later implemented in the commercial solution. A nonlinear sigmoid mapping is used to map the value of the linear combination of the features to a scale between 0 to 100 which has then became the de facto standard scale for the DOA monitors. BIS calculates the bispectral index from 2 second EEG epochs. Other components of BIS include the detection of burst suppression waveform with 2 different algorithms and 2 ratios of spectral powers. BIS has been shown to decrease monotonously with increasing depth of anesthesia [Rampil 1998] and its values have been shown to correlate with the concentrations of hypnotic agents [Doi et al. 1997, Katoh et al.

2000, Lysakowski et al. 2001]. However, during stable and deep sevoflurane anesthesia, BIS has been reported to increase during epileptiform activity [Kaisti et al. 1999] or to fluctuate abnormally [Chinzei et al. 2004].

2.5.3 EEG activity during intensive care and its monitoring

Patients with the most life-threatening conditions are treated in hospital intensive care units (ICUs). The physiological processes of ICU patients are close to collapse and the patients often need support to their ventilation and blood circulation, for example. For monitoring the status of the physiological processes, many different biosignals need to be monitored. These include electrocardiogram (ECG), blood oxygen saturation, blood pressure, body temperature and blood markers.

The usefulness of EEG in the ICU is currently studied intensively for several reasons [Jordan 1999, Hirsch 2004]:

- EEG is sensitive to the most common causes of cerebral injury: hypoxia and ischemia. Brain tissue is often the first to suffer from reduced oxygen delivery which eventually may lead to a permanent brain damage. If the cerebral blood flow falls too low, it is indicated in the EEG as a suppression of the high frequency activity. If the ischeamia continues, the death of the brain cells is indicated by the decrease in the EEG amplitude finally leading to a complete EEG silence, which is a sign of brain death.
- EEG may detect neuronal recovery when the clinical examination cannot: Patients with suspected neuronal damage are often unresponsive because of sedation and possible neuromuscular blocking agents. Such patients cannot be tested with the traditional neurological tests requiring responsiveness [Teasdale & Jennett 1974]. So, their desired neurological recovery is difficult to assess. The neurological recovery is often visible in the EEG already before the return of the responsiveness as an increase in the amplitude, return of high frequency activity and temporal variability in the long-term EEG records.
- EEG is the best available method for detecting epileptiform activity: subclinical epileptic seizures (those that would remain unnoticed without EEG monitoring) seem to be common in ICU patients [Towne et al. 2000]. Prolonged epileptic seizure can lead to a permanent brain

damage and increased mortality [Wijdicks et al. 2006]. Continuous EEG monitoring is the only means to detect the subclinial seizures.

Because of the sedative medication needed by most of the ICU patients to relieve anxiety, the EEG content of ICU patients without neurological dysfunctions mainly consists of delta and theta waves. Malignant EEG waveforms encountered in comatose ICU patients include [Young et al. 1997]:

- Triphasic waves, a slow-wave pattern mostly associated with metabolic disorders.
- Burst-suppression, an EEG pattern with intermittent EEG suppression indicating reduced brain metabolism and possible death of neuronal cells if encountered in patients without affecting medication.
- Unreactive coma pattern, a waveform with stationary alpha or theta waves or spindles without temporal variability.
- Epileptiform activity, a waveform representing increased exitation.
- Complete suppression, sign of maximally reduced brain metabolism.

Epileptic seizures seem to be surprisingly common in ICU patients. In an EEG examination, 8% of comatose ICU patients were found to have SE without its external symptoms [Towne et al. 2000]. EEG analysis is a mandatory tool for the diagnosis of SE [Treiman et al. 1998]. However, long-term monitoring and review of EEG by a neurophysiologist in the ICU is not always possible due to the limited resources especially during night shifts and weekends.

The variety of malignant EEG patterns in ICU patients poses serious challenges on the design of EEG monitoring. EEG signal processing in the ICU is a novel research field and only a few signal processing applications have been presented.

In the study of Si et al [Si et al. 1998], a system for the EEG monitoring in the pediatric ICU is presented. Data were collected from 74 patients in the pediatric ICU with the purpose to generate an automatic system that would estimate the abnormality of the EEG similarly as a trained EEG expert does. The signal features calculated included 1) EEG amplitude from the past 5 minutes; 2) Asymmetry, as calculated by the logarithm of the ratio of band power in the left hemisphere divided by the band power in the right hemisphere; 3) Front/back differentiation as calculated by the logarithm of the ratio of band power in the posterior region divided by the band power in the anterior region.

They used fuzzy membership learning and neural networks to obtain the classification to seven classes reflecting the severity of the abnormality.

Agarwal et al. presented a method for compressing long-term EEG recordings into two pages [Agarwal et al. 1998]. The method breaks down the EEG into stationary segments and features are used to assign classes for the segments. The presented method is based on the finding that certain EEG patterns tend to cycle in a recurrent manner. The method uses the Nonlinear Energy Operator (NLEO) for the segmentation of the EEG [Agarwal & Gotman 2001]. Features used for the classification of the segments are: 1) average amplitude of the segment; 2) mean frequency of the segment; 3) frequency-weighted energy measure also obtained with the NLEO. For the clustering of the segments, an ad-hoc k-means clustering method was utilized. The target EEG classes for the classification were 7 classes representing the severity of the abnormality.

Many studies have tested BIS in ICU setting with conflicting results. The study by Shibata et al indicated that BIS could be used in the survival prognosis of ICU patients [Shibata et al. 2005]. Vivien et al found that BIS is useful in the assessment of brain death in ICU patients [Vivien et al. 2002]. However, for the assessment of sedation, BIS has been found both inappropriate [Nasraway et al. 2002] and appropriate [Simmons et al. 1999]. Frenzel et al. found that BIS is correlated with the assessment of sedation of only some ICU patients [Frenzel et al. 2002]. The further study by Vivien et al revealed that the existence of electromyographic activity increased the BIS values significantly [Vivien et al. 2003] in ICU patients. This finding supports the assumptions that BIS should not be applied for the monitoring of sedation in general ICU patients and algorithms specifically targeted at ICU monitoring are needed.

2.6 Analysis of physical activity

Physical activity is defined as behaviour that results in any movement contributing to the total energy expenditure of the human [Caspersen et al. 1985]. In the studies concerning the effects of physical activity on the human body, accurate quantitative measurements of the physical activity are needed.

A common way to estimate physical activity is self-reporting, i.e. the subjects complete questionnaires, interviews or surveys. In large epidemiological studies, self-observations have been the primary tool for the assessment of physical activity as they are practical, easy to use and they have low study cost. However, directly measuring physical activity by physiological monitoring or motion

sensors offers potential advantages over self-reporting by reducing bias resulting from the poor memory and overreporting and underreporting [Haskell & Kierman 2000].

Energy expenditure is the most studied measurable component associated with physical activity. Traditional methods for the measurement of energy expenditure include indirect calorimetry (usually meaning the estimation of energy expenditure by measuring respiratory gases) and doubly labelled water tests (measurement of the produced carbon dioxide related to the energy expenditure by laboratory analysis of body fluids). However, neither of these methods is suited for long-term recording of human activity outside a laboratory environment. Indirect calorimetry requires a gas mask to be worn by the subjects, which disturbs daily living. The doubly labelled water test on the other hand requires periodic sampling of body fluids.

For long-term unobtrusive monitoring of energy expenditure, heart rate monitors have been used. If individually calibrated, heart rate monitors can be used to measure the energy expenditure. The relation between heart rate and energy expenditure is roughly linear for high intensity activities. However, for low intensity activities the relation is not linear and an accurate estimation of the energy expenditure cannot be derived [Haskell & Kierman 2000]. Heart rate is also affected by other factors such as psychological stress which may cause bias in the measurements. Because of these problems, more sophisticated methods based on heart rate have been developed to overcome these limitations and the research on methods that do not require calibration is under constant research [Spurr et al. 1988, Rennie et al. 2001, Firstbeat 2007].

Other sensor types utilized in the analysis of physical activity include e.g. video recordings, floor sensors, and pedometers. The movement pattern specific for each activity can be recognized from a video signal that captures the subject from a distance [Haritaoglu et al. 2000, Uddin et al. 2008, Niu & Abdel-Mottaleb 2004]. Floor sensors can be used to detect the changes in the indoor location of the subject [Murakita et al. 2004, Rimminen et al. 2008]. Both video cameras and floor sensors only work in the locations where they have been installed. Pedometers are simple devices for the rough estimation of walking distance and also other activities involving steps. Many of them also provide estimates of the energy expenditure caused by the walking. However, there does not exist a gold standard calibration method for pedometers which makes them in general unsuitable for the estimation of energy expenditure [Kashiwazaki et al. 1986]. In addition, they only measure activities that involve footsteps and do

not properly estimate the energy expenditure during e.g. such activities as weightlifting or cycling.

There are dedicated wearable devices for the estimation of energy expenditure such as CSA, TriTrack-R3D, RT3, SenseWear Armband and Biotrainer-Pro (see [King et al. 2004] for comparison). These devices contain accelerometers as their main measurement component. In addition, they may contain other sensors such as those measuring the heat generated by the body.

Although most studies on the measurement of physical activity have concentrated on the estimation of energy expenditure, it cannot describe all the concequences of physical activity. An international consensus statement regarding physical activity, fitness, and health [Bouchard & Shephard 1994] identifies six areas affected by physiological effort: body shape, bone strength, muscular strength, skeletal flexibility, motor fitness, and metabolic fitness. All of these have their own distinct impact on an individual's general well-being, and thus, estimating energy expenditure alone is not sufficient in order to assess the overall impact of the physical activities on the individual's well-being. A more detailed analysis of physical effort can be obtained by activity recognition, i.e., by detecting the exact form of activity the subject is performing. For this type of more detailed activity analysis, wearable accelerometers are studied in this thesis.

2.6.1 Body accelerometry

Advances in sensor technology are making acceleration sensors, i.e. accelerometers, smaller, cheaper and less power consuming [Mathie et al. 2004]. Their feasibility for tracking human body motions has been shown on many occasions. Because of these factors, they have become popular in the research of wearable technology.

In this thesis, body accelerometry is defined to comprise the technology of measuring the motion of the human body with acceleration sensors worn on different parts of the body. Such sensors are called 'wearable'.

Accelerometers are defined as instruments that can measure acceleration forces that are affecting them. They can be sensitive to acceleration in only one direction, but the advanced accelerometers are nowadays able to measure all three dimensions simultaneously. Although there is a variety of mechanically and electronically different accelerometer types, they all utilise the same concept of a spring mass system [Mathie et al. 2004]. A mass is attached to a spring which holds the position of the mass constant when no force is applied to the mass. An applied force either stretches or compresses the spring. The

displacement of the spring or the mass is measured and scaled to represent the acceleration. Each measurement dimension needs a separate spring mass system.

Accelerometers are sensitive to forces caused by the movements of the sensor and to the gravitational force. Some accelerometers do not generate a DC-level output and thus do not reflect the contant gravitational force. However, such accelerometers are seldom used in the body accelerometry as the measurement of gravitation force has several benefits. The accelerometers can be calibrated and static body and limb positions can be detected with it.

Mathie et al. have identified three main purposes for ambulatory monitoring of body motion with accelerometers [Mathie et al. 2004]:

- Objective assessment of body movements. In these studies, typically features that characterize certain conditions and diseases are sought. Typical examples are studies for the assessment of gait.
- Monitoring of adverse events. In these studies, features that show rapid changes in the body status are used. Such rapid changes could include falls and epileptic seizures.
- Long-term monitoring in unsupervised free living. In this diverse cathegory, features that can monitor slowly changing trends in the behaviour of the subject are utilized. The monitoring solutions for activity recognition and for supporting independent living belong to this category.

Additionally, in the studies of sleep and circadian rhythm, actigraphy has been utilized [Ancoli-Israel et al. 2003]. Actigraphs are devices which are used to record the limb movements of the subject. They are usually placed on the wrist and their measurement is based on an accelerometer. The sleep/wake rhythm of the subject is detected based on the variations in the acceleration signal.

The positioning of accelerometers on the body depends on the targeted application. For example, leg movements have been studied with accelerometers attached to the thigh or ankle [Aminian et al. 1999], energy expenditure has been estimated with accelerometers placed close to the center of mass of the human body [Bouten et al. 1997] and Parkinson disease has been monitored with sensors placed on the wrist [Veltink et al. 1995] and on the center of mass [Sekine et al. 2002]. For advanced activity classification, sensors on more than one position are used [Bao & Intille 2004].

2.6.2 Body accelerometry in activity recognition

Although activity recognition in wide sense can be considered to include the recognition of all the actions performed by a subject, in this thesis activity recognition means the recognition of the form of physical activity (e.g. walking, running, sitting, etc.) of a human subject.

Wearable accelerometers are well-suited for activity recognition as they contain information about the frequency and intensity of movements as well as the body position. The intensity and frequency content of the body accelerometer signal is different for different activities. Running measured from the ankle produces acceleration peaks of the magnitude 8.1–12.0 g [Lafortune 1991, Woodward & Cunningham 1993]. Regular walking is reported to produce accelerations in the order of less than 1 g [Cappozzo 1982]. As the extreme case, acceleration of more than 80 g has been measured from the wrist of a baseball pitcher [Paradiso 2006]. An example of acceleration signal measured from the ankle during walking is shown in Figure 9.

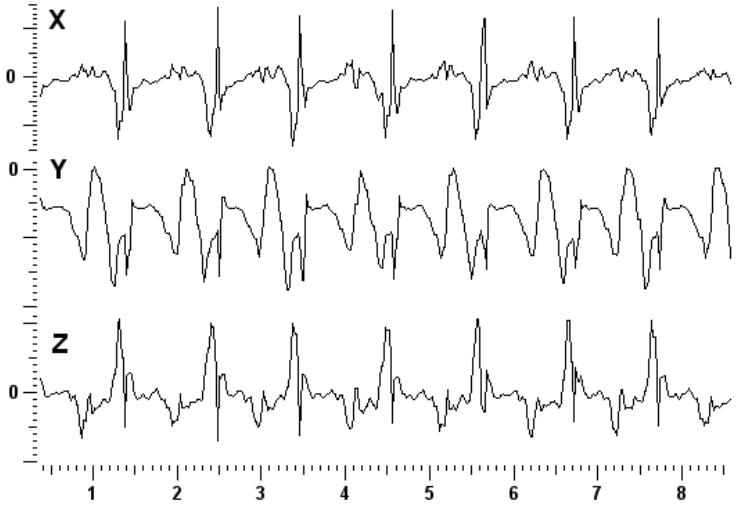

Figure 9. Acceleration signal measured from the ankle during walking. The three dimensions of the sensor are shown separately (X shows acceleration in the left-right direction, Y in the vertical direction, and Z in the back-forth direction). The gravitational force is visible in Y as a negative DC component in the signal. The vertical axes are arbitrary units. The horizontal axis is time in seconds. The sampling frequency of the signals is 50 Hz.

For multiclass activity recognition with wearable sensors, a multisensor approach is commonly used. Accelerometers are often placed on the hip [Bao & Intille 2004], waist [Mathie et al. 2003], chest [Aminian et al. 1999, Foerster et al. 1999], arm [Bao & Intille 2004], ankle [Bao & Intille 2004] and thigh [Bao & Intille 2004, Aminian et al. 1999, Foerster et al. 1999]. Although multisensor approaches undoubtedly produce better results, they may not be feasible in commercial applications. For that reason, Lester et al have introduced an activity recognition system with just one accelerometer sensor unit [Lester et al. 2006, Lester et al. 2005] that can be placed on different parts of the body depending on the situation.

The most important frequency band for the monitoring of daily activities is considered to be 0.3–3.5 Hz [Sun & Hill 1993]. Bouten et al. gave a rule of thumb that for the monitoring of daily activities accelerometers should be able to measure ±12 g and their frequency range should be 0–20 Hz [Bouten et al. 1997].

The three-step signal processing approach of preprocessing, feature extraction and classification is commonly performed in activity recognition from the body accelerometry. Typically, acceleration signal features are calculated with sliding time windows and with features assuming piecewise stationarity within the time windows.

The time domain signal features of activity recognition from body accelerometry typically include:

- signal magnitude (area under the 3D acceleration magnitude curve) [Mathie et al. 2003, Mathie et al. 2004, Karantonis et al. 2006];
- rectified averaged AC values [Foerster & Fahrenberg 2000];
- first and second moments (average, variance, energy) [Bao & Intille 2004, Lester et al. 2006]. Standard deviation, which is a derivate of the second moment, is also used [Lee & Mase 2002];
- correlations between acceleration signals from different locations [Bao & Intille 2004];
- median and absolute deviation [Aminian et al. 1999].

The frequency domain signal features include:

- frequency domain entropy [Bao & Intille 2004, Lester et al. 2006] ;
- power in certain frequency bands [Lester et al. 2006, Foerster et al. 1999, Foerster & Fahrenberg 2000].

Additionally, wavelet-based approaches have been suggested that cannot be classified belonging either to time-domain or frequency-domain categories [Sekine et al. 2002, Sekine et al. 2000].

The classification methods used in the activity recognition are fairly simple starting from the most simple case of fixed thresholds [Aminian et al. 1999, Mathie et al. 2003]. Other methods include decision tables, nearest-neighbour classification, Bayesian models, and decision trees [Bao & Intille 2004]. Clustering approaches have also been utilised [Foerster et al. 1999]. For modelling the temporal connections between different activities, Hidden Markov Models (HMM) have been popular [Lester et al. 2006]

The most recognized commercial solution to activity recognition is the Intelligent Device for Energy Expenditure and Activity (IDEEA) [Zhang et al. 2003]. IDEEA has been tested with 32 types of physical activity and validated with 76 subjects. The activity types detected by IDEEA include sitting, standing, lying, running, walking, cycling, jumping, stair ascending and descending, and different transitions, among others. The usability of IDEEA is limited by the fact that it comprises 5 wired sensors attached to the chest, thighs and feet. Thus, the system is not suitable as a consumer product and is primarily targeted at professional use.

3. Objectives of the thesis

The general objective was to present methods and their results for the classification of signals originating from the human body. The following describes in detail the research problems of the two study entities included in this thesis.

3.1 Detection of epileptiform waveforms

The objective of the studies **E1**–**E2** was to develop and validate algorithms for the classification of EEG waveforms encountered during sevoflurane anesthesia with special interest on the epileptiform EEG activity. The objective of the studies **E3**–**E4** was to validate the algorithms developed for the detection of epileptiform EEG activity in ICU setting for the prediction of patient outcome.

3.2 Recognition of physical activity

The objective of studies **A1**–**A3** was to develop and validate practical algorithms for the classification of daily activities and sports primarily based on signals from wearable accelerometers.

4. Study outlines

4.1 Detection of epileptiform waveforms

In publications **E1** and **E2**, the same dataset was studied, which consisted of EEG recorded from 60 patients undergoing elective surgery. The data were pooled from two earlier published studies [Vakkuri et al. 2000, Yli-Hankala et al. 1999]. The patients received sevoflurane anesthesia during the recordings. The EEG was obtained from the following electrode pairs: Fp1-A1, Fp2-A2, Fpz-F7, and Fpz-F8. The sampling frequency of the EEG was 128 Hz. In addition, BIS depth-of-anesthesia index was recorded with a designated monitor. To obtain a reference for the algorithm development, a neurophysiologist classified the EEG waveforms encountered in the recordings.

In publication **E1**, a large variety of features was extracted from 5 second EEG segments. The extracted features are listed in Table 1.

Table 1. EEG features extracted in publication **E1**.

Time domain features
Mean amplitude
Median amplitude
Root mean square amplitude
Peak-to-peak amplitude
Features from wavelet decomposition
Standard deviation of coefficients
Skewness of coefficients
Kurtosis of coefficients
Wavelet subband entropy
Frequency domain features
Spectral peak power
Spectral peak frequency
Spectral edge frequency 95%
Spectral edge frequency 50%
Spectral entropy
Power (8.2- 20 Hz) / Power(1.0-8.0 Hz)
Spectral entropies, relative powers, and absolute powers of the bands 1.0–3.8 Hz, 4.0–8.0 Hz, 8.2–13.0 Hz, 13.2–20.0 Hz, 20.2–47.0 Hz, and 1.0–50.0 Hz

For classification, a probabilistic decision tree model was used. The structure of the tree was designed based on the *a priori* knowledge of the different waveforms and their clinical meaning. The data were divided into training (30 patients) and validation sets (30 patients). The features and the threshold values of the decision tree were optimized with the training data. The performance assessment results were obtained with the validation data.

After having identified the most promising features for the discrimination of EEG waveforms in publication **E1**, a more detailed analysis targeted on epileptiform activity was performed in publication **E2**. This time, only WSE was calculated from all the EEG channels based on 5-level wavelet decomposition. Sequential floating forward search was used for the feature selection [Pudil et al. 1994]. Two indexes were developed: one for the quantification of the slow monophasic component of EEG, which preceeded the epileptiform spikes, and one for the quantification of epileptiform spikes. For the development of the

algorithms, the data were similarly divided into training and validation data as in publication **E1**. The temporal evolutions of the developed indexes were compared to BIS readings to evaluate the potential of the indexes to detect the falsely high BIS readings during epileptiform activity.

In publication **E3**, EEG data obtained from 20 patients resuscitated after out-of-hospital cardiac arrest were studied. After arrival to the ICU, the patients were treated with a 24-hour hypothermia protocol. EEG recording was also started upon arrival. EEG was recorded from channels Fp1-At1, Fp2-At2, At1-A1, and At2-A2. The sampling frequency was 500 Hz which was downsampled to 128 Hz for further analyses. The recordings were made continuously until the patients were extubated, transferred to the ward, or when five days had passed since the cardiac arrest. The information about patient outcomes, meaning whether they survived after the treatment or not, was used as the reference in the analysis. WSE from the detail coefficients of the second decomposition scale roughly corresponding to frequency band 16–32 Hz was calculated for each 5-second EEG segment. In addition, the signal powers in the band 16–32 Hz and in band 1–60 Hz were obtained for reference purpose. For each hour of recorded EEG, the average values of each of the three features (WSE and the two band powers) were calculated and their distributions were examined to find out if they differed between the survivors and non-survivors.

In publication **E4**, the same data set as in publication **E3** was used with the extension of data from 10 more patients thus resulting in EEG data from 30 resuscitated cardiac arrest patients. For this study, the EEG signals were also analysed by a neurophysiologist for the following EEG characteristics: Continuity, suppression, burst suppression, discharges, spindles, myoclonia, and status epilepticus. The following EEG features were obtained: burst-suppression ratio (BSR), State Entropy (SE), Response Entropy (RE), and wavelet subband entropy (WSE). Statistical testing was performed to evaluate the dependencies between the EEG features compared to the outcome groups and EEG characteristics.

4.2 Recognition of physical activity

The activity data analysed in publication A1 was collected from 16 recruited volunteers. Altogether 22 signals from body-worn devices were collected. Accelerometers were placed on the wrist and chest. They had a sampling rate of 200 Hz for the chest and 40 Hz for the wrist sensor. The dynamic range of the

accelerometers was -2 g … 2 g. Altogether 31 hours of annotated activity data were collected and stored on a compact PC for later offline analysis. The test persons followed a predefined scenario of activities to perform. The scenario contained the following activity classes: 1) lying, 2) sitting/standing, 3) walking, 4) Nordic walking, 5) running, 6) rowing (with a rowing machine) and 7) cycling (with an exercise bike). The exact durations and locations of the activities were decided by the subjects. The duration of each measurement session was approximately 2 hours. The test person was accompanied by a supervisor who used a special program running on a PDA to mark the changes in activity for reference purposes. The time-domain features extracted from acceleration signals included mean, variance, median, skewness, kurtosis, 25% percentile and 75% percentile calculated using a sliding window. Frequency-domain features were spectral centroid, spectral spread, estimation of peak frequency, estimation of power of the peak frequency and signal power in different frequency bands. Both 4-second and 10-second windows were used in the feature calculation. The feature selection was done visually by comparing the distributions of the features between the target classes. For classification, two decision trees models and an artificial neural network (ANN) were applied. The classifiers were trained by using the feature signals as inputs and PDA annotations as targets. For all the three classifiers the classification results were acquired by leave-one-subject-out cross validation.

For publication **A2**, the study protocol was revised and a second data collection of activity data was performed. This time, 12 subjects were recruited. The duration of each measurement session was increased from 2 hours to around 6 hours. The activity classes in this study were: 1) lying; 2) sitting and standing; 3) walking; 4) running; 5) Nordic walking; 6) rowing with a rowing machine; 7) cycling with an exercise bike; 8) cycling with real bike; and 9) playing football. A major part of the recordings was performed without supervision and during that time, the subjects were allowed to carry on with their normal daily living. However, they used a PDA program to annotate their activities and locations. Acceleration signals were obtained from the wrist and hip with sampling frequency of 20 Hz and sensor output range of -10 g … 10 g. Time domain features extracted from the acceleration signals included mean, variance, median, skewness, kurtosis, 25% percentile, and 75% percentile. Frequency-domain features included the estimation of power of the frequency peak and signal power in different frequency bands. The performance of each feature was evaluated by the area under the receiver operator characteristic (ROC) curve.

Four different classifiers were used: two decision tree models, one artificial neural network and a hybrid model merging small neural networks into a decision tree structure. For all classifiers, results were acquired by leave-one-subject-out cross validation.

The purpose of the study reported in publication **A3** was to evaluate the performance of the online activity recognition software designed based on the offline results obtained in publications **A1** and **A2**. Three subjects were recruited. The subjects performed a set of predefined activities without predefined order: walking, running, lying, sitting, standing, and cycling with an exercise bike. They were instructed to perform at least 5 minutes of each of them. The acceleration signals were obtained from wireless sensors worn on the wrist, hip and ankle with sampling frequency of 50 Hz and output range of -10 g … 10 g. The extracted signal features included signal average, variance, frequency of the highest peak in the PSD, and spectral entropy. A decision tree model with fixed thresholds was used in the classification. The thresholds were derived from the earlier publications **A1** and **A2** and thus all the collected data could be used for the validation of the algorithms.

5. Results

5.1 Detection of epileptiform waveforms in anesthesia

In publication **E1**, a scheme for the classification of EEG waveforms encountered during sevoflurane anesthesia was presented. Particular interest was on the epileptiform activity which was manifested as periodic epileptiform discharges (PED) in this data. EEG was recorded from 60 patients during sevoflurane anesthesia. A neurophysiologist annotated the EEG data and a probabilistic decision tree was developed to detect these annotated classes. 48 signal features were extracted from the recorded EEG. The sensitivities and specificities of detecting different waveforms are presented in Table 2.

Table 2. Classification specificities and sensitivies for the detection of the different EEG waveforms encountered during sevoflurane anesthesia.

Waveform	**Specificity**	**Sensitivity**
Awake	69 %	96 %
Burst suppression	51 %	92 %
PED	**83 %**	**87 %**
Normal slow	86 %	64 %
Abnormal slow	65 %	80 %
Abnormal slow with spikes	54 %	84 %

The study in publication **E2** further exploited the results of publication **E1**. In publication **E1**, wavelet subband entropy (WSE) was recognized as the most important feature for the detection of epileptiform activity. In publication **E2**, WSE was studied in detail and used as an index to quantify the epileptiform activity of the EEG during sevoflurane anesthesia. In publication **E2**, it was

shown that WSE can be used to provide complementary information to BIS which can help the clinicians to recognize the falsely high BIS readings during epileptiform activity. Such false readings may compromise patient safety if the doses of anesthetic drugs are adjusted based on them. One of the key findings of publication **E2** is shown in Figure 10 which illustrates how the WSE values decrease when the epileptiform activity (PD, periodic discharges) becomes increasingly prominent. In addition, the inappropriate increase in the BIS values during PD is visible.

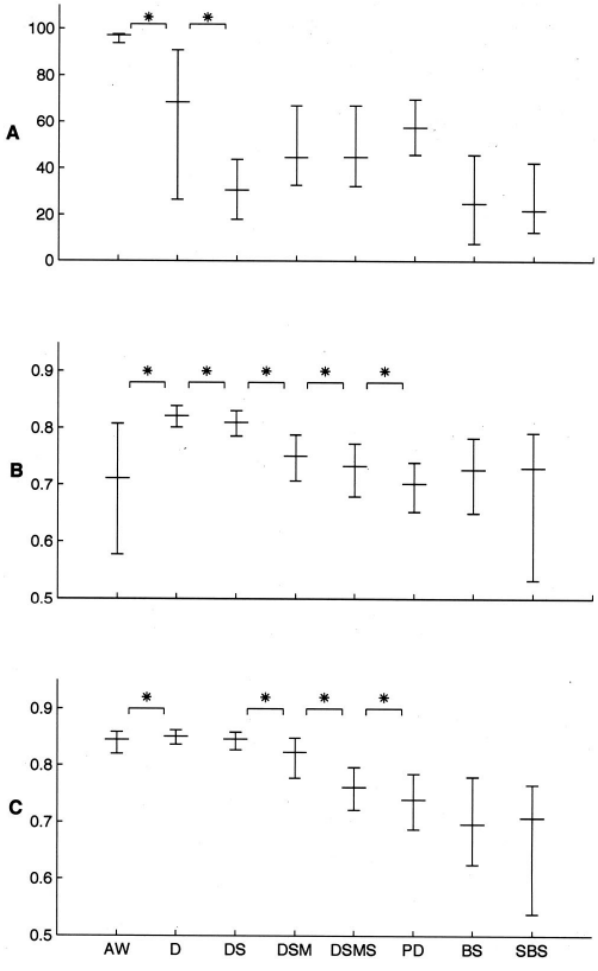

Figure 10. Median and quartile values of (A) Bispectral Index, (B) combined wavelet subband entropy 4–16 Hz, and (C) wavelet subband entropy 16–32 Hz for each electroencephalographic class: awake activity (AW); burst suppression (BS); delta activity (D); slow delta activity (DS); slow delta monophasic activity (DSM); slow delta monophasic activity with spikes (DSMS); periodic discharges (PD); burst suppression with spikes (SBS). The asterisks denote statistical significance ($P < 0.05$) between classes.

5.2 Detection of epileptiform waveforms in intensive care

In publication **E3**, the WSE concept was applied to ICU patients. The study population consisted of 20 patients resuscitated after an out-of-hospital cardiac arrest who were treated and monitored in the ICU. Afterwards, when the outcomes of the patients (survivor / non-survivor) were known, WSE was calculated from the recorded EEG and the average WSE value was obtained for each hour of each recording. The distributions of hourly average values of WSE of the outcome groups were then compared. A statistically significant difference was found between the distributions. The WSE distributions of the outcome groups are presented in Figure 11.

In publication **E3**, the research was continued and more EEG parameters were compared to the outcome of the patients in publication **E4**, where EEG derived features were found to be associated with the outcome of the patients already during the first 24 hours of the ICU treatment. Table 3 summarises the EEG findings of publication **E4**.

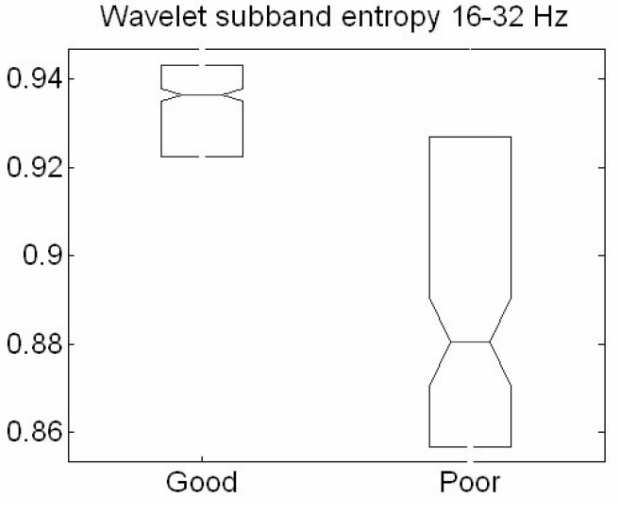

Figure 11. Distributions of WSE values for the outcome groups in publication E3.'Good' refers to WSE values from the survivors and 'poor' to those from the non-survivors. The lines inside the boxes indicate the locations the median values. The edges of the boxes are located at the 25th and 75th percentiles of the distributions.

Table 3. EEG findings in publication **E4**. The EEG parameters are studied in two time intervals, 0–24 hours and 24–48 hours after the arrival to the ICU. The EEG-parameters are WSE, BSR (burst-suppression ratio), RE (Response entropy), and SE (State entropy). The statistically significant differences ($p \leq 0.05$) between the outcome groups are printed in bold. The results are presented as medians and ranges.

0–24 h		**Good Outcome (n = 21)**	**Poor Outcome (n = 9)**
	WSE	0.84 (0.75–0.85)	0.83 (0.69–0.85)
	BSR	**18 (0–81)**	**65 (4–74)**
	RE	**20 (3–51)**	**10 (4–22)**
	SE	**19 (3–50)**	**9 (4–22)**
24–48 h			
	WSE	**0.84 (0.80–0.86)**	**0.82 (0.65–0.85)**
	BSR	**0 (0–17)**	**2 (0–26)**
	RE	67 (26–83)	55 (29–78)
	SE	58 (24–76)	46 (28–68)

5.3 Activity recognition in supervised conditions

In publication **A1**, 18 different quantities were collected with wearable sensors during recordings from 16 subjects. In the feature selection phase, accelerometers proved to be superior to signals from the other sensors for the discrimination of the recorded activities: lying, sitting/standing, walking, Nordic walking, running, rowing (with a rowing machine) and cycling (with an exercise bike).

As a result of the feature selection process, six features were selected for the classification process: 1) peak frequency of vertical chest acceleration, 2) median of vertical chest acceleration, 3) peak power of vertical chest acceleration, 4) variance of back-forth chest acceleration, 5) sum of variances of 3D wrist accelerations, 6) power ratio of frequency bands 1–1.5 Hz and 0.2–5 Hz measured from left-right magnetometer on chest. For classification, three classifiers were utilized:

- Custom decision tree which incorporates tree modelling with human domain knowledge and decision threshold selection based on statistical analyses
- Automatic decision tree which used Gini impurity index for the tree model generation and threshold selection

- Artificial neural network (multi-layer perceptron) which was used as a reference classifier.

The classification results for all three classifiers are summarized in Table 4. All results are obtained with leave-one-subject-out cross-validation (data from 4 subjects were excluded because of technical problems). The amount of classified data was approximately 31 hours.

Table 4. Summary of the classification results in publication **A1**. The values are percentages of correctly classified samples.

	Recognized activity		
Annotation	Custom decision tree	Automatic decision tree	Artificial neural network
Lie	**87**	83	74
Row	**69**	56	59
Exbike	79	**82**	75
Sit/Stand	**96**	95	**96**
Run	**97**	**97**	22
Nordic walk	**90**	72	52
Walk	58	78	**79**
TOTAL	82	**86**	82

5.4 Activity recognition in unsupervised conditions

For publication **A2**, a second, revised, round of data collection and analysis was performed. Whereas in publication **A1** activity data were collected under supervision, in this data collection the subjects were additionally instructed to collect and annotated recordings made without supervision.

For this data set, the following signal features were selected to be used in the classification phase: 1) peak frequency of the vertical acceleration measured from the hip; 2) range of the vertical acceleration measured from the hip; 3) mean value of the vertical acceleration measured from the hip; 4) peak frequency of the horizontal acceleration measured from the wrist; 5) sum of variances of 3D acceleration measured from the hip; 6) spectral entropy of the

vertical acceleration measured from the hip; 7) speed measured from the GPS device.

For classification, the same three classifier models as in publication **A1** were utilized and in addition also a hybrid model in which the simple threshold decisions of each decision node of the tree structure of the custom decision tree were replaced by a small neural networks.

Table 5. Summary of the classification results in publication **A2**. The values are percentages of correctly classified samples.

	Recognized activity			
Annotation	Custom decision tree	Automatic decision tree	Artificial neural network	Hybrid model
Lie	**98**	96	**98**	97
Row	58	84	85	**87**
Exbike	20	**79**	4	18
Sit/Stand	94	53	96	**97**
Run	**91**	83	90	89
Nordic walk	**85**	66	66	70
Walk	50	62	67	**71**
Football	63	55	47	**78**
Bike	52	**74**	67	72
TOTAL	83	60	87	**89**

The classification results for all three classifiers are summarized in Table 5. All results are obtained with leave-one-subject-out cross-validation. The amount of classified data was approximately 68 hours.

5.5 Online activity recognition

In publication **A3**, The calculation of the following features was implemented onto Windows Mobile environment running on the PDA: 1) signal average; 2) signal variance; 3) frequency of the highest peak in the PSD; 4) spectral entropy. All features were calculated from the accelerometer on the ankle.

As a proof-of-concept, activity data were collected from 3 subjects and consisted of 5 activity classes: lying, sitting & standing, walking, running, and

cycling. For classification, a simplified version of the custom decision tree model presented in publications **A1** and **A2** was implemented onto the PDA. The average classification accuracy for the three subjects was 94%. Confusion matrix of the classification results is presented in Table 6.

Table 6. A confusion matrix of the classification results in publication **A3**. The values are percentages.

	Recognized activity				
Annotation	Lie	Sit/Stand	Walk	Run	Cycle
Lie	**100**	0	0	0	0
Sit/Stand	0	**100**	0	0	0
Walk	0	2	**96**	0	2
Run	0	4	21	**75**	0
Cycle	0	4	0	0	**96**

6. Discussion

6.1 Accomplishment of the objectives

6.1.1 Detection of epileptiform waveforms

The objective of the studies **E1**–**E2** was to develop and validate an algorithm for the classification of EEG waveforms encountered during sevoflurane anesthesia with special interest on the epileptiform EEG activity.

The algorithm for the classification of EEG waveforms was successfully developed in publication **E1**. Publication **E2** then concentrated on the quantification of epileptiform activity. A successful quantification was obtained as the WSE values during different epileptiform waveforms and during the waveforms preceeding them were shown to be statistically different.

The objective of the studies **E3**–**E4** was to validate the algorithms developed for the detection of epileptiform EEG activity in ICU setting for the prediction of patient outcome. A statistically reliable prediction model could not be generated with the limited study population used. However, a statistical relationship between WSE and the patient outcome was established in publication **E3**. The results were extended in publication **E4** by showing a statistical relationship with a larger study population and by presenting preliminary classification results.

6.1.2 Recognition of physical activity

The objective of studies **A1**–**A3** was to develop and validate practical algorithms for the detection of daily activities and sports performed by the subject primarily based on signals from wearable accelerometers.

The objective was accomblished in publications **A1** and **A2**. The results of publication **A3** exceeded the original objectives with the developed online activity recognition system.

6.2 Impact of the publications in their research fields

Although the general changes in EEG during anesthesia are well-known, the exact characteristics of EEG during sevoflurane anesthesia, including epileptiform activity, have been described only lately [Vakkuri et al. 2001, Vakkuri et al. 2000, Yli-Hankala et al. 1999]. Publication **E1** is the first quantitative EEG study where the automatic classification of the epileptiform EEG waveforms in sevoflurane anesthesia is presented.

The inconsistent behaviour of BIS during sevoflurane anesthesia has been reported previously [Woodforth et al. 1997, Vakkuri et al. 2001, Vakkuri et al. 2000, Yli-Hankala et al. 1999, Jääskeläinen et al. 2003]. However, publication **E2** goes further by quantifying the BIS readings during epileptiform activity and showing their inconsistency when compared to the concentration of the anesthetic agent. In addition to presenting the inconsistency of BIS readings, publication **E2** introduces an EEG parameter, wavelet subband entropy (WSE), for the quantification of the epileptiform activity. The publication is unique, as no similar indexes for the quantification of epileptiform activity during anesthesia have been suggested in the literature. However, the problematic nature of epileptiform EEG activity is acknowledged and some DOA monitors claim to recognize it separately [Narcotrend 2005] to avoid misleading index values.

Publication **E3** showed that the index of epileptiform activity developed in publications **E1** and **E2** could provide information for the survival prognosis of ICU patients. Indirectly it also supports the assumption that epileptic seizures are common in resuscitated cardiac arrest ICU patients and are related to poor outcome.

The prognostic characteristics of different EEG findings are partly unclear as in the literature the findings have been merged into categories of malignant and being characteristics [Wijdicks et al. 2006]. In publication **E4**, the importance of epileptiform EEG activity in the prognosis was emphasized as all patients with status epilepticus (SE) died. In addition, WSE was shown to be significantly lower for the SE patients and also in general for the non-survivor group. The publication simultaneously studied EEG-derived features and blood markers for the prediction of patient outcome. One of the findings of publications **E4** was

that the EEG-derived features are associated with the patient outcome earlier than many traditional blood markers.

There are only a few studies which have considered activity recognition in out-of-lab or realistic laboratory settings [Bao & Intille 2004, Foerster et al. 1999, Uiterwaal et al. 1998]. To the author's knowledge, publications **A1** and **A2** are based on the largest out-of-lab data set collected and analysed for the activity recognition purposes. There is a larger variety of activities and ways to perform them real-life environment than in laboratory. This is shown to decrease the activity classification accuracy [Foerster et al. 1999]. However, publication **A2** demonstrated the robustness of the developed algorithms as the classification accuracy increased only slightly when the out-of-lab data was left out of the analysis. The recognition accuracies obtained in publications **A1** and **A2** are among the highest reported for such a multi-class activity recognition problem [Bao & Intille 2004, Preece et al. Accepted for publication].

The current challenge in the activity recognition research is to develop unobtrusive wearable solutions that could later become consumer products. Publication **A3** is among the few studies which have demonstrated practical solutions for daily activity recognition. Other similar works include [Lester et al. 2006, Karantonis et al. 2006].

6.3 Limitations of the studies

Publications **E1** and **E2** presented methods for the detection of epileptiform activity in sevoflurane anesthesia. In order to be implemented in DOA monitors, the algorithms should be tested also with EEG waveforms caused other anesthetic drugs to validate their specificity to the detection of the epileptiform activity.

Publications **E3** and **E4** consider the detection of epileptiform activity in the EEG of ICU patients. The number of different combinations of illnesses of the patients and drugs used in ICU is enormous and many of them have effects on the EEG waveforms. This limits the applicability of the results in publications **E3** and **E4** as they show the performance of quantitative EEG parameters for one particular patient population: patients resuscicated after cardiac arrest and treated with hypothermia and sedated with midazolam and fentanyl.

The original purpose in publication **E4** was to calculate the prediction powers of different quantitative EEG parameters for outcome prediction. However, it became later clear that the study population was too small for reporting prediction models and accuracies in clinical journals.

Reporting a prediction model based on a combination of EEG features and blood markers in publication **E4** would have been of great interest to many clinicians. However, the study population was too small for such purpose. The prediction analysis was limited to presenting preliminary results without details about the classification rules.

In publications **A1**–**A3** concerning activity recognition, altogether 31 data collections were performed. The applicability of the results of the publications is limited by the homogeneity of the subjects. In all of the studies, the average body mass index (BMI) of the study population was below 25 indicating that the study populations were on average normal weight. The users of health-promoting activity recognition systems however could be those with modest weight management problems. The presented activity recognition algorithms are not evaluated with such users.

The measurement range of accelerometers in publication **A1** was less than recommended [Bouten et al. 1997] and the same applies for the sampling frequency of the acceleration signal in publication **A2**. These limitations have influenced the results of the studies, which is considered in detail in the publications.

Considering the use of solely accelerometer-based algorithms for activity recognition, the results in publications **A1** and **A2** are of limited reliability in the sense that in both of them also information from other sensors has been used in obtaining the classification results: frequency band power of magnetometer signal in publication **A1** and speed measured from a GPS signal in publication **A2**.

6.4 Suggestions for further research

The research presented in publications **E1** and **E2** was targeted to a known problem in the existing DOA monitors – the falsely high readings during epileptiform activity. It should be tested that the developed algorithms do not react to non-epileptiform EEG waveforms encountered in anesthesia induced by other anesthetics. After such validation, the developed algorithm could be implemented to the DOA monitors.

The vast number of different illnesses, treatments and medications used in ICU patients pose a challenge to the further validation of the methods presented in publications **E3** and **E4**. Although all the different ICU patient groups cannot be tested, a larger validation study with heterogenic general ICU population could offer more information about the suitability of the algorithms for clinical practice.

In all of the activity recognition publications **A1**–**A3**, activity classification results have been calculated only based on the data in the corresponding time window. However, there are temporal connections between activities that could be utilized to improve the classification results. For example, it is unlikely that a subject would instantly change from lying to cycling without any other activity in between. On the other hand, changes from lying to standing or walking are pretty likely. Utilizing such a priori information could potentially improve the classification results.

6.5 General discussion

In the classification of biosignals, intrasubject and intersubject variability in the measured signals play an important role. Because of them, the classification accuracies of biosignal-based solutions need to be evaluated with large enough study populations. In addition, to demonstrate the general applicability of the presented algorithms, they must be validated with different data than those used for the design of the algorithms.

In the publications of the thesis, the following procedures have been performed to obtain unbiased performance assessment of the classification results:

1. **Collection of large, well-annotated data set from multiple subjects.** Although there are scientific ways of defining a large enough population for biosignal studies, such as power analysis, limited resources often set limits for the extent of data collection. In publications **A1** and **A2**, 21 hours of data from 16 subjects and 68 hours from 12 subjects, respectively, were collected. Both of these data collections are among the largest presented in the field of activity recognition. In publications **E1** and **E2**, 6 minutes of EEG were recorded from 60 subjects. In publication **E3**, 914 hours of EEG from 20 subjects were used in the analysis and for publication **E4** this was extended to 1290 hours from 30 subjects.
2. **Division of data so that no same data are used for the design and validation of the algorithms.** Data division is performed in publications **A1** and **A2** by a leave-one-subject-out cross-validation and in publications **E1** and **E2** by dividing the data into development and validation data sets both containing approximately half of the data. In publication **A3** all

data were considered validation data as the classification algorithm had been adapted from the earlier publications **A1** and **A2**. In publication **E3**, no classifications were made and no divisions were needed. In publication **E4**, the classification results presented were considered preliminary and no division was applied. It was stated in the publication that the classification model and rules used need to be validated in a separate study to prove their reliability.

7. Conclusions

In this thesis, an index for the quantification of epileptiform EEG activity was presented and statistical relationship between the index and annotated epileptiform activity was found both in general OR anesthesia and ICU treatment.

An offline activity recognition system was developed and validated. Also the first steps of developing it further into an online system were presented.

In both of these research problems concerning the classification of biosignals, solutions with state-of-the-art scientific results and true applicability were obtained.

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Title

Methods for the Classification of Biosignals Applied to the Detection of Epileptiform Waveforms and to the Recognition of Physical Activity

Abstract

Biosignals are such signals that quantify the physiological processes of a living organism. Classification of biosignals aims at inferring the physiological condition of the organism based on the biosignals obtained from it. In this thesis, the classifications of two biosignals originating from the human body are studied in detail: the electroencephalogram (EEG) and acceleration signals recorded from body-worn sensors (body accelerometry).

EEG quantifies the electrical activity of the brain. In this thesis, EEG recorded in hospital operating room and intensive care unit environments is classified to detect epileptiform brain activity which is a potentially brain-damaging phenomenon. Wavelet subband entropy of EEG is shown to be statistically associated with epileptiform activity both in operating room patients under sevoflurane-induced anesthesia and in intensive care unit patients resuscitated after cardiac arrest. The results support the hypothesis that epileptiform activity can be continuously monitored in both clinical settings.

Body accelerometry quantifies the movements of the human body with body-worn sensors. In this thesis, body accelerometry is classified for activity recognition purposes, i.e. the purpose is to detect the type of physical activity of the subject from the body acceleration signals. State-of-the-art offline classification results are obtained in two studies. In addition, conversion of the presented offline activity classification algorithms to an online version is demonstrated. The results confirm that multiple classes of daily physical activities and sports can be reliably recognized with body accelerometry.

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Nimeke

Menetelmiä biosignaalien luokitteluun sovellettuna epileptiformisten aaltojen havaitsemiseen ja fyysisen aktiviteetin tunnistamiseen

Tiivistelmä

Biosignaalit kuvaavat elävien organismien fysiologisia prosesseja. Biosignaalien luokittelun tavoitteena on päätellä organismin fysiologinen tila siitä kerättyjen biosignaalien avulla. Tässä väitöskirjassa tutkitaan kahden ihmisruumiista kerätyn biosignaalin luokittelua: aivosähkökäyrän (EEG:n) ja puettavista antureista kerätyn kiihtyvyyssignaalin.

EEG mittaa aivojen sähköistä aktiivisuutta. Tässä väitöskirjassa sairaalan leikkaussalissa ja teho-osastolla kerättyä EEG-signaalia luokitellaan epileptiformisen aivotoiminnan tunnistamiseksi, joka on mahdollisesti aivoja vaurioittava ilmiö. EEG-signaalista lasketun wavelet-hajotelman kaistan entropian osoitetaan olevan tilastollisesti riippuvainen epileptiformisesta aivotoiminnasta sekä leikkauspotilailla sevofluraanianestesiassa että sydänpysähdyksestä elvytetyillä tehohoitopotilailla. Tulokset tukevat olettamusta, että epileptiformista toimintaa voidaan tarkkailla molemmissa kliinisissä ympäristöissä.

Vartalon kiihtyvyysmittaukset puettavilla antureilla tuottavat biosignaaleja, jotka kuvaavat vartalon liikettä. Tässä väitöskirjassa näitä signaaleja luokitellaan, jotta henkilön fyysisen aktiviteetin tyyppi pystyttäisiin määrittelemään. Tieteellistä huippua edustavia luokittelutuloksia saavutetaan kahdessa tutkimuksessa. Lisäksi testattujen menetelmien soveltamista reaaliaikaiseen aktiviteetin tunnistamiseen havainnollistetaan. Tulokset vahvistavat, että monia päivittäisiä fyysisen aktiviteetin muotoja voidaan luotettavasti tunnistaa puettavista kiihtyvyysantureista saatavista signaaleista.

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