

EEG analysis for monitoring of anesthetic depth

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EEG Analysis for Monitoring of Anesthetic Depth

by
M. van de Velde
P.J.M. Cluitmans

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This report was submitted in partial fulfillment of the requirements for the degree of Master of Electrical Engineering at the Eindhoven University of Technology, Eindhoven, The Netherlands

The work was carried out from September 1990 until May 1991 under responsibility of Professor J.E.W. Beneken, Ph. D., at the Division of Medical Electrical Engineering, Eindhoven University of Technology, under supervision of P.J.M. Cluitmans, Ph. D.

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Abstract

The main subject in this report is "EEG analysis". For this purpose a new software application was developed that enables investigation of parameters derived from EEG signals and provides flexible spectrum evaluation of EEG data.

The work was carried out within a research project that aims at automatic assessment of "anesthetic depth" during surgical procedures. The project is mainly concerned with so called "auditory evoked potential" studies, and is now extended into the field of EEG analysis. Previous anesthesia research and the EEG data measured during recent studies were taken as starting points for this study.

The developed EEG analysis application was tested and evaluated through analysis of the data mentioned, and we may conclude that the program serves its purpose well. Investigated EEG parameters show correlations with anesthetic depth, although general applicable conclusions cannot be drawn.

Van de Velde, M. and P.J.M. Cluitmans

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1 Introduction

The purpose of the study "EEG analysis in anesthesia" is the extension of a method to measure the functioning of the central nervous system (CNS) of anesthetized persons undergoing a surgical procedure. For better understanding of the objective of the project a brief perspective on the subject and the framework of the research will be described below.

1.1 Monitoring In anesthesia

During surgical procedures anesthetics are being used all over the globe. This widespread use of anesthetic agents has grown simultaneously with the recognition of the need for patient monitoring during the state of narcosis. Already before 1850 the anesthetic properties of substances like ether and chloroform were discovered, and soon these drugs were introduced as anesthetics. The monitoring and registration of vital signs of patients however, began only in the second half of the 19th century, but ever since the registration of patient parameters is seen as a necessity and has been in constant development [Booij, 1989]. Nowadays, anesthesiologists monitor quite a few clinical parameters, amongst which especially the respiratory and circulatory functions are important. They also try to establish and maintain a certain "level" of anesthesia: the patient should not notice anything of the operation but also must not be too "deeply" anesthetized, for this may cause permanent physiological damage or a delayed recovery.

General anesthesia is divided into several stages in relation to clinical signs, from pre-operative stage, after a premedication is administered to the patient, to the maintenance stage of anesthesia. The levels of anesthesia are more difficult to recognize with the use of modern, balanced anesthesia techniques. These techniques use a combination of drugs each of which depresses one of the four components of anesthesia: either sensory block (analgesia), motor block (relaxation), reflex block or mental block (amnesia) [Booij, 1989]. The deduction of good conclusions about the influence of a specific anesthetic on the level of anesthesia can be complicated by the occurrence of side-effects caused by the drug, e.g. most analgesics also affect mental block.

The last three decades many investigators have reported the incidence of unnoticed awareness during surgery. This undesirable phenomenon may occur during any phase of an operation, although some special categories of surgery (where lower dosages of anesthetics are used) show a higher incidence of awareness or recall than other types of surgery (see for instance Blacher [1984], Bogetz et al. [1984] and Booij [1989]). Anesthetists may overlook such a state in a patient because of the lack of a simple means to assess depth of anesthesia, especially the state of awareness in a patient [Cluitmans, 1990]. The main approach to improve monitoring of anesthetic depth is neurophysiological monitoring. Research in this field is mainly concerned with electroencephalogram analysis and evoked potential studies:

- Electroencephalogram (EEG) analysis is the interpretation of brain waves recorded from the scalp by means of studying the raw EEG or by calculating EEG derivatives: e.g. frequency or power distribution, amplitude, correlations between recorded signals, etc. An important application of analysis of the electroencephalogram is the use of such techniques in operations where the flow of blood to the brain may be endangered; cerebral ischemia (insufficient bloodflow) and/or hypoxia (oxygen deficiency) may occur.
- In evoked potential (EP) studies a sensory organ of a patient is stimulated while recording the electroencephalogram. When multiple stimuli are given and the electrical activity is recorded after each stimulus, consistent potential changes can be recorded by averaging the responses, thus eliminating background activity. These potential changes, recorded as waveforms on the EEG, are very similar in all humans [Pryse-Phillips, 1989].

During the last ten or fifteen years, monitoring-research has grown considerably because of the new technological possibilities towards computerization in the operating room.

1.2 The Servo-anesthesia project

The division of Medical Electrical Engineering at the Eindhoven University of Technology initiated the project "Servo-anesthesia" to be able to contribute to research in patient monitoring, especially in supporting the task of the anesthesiologist. The goal of this project is to determine whether automation of narcosis in the operating room is feasible and useful, and if so, how this can be achieved.

1.2.1 Anesthetic depth research

One of the studies performed within the project is the research-program **Neurophysiological monitoring of anesthetic depth**. Till now, main interest has been in the study of the influence of anesthetics on auditory evoked potentials (AEPs) and the improvement of the method for measuring these signals from the auditory nervous pathway by applying both the conventional and a new, a non-linear analysis (NLA) EP technique, where random "trains" of impulses are used. A pilot study on cats and a clinical study with humans showed promising results for the future, and a broadening of the study was recommended, for this may improve the reliability and drug-independency of the technique [Cluitmans, 1990].

A data-acquisition system and a database system were developed as part of this study. The Event Recording and Data Acquisition system (ERDA) and the Electrophysiologic Monitoring DAtaBase System (EMDABS) enabled the research team to collect and store all relevant data during the operations where the evoked potential techniques were being applied [De Jong, 1986; Kuipers, 1991; Pfaffenhöfer et al., 1991]. Since the calculation (or "filtering") of evoked potentials from the EEG needs a large number of responses for averaging, one comes to think of the information that is not being used, i.e. the raw electroencephalogram. Research throughout the years has implicated the possible relational aspects of the EEG when referring to levels of anesthesia. When considering awareness however, publications are less clear; obviously the relation between "levels" and awareness during anesthesia is more difficult to establish. Research on a broad scientific basis also is handicapped by the differences in the usage of drugs and therefore by the different conclusions, in spite of the sometimes promising results.

The stored data enables us to process the raw EEGs that were measured during the studies, and thus provides for a combined study of auditory evoked potentials and EEG analysis. This report will concentrate on the latter subject: **EEG analysis for monitoring of anesthetic depth**, and especially on the development of a *means* to analyse EEG signals/parameters, in order to search for correlates with anesthetic depth.

A description of the EEG analysis tool is obtained after investigation of research in this field (chapter 2), and elaborated in general (chapter 3) and in mathematical detail (chapter 4). Testing of the tool through actually analyzing EEG signals is described in chapters 5 and 6. Conclusions from this research are presented in the final chapter 7.

1.2.2 A perspective on the project

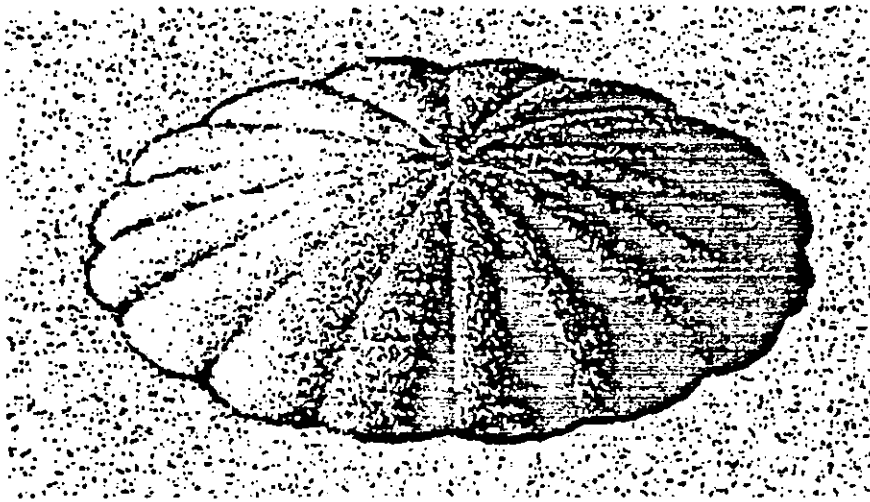
The "Monitoring of anesthetic depth" project, as part of the Servo-anesthesia project, will tend to increase in proportions, because of the complex matters involved. If parallel processing of the electroencephalogram and evoked potentials (esp. auditory EPs) can be accomplished, it will still be of importance to try to extract features relating to anesthetic depth automatically. Pattern recognition techniques may be used by applying artificial neural net models to the AEP complexes.

Another important factor is the improvement of signal validation and automatic detection and removal of artifacts. Already some algorithms are available [*Jansen, 1989*], but in the future reliable data acquisition must also be enabled during difficult conditions like electrosurgery [*Cluitmans, 1990; Pronk, 1986*].

The ultimate goal of the research is to make a closed loop system, which measures and interprets patient parameters and controls the administration of anesthetic agents. Many of the quality control steps performed manually today will be done automatically [*Levy et al., 1984*]. The incorporation of an adaptive control system can be seen as a major development, but the use of automatic control lies in the future [*Rampil et al., 1984*]. This can only be done by taking into account all factors influencing the EEG. Further research has to be carried out for documenting quantitatively the relevant relationships of the variables involved [*Pronk, 1986*]. The database system EMDABS will make this possible. When looking at the amount and sort of information to be processed for interpretation by such a control system, a tendency grows to think of an expert systems approach for the overall design of the anesthesia-monitoring system. The knowl-

edge and expert system toolbox developed in previous work in the "Servo-anesthesia" project may be used for this application [Van der Aa, 1990; Blom, 1990].

The use of EEG for peri-operative patient monitoring systems is thought of as having become a practical proposition with advances in technology for analysis and display. Many applications of EEG which were pioneered in the early years of EEG monitoring are re-evaluated [Pronk, 1986]. With technical problems solved, it should be possible to develop an objective, reliable system for intraoperative monitoring of the mental state of anesthetized persons [Cluitmans, 1990].



M.C. Escher: Detail of "Hol & Bol" ("Convex & Concave"), 1955

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2 EEG Monitoring in Anesthesia

This chapter first describes some basic considerations about the EEG and what mechanisms it reflects, and then summarizes some techniques that can be used to process the EEG. A review of general basic EEG research, as well as recent anesthesia research is presented in the third paragraph. An evaluation closes the chapter.

2.1 The electroencephalogram

The first recording of an electroencephalogram was made in 1929 by a German named Hans Berger. Since then a lot of researchers have investigated the value and usefulness of this visualized brain activity. In order to be able to measure the EEG uniformly a standard has been defined by the international 10-20 system which specifies the placement of 22 electrodes on the scalp [Spehlman, 1981]. The use of such numbers of electrodes however, is not convenient during surgery and will not help for a fast introduction in the operating room of any anesthesia monitor. For an application in the operation theatre like the monitoring-system the Servo-anesthesia project aims at, only a few electrodes should be necessary.

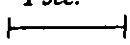


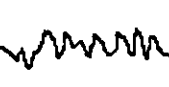
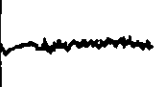
Spehlmann [1981] gives a simple but clear description of the EEG: „the source of the electroencephalogram are electrical potentials generated by nerve cells in the cerebral cortex in response to various kinds of input, including those from pacemakers of rhythmical activity in the depth of the brain. These fluctuating

potentials summate and penetrate to the scalp where they can be recorded as the scalp EEG".

The electrical activity of the cortical neurons is mainly dependent on their metabolism [Pronk, 1986] and, due to coherence, for some groups of neurons also on the mental state of a person; consider for instance a state of selective attention in hearing: the physiological signs in the attended channel (the *left* or *right* ear) can be shown to be larger [McCallum, 1989]. Measuring this neuronal activity thus provides a means for interpreting the metabolism of the brain and to some extent the level of arousal or attentiveness of a person. For example through concussion or anesthesia, the resulting reduction of the activity of the nervous system may lead to confusion or unconsciousness. Even then, it could still be possible for the senses to pass messages to the brain over the direct neural pathways. The brain is functioning through highly complex mechanisms of which only little activity is measured by scalp electrodes, and consequently only a small amount of information can be extracted from the EEG.

For convenience, some general patterns have been roughly classified in accordance with the frequency that is most clearly present in the EEG. This classification is indicated with greek symbols. When this frequency lies between 0 Hz and 4 Hz, the EEG is said to be of δ -rhythm, from 4 Hz to 8 Hz is called θ -rhythm, from 8 Hz to 12 Hz the term α -rhythm is used and from 12 Hz to about 30 Hz the rhythm is known as β -rhythm.

Table 2.1 Classification of EEG frequency ranges

signal 1 sec. 				
range (Hz)	0 - 4	4 - 8	8 - 12	12 - 30
class	δ	θ	α	β

In spite of difficult interpretation of recordings of brain waves, the EEG is considered to be a principal measure of the effect of anesthetics. A great advantage

of this approach to monitoring of anesthetic depth is its applicability with both inhaled and injected agents [Eger, 1984].

2.2 Analysis techniques

The most important automated analysis technique for processing the EEG is **spectral analysis**; i.e. the calculating of different frequency components of the EEG. This is usually done by Fourier analysis. The resulting spectrum can be displayed in several ways, of which the "compressed spectral array" (CSA) [Bickford *et al.*, 1972; Bickford *et al.*, 1973; Bickford, 1979] is most commonly used. This is a pictorial of EEG-frequencies, in which the EEG power spectrum of several electrode-channels is displayed semi-3-dimensional: spectra are put "behind" each other in chronological order, and placed in an array on display according to the electrode position (see figure 2.1). One disadvantage of the CSA may be the somewhat indistinct presentation of the time-axis, which may obscure the relation time versus power. This relation is restored in an alternative

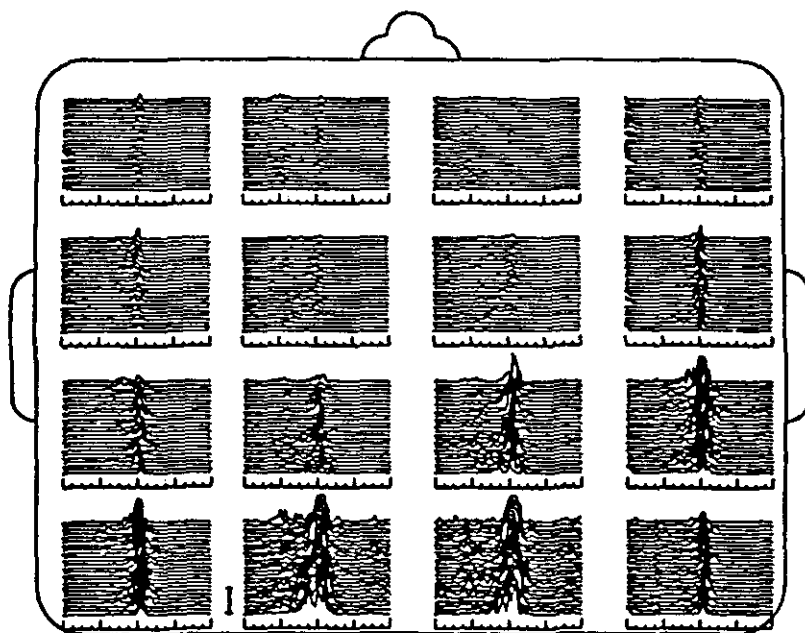


Figure 2.1 Example of a "Compressed Spectral Array"
(from Bickford [1979])

display (see figure 2.2): the density spectral array (DSA), where the relative power values are indicated with smaller or larger dots [Levy *et al.*, 1980].

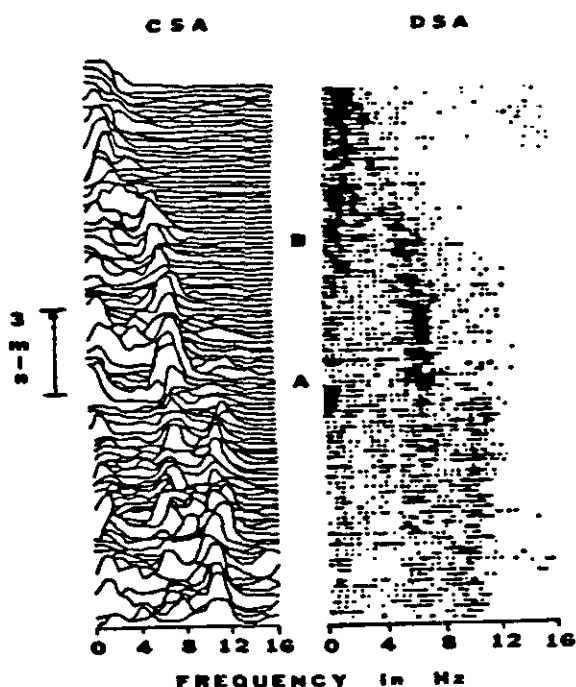


Figure 2.2 CSA and DSA display
(from Levy *et al.* [1980])

Several **characteristic frequencies** of the EEG spectrum have become known under specific names [Interspec Inc., 1985]:

- The *peak power frequency* (PPF).
This is the frequency of the largest power component.
- The *spectral edge frequency* (SEF).
The largest frequency at which still a significant amount of power is present is called SEF (below this frequency 97% of the total power is captured).
- The *median power frequency* (MPF).
This is the frequency at which 50% of the total power is contained in lower frequencies and 50% of the total power is contained in higher frequencies.

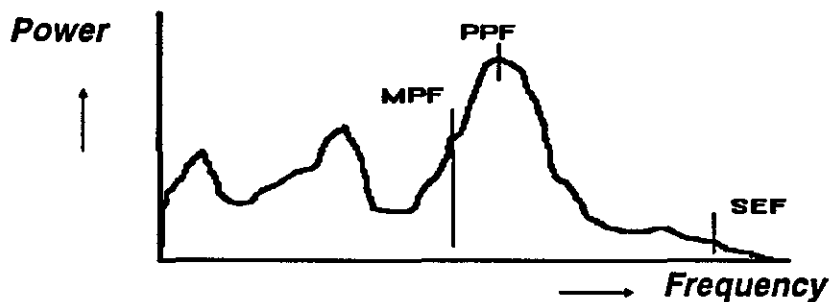


Figure 2.3 Characteristic frequencies

For the calculation of the Fourier transform, the sampling frequency, the filtering technique and length of time interval to be frequency transformed have great influence on the spectrum.

Quite another approach is given by the cerebral functioning analyzing monitor (CFAM) [Sebel *et al.*, 1983]. This device modifies the EEG further than conventional power calculation. Separately the frequency distribution and the amplitude distribution of two channels are plotted against time. This makes it more easy for an anesthetist to watch separate changes in both distributions, but at the same time (over-) intensifies the monitoring function of the anesthetist when compared to a single display of only power distribution.

Frequencies in the EEG are also estimated by the so called zero crossing or period/amplitude technique. The EEG is directly processed by recording the time and highest amplitude between crossings of a baseline signal (DC signal). The use of this technique implies several problems, for instance its sensitivity to minor fluctuations in the EEG [Levy *et al.*, 1980]. It may be nice for detection of spike artifacts in the EEG [Levy *et al.*, 1984], but in low frequency components the crossings may not be detected [Pronk, 1986], and therefore this technique does not provide a general applicable method for EEG-spectrum calculation, especially not when considering the possible importance of the lower frequency ranges in trying to estimate anesthesia levels. Moreover, the computational capacity of modern computers enables us to calculate spectra in very short time, whereby the "direct" EEG processing of zero crossing becomes superfluous.

Specific parameters. *Correlation coefficients* are being used as a measure of the degree of "relatedness" between two quantities. Cross-correlation determines the relatedness of two different functions, while auto-correlation functions

are calculated of one function and the same function shifted in time. The time-shift is of great influence; coefficients are mostly calculated for several values of the time-shift. These signal processing techniques can be used on time-related signals (e.g. different EEG signals), as well as on spectra, or on other quantities [Basar, 1980]. For detection of specific waveforms, automated pattern recognition or template matching could be used. Also in such applications, artificial neural nets are being applied. The use of these techniques stretches beyond the scope of this study.

◆ Some value may be attached to *stabilization factors*. These can be defined in several ways, complex (see Basar [1980]) or more simple: the ratio of the certain *range* within which the distribution of a quantity has to stay in, and the *time* that the quantity stays within that range. Frequency stabilization or phase stabilization (in simultaneously recorded channels) may take place in several frequency bands after a stimulus [Basar, 1980]. When compared to previously calculated factors, the stabilization factors could indicate changes in the state of a patient. Applying such factors in the "Neurophysiologic monitoring" project could prove to be useful, but the application of the NLA technique will influence the results, because of the use of trains of high frequency auditory stimuli.

2.3 Interpreting the (processed) EEG

2.3.1 Anesthesia levels in the EEG

In normal, attentive state of persons, the EEG generally shows a low amplitude activity. In the stages of relaxation, drowsiness and sleep, amplitude grows and frequency drops. If a person is anesthetized, generally the same effects occur: increasing amplitude and slowing rhythmical activity. However, this happens only to a certain level of anesthesia. Deeper anesthesia levels show again a decrease in amplitude and an even further slowing EEG. A classification into 7 levels has been made. In short, the levels correspond with the following patterns [Collins, 1976]: 1. flat pattern, low amplitude, the α -activity present in normal state has disappeared, 2. rhythmical high-amplitude sub- α activity, 3. complex pattern, slower activity & amplitude begins to fall, 4. slight suppression, decreasing amplitude & short periods (2 seconds) of flat patterns, 5. moderate suppression, flat EEG for periods of about 5 seconds (burst suppression), 6. severe suppression, the wave groups do not appear more than once every 10

seconds, 7. complete suppression of measurable waves. This "general" scheme is mainly applicable to volatile anesthetics.

Irregular activity. Extreme anesthesia or surgical stimulation [Van der Ende et al., 1990] may cause a "reactivation" of EEG activity; the sequence of levels as described above may be reversed. This may happen after a fairly consistent pattern in the EEG. *Transitions* between levels may show different electroencephalographic signals, and mixtures of "fast", α or β , and "slower" waves — as encountered in sleep patterns — may occur during recovery from anesthesia [Bovill et al., 1982; Faulconer et al., 1960]. Levels 4 to 7 of the general scheme show additionally irregular electrical burst activity of "high" voltage δ -waves, depending on the degree of suppression [Sebel et al., 1981; Collins, 1976].

◆ It should, however, always be possible to recognize changes [Interspec Inc., 1985], but one must be aware of the possibility of presence of physiological changes like hypoxia and ischemia [Grundy, 1985]. These effects can also make the EEG frequency spectrum shift towards lower frequencies, but may as well be caused by deeper anesthesia.

Characteristic frequencies. Changes in the EEG as mentioned above, can be observed by looking at the frequency distribution in the power spectrum. Shifts in characteristic frequencies (PPF, SEF, MPF) are used as parameters for indicating changes in the level of anesthesia in the patient. Generally, in deeper levels of anesthesia the characteristic frequencies are lower. Observing the peak power frequency may provide information about general changes in the pattern of the EEG, but the spectral edge frequency [Rampil et al., 1984; Withington et al., 1986] and the median power frequency [Schwilden et al., 1987a, 1987b, 1989; Simons et al., 1989] are considered to provide more reliable information about the level of anesthetic suppression. Also the onset of specific frequency ranges may be used as an indicator for changes in the mental state of patients (see below).

Alpha-rhythm. Several researchers, amongst which *Findeis et al.* already in 1969, point to the possibility that, when a patient is in state of suppression, the onset of α -rhythm or sub- α -rhythm (5 Hz) could indicate the onset of awareness. This was investigated recently: the results of the research showed that observing the " α -peak" gives information about awareness in an important number of cases [Van der Ende et al., 1990; Schwilden et al., 1987b; Simons et al., 1989]. Indicated was also that α -rhythm may be evoked by using auditory stimula-

tion (!). Asymmetry in different EEG signals was considered to be related to a deterioration of brain functions.

High-frequency activity. In low level anesthesia the presence of high-frequencies was indicated by *Bart et al. [1971]*, *Clark et al. [1971]* and *Levy [1986]*. A distinct β -rhythm in small frequency bands centred at about 24 Hz occurred at low concentrations of anesthetics and suggested a relation between such β activity and amnesia [*Levy, 1986*]. Another research by *Smith et al. [1979]* showed the significance of changing frequency peaks in a frequency band from 19.4 Hz to 27 Hz in *rapidly* changing anesthesia.

Since the EEG represents only a small amount of the activity of the neurons, the use of **combinations** of features extracted from processed data can be recommended. An example of an automatic EEG pattern recognition system using several features was demonstrated by *Berezowskyj et al. [1976]*. The system made use of characteristic frequencies as described above and the spectral energy of some frequency bands, and was able to relate 55% to 80% of the EEG spectra to the correct levels of anesthesia.

2.3.2 Clinical depth of anesthesia

Criteria for estimating levels of anesthesia objectively. In recent research anesthesia mostly is divided into 4 or 5 levels by making plain observations of the state of patients. In a clinical study with patients under total intravenous propofol-alfentanil anesthesia, previously performed as part of the Neurophysiological monitoring project, the following scheme was used as a reference [*Cluitmans, 1990*]:

level 1:	baseline recording: awake (premedicated);
level 2:	patient sedated, but responsive to calling of his/her name;
level 3:	visible motoric responses, either spontaneous or to a noxious stimulus, but no response to calling of name;
level 4:	no visible motoric responses, but autonomous responses still present, either spontaneous or to noxious stimuli;
level 5:	no visible motoric or autonomous responses present.

All research is performed in collaboration with anesthetists, who have to assess the level of anesthesia by using their extensive clinical experience. Otherwise no relations between parameters under investigation and anesthetic depth or awareness could be established, for one cannot ask the patient about his or her

mental state! However, sometimes the anesthesiologists do not know exactly the level of anesthesia. This supports the search for easy to use parameters, but also indicates that the anesthetic levels assessed by any anesthetist should be used with care.

2.3.3 Additional considerations

Besides interpreting the EEG from the "raw" or processed data, it is important to look at referential EEG recordings from the same person. Interpretation should never be done automatically if this "baseline" recording, performed in stable state of the patient, is not examined. Researchers and anesthetists must keep in mind that different patients can have specific patterns. *Simons et al. [1989]* indicated that a small number of persons never show an α -rhythm. However, according to *Collins [1976]* this is considerable: 20% ! This also demonstrates that whatever technique or parameter is being used, the recording and registration of the relevant data is indispensable for post-operative evaluation. In our project, this means the incorporation of a description of the EEG processing methods and parameters in the datamodel of EMDABS.

The use of various drugs influences the observed patterns in the EEG. Some anesthetics — e.g. opioid analgesics [*Sebel, 1985*] — or combinations of agents [*Cluitmans, 1990*] cause the burst suppression pattern to vanish. Furthermore the influence of using different drugs can be noticed in the EEG by the absence of one or several patterns (levels) as described in § 2.3.1, or by changes in the occurrence of slow waves [*Collins, 1976; Sebel, 1985*].

There are several things of interest when the power spectrum of an EEG is to be calculated. Some technical and practical details influence the resulting spectrum:

- in the operating room mains-interference may occur; and therefore a *filtering technique* may be used to make interferences of all electrical apparatus as minimum as possible — however, this certainly causes distortion of the EEG;
- the *sampling frequency* has to be at least twice the maximum frequency of the EEG spectrum that we want to investigate (Nyquist's theorem);
- the *analog to digital conversion* (ADC) has to be sufficient;
- the *calibration* of the measured data must be accurate — gains of amplifiers sometimes drift;

- and the length of the *time interval* to be processed will have to be chosen between a few and about 15 seconds, in order to provide a stationary EEG spectrum [Pronk, 1986];
- the previous technicality is indicated also by the following: if waveforms like burst suppression or artifacts appear in the EEG, the power spectrum must be calculated with greater care. Detection of such waveforms is required and adaptation of the calculation process (e.g. longer time intervals) will be necessary.
- however, in transient (non-stationary) analysis, the application of processing short intervals (epoch lengths of about 2 seconds) proves to be powerful [Levy, 1987] and must be examined for use in measurements.

2.4 Evaluation & discussion

As stated before, the first aim of this study is to extend the Neurophysiological (evoked potential) monitoring project into the domain of simultaneous EP and EEG diagnosis of anesthetic depth. Therefore, a general applicable means for observing EEG changes like the CSA should become available. Making an entire *array* of spectra like the CSA (as shown in figure 2.1) is not necessary or even possible, because the measurements that were performed earlier in the project consisted of only two-channel recordings. It is very likely that this methodology shall be used again in future measurements, maybe only with slight modifications.

The development of a spectrum evaluation tool will focus (as described in the next chapters) on building a "CSA" or "compressed spectral display" showing one EEG measurement channel at a time, with the help of which stored EEG data can be reviewed as chronological spectra.

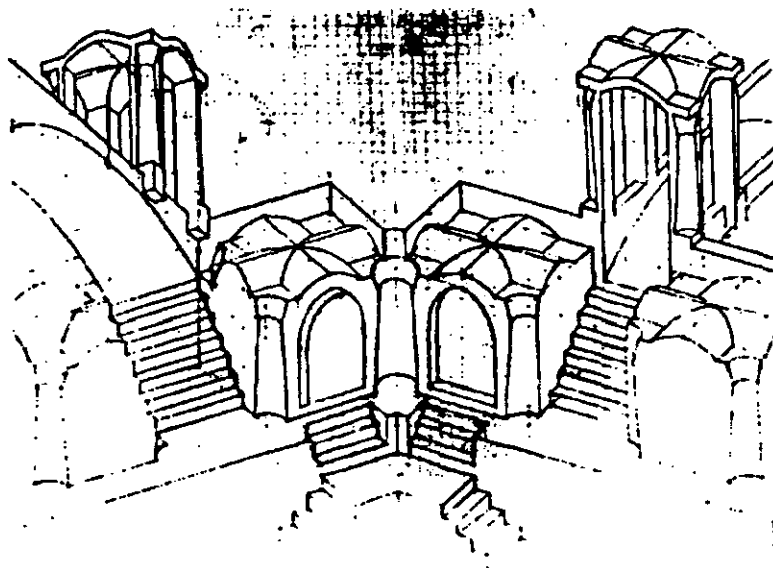
Such a technique may be preferred over the DSA technique, which used tinier or fatter dots to display relative values of power in order to make the relation time versus spectrum more clear, but at the same time making it more difficult to interpret the spectrum itself. The composed lines in the CSA, representing spectra, are more pleasant for the eye, and easier to interpret accurately. Actually, the time relation of a CSA technique to be used in a compressed spectral

display can be improved by making use of colors, by allowing different angles of view, and yet in another way: what I would call a "concave compressed spectral display". The normal display of spectra as used in the CSA is called convex, i.e. spectra are "bulging" out of a "horizontal" surface. This type of display can be complemented by showing spectra in a concave manner, revealing hidden details of particular spectra, and vice versa. This will be clarified in the next chapter.

Furthermore, the spectrum calculation algorithm should enable the use of different epoch lengths, say from about 2 seconds to 20 seconds. A supplemental algorithm should be available to detect defections like burst suppression, for instance with parameters like "signal" stabilization factors. Detection of artifacts will not be implemented in a spectrum display program, first because of the short duration of artifacts (short most of the time; and slow trends in measurements will not influence spectra very much) and resulting peaks in power will be easy to recognize, and secondly because this can be considered a separate part of an overall system (see for instance *Jansen [1990]*, and *Värri [1988]*).

Testing a new research tool can be done with the data acquired previously in clinical sessions performed for AEP analysis. The amount of raw data (7 cat studies, 34 human studies stored on optical discs) and the quality (e.g. the sampling frequency was high enough: 5 kHz) will be sufficient for a thorough evaluation of a spectrum display program.

When this work is done, further EEG research is possible. The most promising results in assessing anesthesia levels or awareness were accomplished by the investigation of specific frequency ranges, like the "evoked" α -rhythm or high β -rhythm (20 to 30 Hz peaks - see § 2.3.1). Also the examination of the characteristic frequencies (MPF, PPF, SEF) may be important. I suggest to investigate simultaneously the changes in *several* frequency bands, for instance by looking at *averages* of, and *relative changes* in the characteristic frequencies when analyzed together. Previous research usually concentrated on only one or maybe two parameters, which is of course very good to investigate the relation between anesthetic depth and the specific parameter, but we want to take anesthesia levels and especially awareness as a starting-point and then try to detect these levels by using every means.



M.C. Escher: Study for "Hol & Bol" ("Convex & Concave"), 1955

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3 CCSA: a spectral analysis tool

Before describing the actual development of the CCSA ("Convex/concave Compressed Spectral Array") EEG analysis tool — in chapter 4 — some requirements and constraints of such an application are presented in this chapter.

3.1 Application requirements

The main goal of an EEG spectrum evaluation program within the Anesthetic depth project is to enable research on the quality and usefulness of (new) parameters to be derived from an EEG in relation to depth of anesthesia. Since future research-projects may vary in point of interest and scope and may incorporate several different researchers, a general analysis tool should be easy to work with and very flexible as to *what* can be evaluated, and therefore must enable an investigator to adjust a certain number of settings. Users of the application should have some insight in the calculation processes, since frequency transformation involves quite a few mathematical matters. However, as this new analysis tool is to be applied in medicine, mere medically trained persons with general knowledge of what can be seen in EEG spectra should also be able to experiment with the application.

3.1.1 General provisions / layout

With respect to the considerations mentioned above, the design of a general applicable means to evaluate EEG spectra was shaped into the form of a user

interactive computer application. The application should facilitate easy adjustment of parameters. For this a menu structure was chosen.

Menus. Menus were made, which — if opened — are displayed as overlay on the display background (this makes the menu structure obvious to the user).

◆ Parameters to be adjusted in menus are for example the sample frequency at which EEG data was sampled, the value of the maximum frequency to be reviewed in the EEG spectrum, the epoch length to be processed and other parameters that influence the calculation and display of an EEG power spectrum. A summation of possibilities in options and parameter adjusting will be given in § 3.1.3.

◆ In order to make the application well surveyable, options that more or less belong together are grouped together in one menu. Some options will only have a yes/no setting, and for these several shortcut possibilities should be enabled, since a user might want to switch the parameter setting more easily than: first opening a menu, choosing the setting, and then closing the menu, in order to plot a CSA with the new setting. For this, a selection is made of the parameters to be put “under” the function keys on the keyboard of the computer. The menu structure/flowchart and a description of the use of the function keys is given in appendix B.

Designing the screen layout. The display of a 1-channel CSA is the main purpose of the program, and this display should show considerable detail in the spectra of the EEG. Therefore a large portion of the available display area (a monitor screen) is reserved for the CSA. As most of the parameter settings (see § 3.1.3) reveal themselves in the CSA — for example the number of spectrum lines — only a few settings need to be visible permanently on the screen (such as the name of the file that is being processed). A display area in which these settings are displayed is placed at the right of the screen. At the bottom of the screen the function keys and their use are displayed, but also in this area messages or errors can be displayed, informing a user what to do next or what error occurred. A drawing of the screen layout is given in appendix A.

Display of spectra. The actual CSA is built by shifting previously plotted spectra “backwards” (i.e. upwards and to one side — semi-3-dimensional) and plotting a newly calculated spectrum in front of the shifted spectra. From this a CSA is made where the time decreases further backwards; the most recent spectrum is displayed in the front.

◆ In the CSA technique, spectra are displayed close behind each other (this is called *compression* [Bickford, 1972, 1973]) where the “overlap” of spectra is *sup-*

pressed, see figure 3.1a. Because of the use of this technique, possible interesting details may be concealed. This type of display can be complemented by making a *concave* CSA, where the spectra are again displayed behind each other, but now with the amplitude plotted downwards (see figure 3.1b).



Figure 3.1 Constructing a CSA: a. convex, b. concave

3.1.2 Data processing requirements

A spectral analysis tool which in first instance, as in our project, is meant to evaluate an EEG on file, must meet the following data processing requirements:

- The program must be able to read the EEG data correctly from file. For this the data format must be specified. For instance, a file may contain data of more channels, which will be encoded within the data samples. Specifications will be given in § 4.1.3.
- Because of the large amount of data obtained during measurement sessions, fast evaluation of the spectra afterwards must be enabled. A user should be able to "step" through a file, one CSA (a specified number of spectrum plots of epoch length) at a time.
- As a user might know in advance precisely where in the data file (at what position, after what time) a phenomenon occurred that he/she wants to evaluate, the file position must be adjustable.
- During measurements the gain of amplifiers may have been adjusted, which influences the calibration of the measured data. A record of this is

kept, and this enables the use of these calibration and offset values in a data-read routine.

The available EEG data within the Anesthetic depth project was sampled at a frequency of 5 kHz because of high-frequency components in evoked potentials. The EEG spectrum, however, needs evaluation only to a frequency of about 100 Hz maximum. The processing of the EEG data to spectrum plots therefore involves some filtering techniques, besides the obvious time to frequency domain transformation. In implementing data calculation and display routines, the future possibility of real time processing is also investigated. When taking real time adaptations into account, the eventual program might prove to be even more widely applicable. These issues will be dealt with in § 4.2 and § 4.3.

During EEG spectra evaluations, a user may change a number of settings. From this, a mere practical issue emerges: when quitting the EEG analysis application, the program's parameter settings should not be lost, since the user does not want to adjust the settings all over again at the next program startup. Therefore a possibility is provided to save the settings.

3.1.3 Interactive parameter adjusting

In the CCSA program (convex/concave compressed spectral array) a large number of (adjustable) parameter will be available. These are presented below.

The following parameters are categorized as **options** (these are parameters that influence the calculation process directly):

- the sample frequency, the EEG frequency (maximum freq. to be plotted), epoch length, begin of CCSA time interval, plotting the next/previous CCSA, plotting/recording to a file of the characteristic frequencies MPF, PPF, SEF and a custom definable frequency; also the factor by which the "spectral edge frequency" is determined is adjustable, since some research may need a slight adjustment of this factor (some investigators use a factor of 97%, while others use a factor of 95% of the total power contents). Spectra can be displayed in squared voltages and as normalized spectra (where every spectrum is normalized on its peak value).

Parameters categorized as **settings** are:

- indication of one of the implemented time windows and indication of FIR filtering (these are actually *calculation* parameters also, see § 4.2.1 and

§ 4.2.2), indication of which channel is to be processed, the angle of the CCSA and the number of spectra in the CCSA, use of color, and plotting a convex or concave CCSA (see figure 3.2).

All of this can be customized and saved in a "settings file".

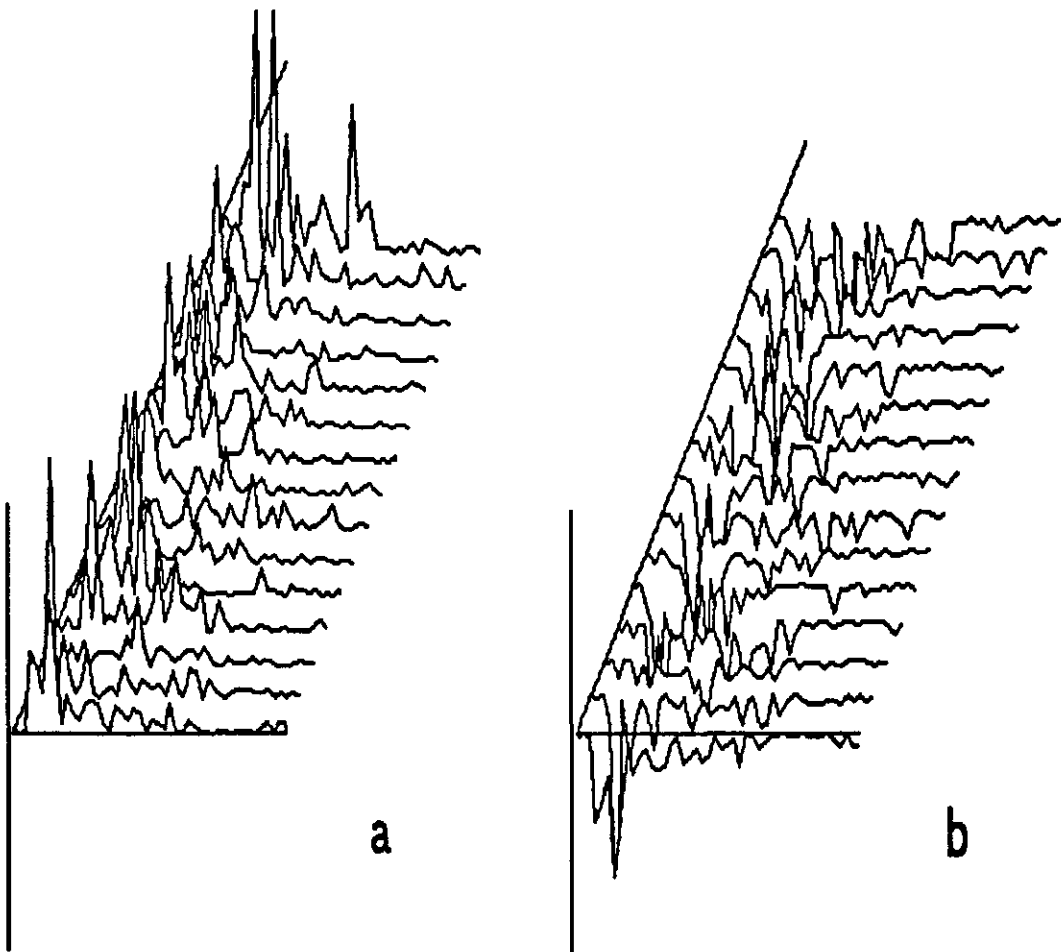


Figure 3.2 Convex (a) and concave (b) CSA display

3.2 Building the EEG analysis application

3.2.1 Software development

When building a software tool that is likely to be used by several researchers, user-friendliness must be of top priority. A well designed user-interface providing informative messages on possible mistakes/actions should be made. With an application like the CCSA, that will be used by persons with technical skills and insight in the data-processing, user-friendliness also has implications on the source code of the application. A clear program structure, descriptive names of identifiers, and use of lots of comments are a necessity, since a future user might want to customize the program. For this, documentation is written describing the usage of the program and describing the internal structure and routines.

The last couple of years, all software implementations with use in the Anesthetic depth project were made in the programming language "C". A major consideration for using this programming language, was the efficient code that modern "C" compilers produce. For possible simultaneous use of the CCSA application and previously (or future) developed programs, the CCSA is also implemented in "C".

3.2.2 Program portability

In trying to build a well structured program, effort is made to establish "program portability". The proposed ANSI standard for the "C" programming language [Kernighan & Ritchie, 1988] is applied as well as possible in writing the program, and for operating the monitor display a separate (extern) graphics library was used [Media Cybernetics, 1988a, 1988b]. This makes the implementation of the program highly portable from one software development environment to another.

Machine independency is obtained by the flexibility of the graphics library, which provides numerous device drivers for different monitors, [Media Cybernetics, 1988b] and by making no special assumptions on the arithmetics (e.g. one's or two's complement type) used on a specific platform. Furthermore, any machine error that occurs during the running of the program, such as memory violation, should be signalled and dealt with.

An obvious condition for writing a portable program is the omitting of any code that has assumptions on particular display size. Flexibility of the program can thus be obtained, and also by using no "hard-code" filenames or constants that may need alteration in the future or in a different environment. Such identifiers are to be grouped together, where a user can easily change them (i.e. use header files — in "C").

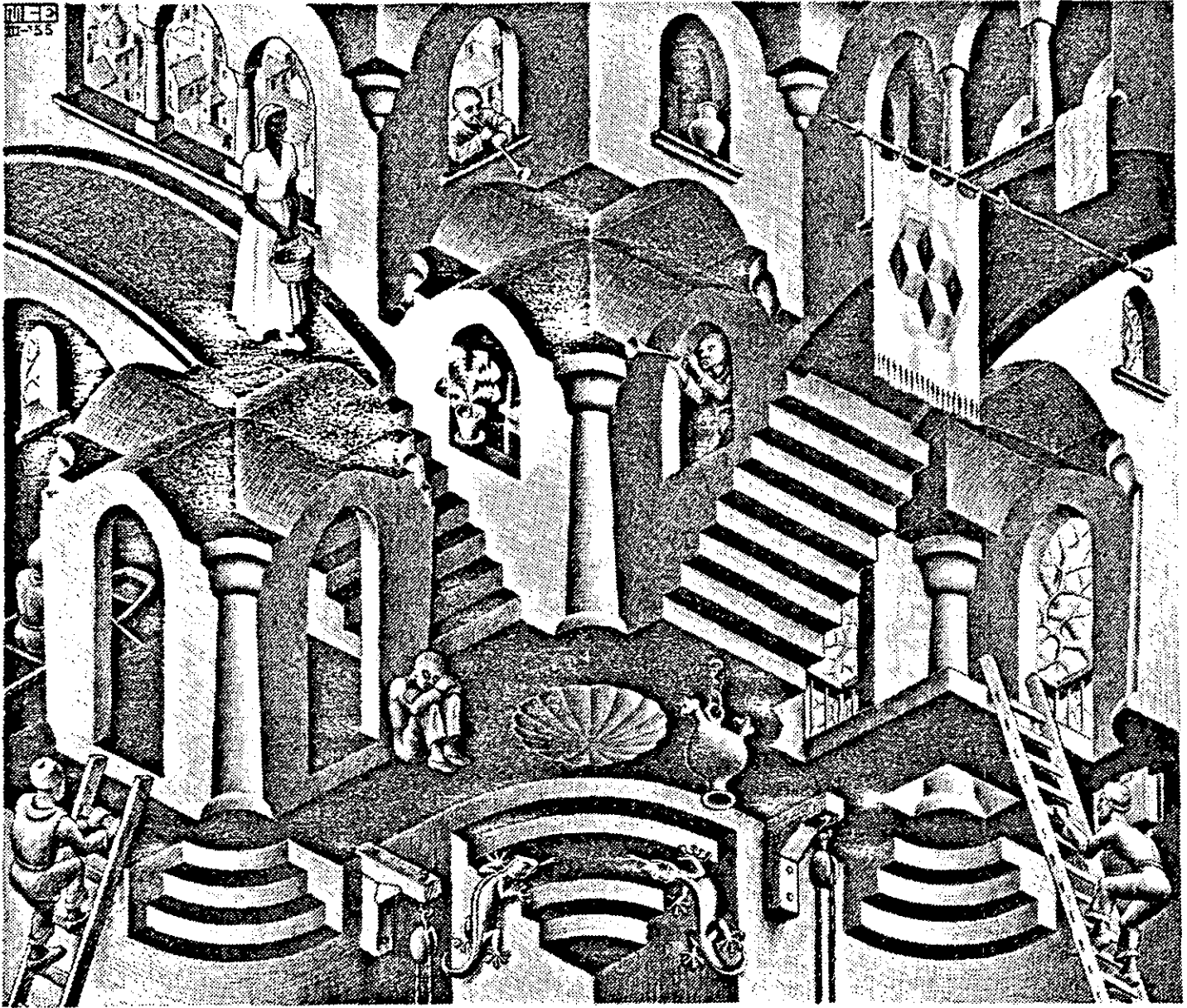
More guidelines on programming portable programs in "C" can be found in *Kernighan & Ritchie [1988]* and in the manual of the *Microsoft® Corporation [1990]*.

3.3 Summary

The development of the "Convex/concave Compressed Spectral Array" (CCSA) EEG analysis application program concentrated on maximum program performance, as to correct data processing and easy use. The development also concentrated on applying advanced programming techniques, in order to obtain a clear program structure and optimal program portability.

Effort was made on designing a good user-interface, with emphasis on features like screen-layout, easy-to-use menus, and informative messages.

Information about the CCSA program can be found in appendices A and B of this report; an extensive documentation can be found at the Eindhoven University of Technology, Department of Electrical Engineering, division of Medical Electrical Engineering.



M.C. Escher: "Hol & Bol" ("Convex & Concave"), lithograph, 1955

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4 Algorithm development

For analysis of EEG data in the frequency domain signal processing is necessary. After first giving specifications for previous studies and measured data in paragraph 4.1, paragraph 4.2 continues with describing filtering techniques, frequency transformation and other aspects of the data processing. Specifics about the performing of data analysis are presented in paragraph 4.3.

4.1 Starting points: previous clinical studies

As part of the "Neurophysiological monitoring of anesthetic depth" project a pilot study with 7 cats under Isoflurane or N₂O-Isoflurane anesthesia and a clinical study with 34 patients undergoing orthopedic surgery under total intravenous alfentanil-propofol anesthesia were performed in Gainesville, Florida and in Nijmegen, The Netherlands respectively (see *Cluitmans [1990]*).

As the dataprocessing of the CCSA program is to be performed on data that were measured during these studies, these data must be specified for a consistent implementation. Relevant informations about the mentioned studies, especially starting points for the EEG analysis, are described in this paragraph.

4.1.1 Measuring equipment

A summary of some of the equipment used during the sessions is given below.

Nicolet Pathfinder I & II electrophysiological monitoring systems (Nicolet Biomedical, Madison, Wisconsin, U.S.A.) were used for conventional evoked potential monitoring, where the stimulus controller module was adapted for use in external triggering.

A Nicolet 1007 auditory stimulator was used together with Nicolet Tip-10 insert type earphones to present clicks to the patient (for evoked potential measurements).

The following band filters were used:

- a 2-pole Butterworth high-pass filter with a cut-off frequency set at 1.5 Hz (cats) and 5 Hz (clinical study),
- a 2-pole Butterworth low-pass filter with a cut-off frequency set at 1.5 kHz.

The evoked potential recording system was implemented on an IBM AT compatible personal computer for storing of 2 channel EEG recordings at a sampling frequency of 5 kHz for each channel.

For a detailed description of all the equipment used in the measurements see *Cluitmans [1990]*.

4.1.2 Session protocol

During separate sessions of the "cats" study and the clinical study data were stored on file. Of all "patients" a baseline recording was made during the pre-anesthetized phase in a session. These baseline recordings were interpreted by the research team for verification of the reliability of the measurements.

For every "level" of anesthesia files were made by recording the EEG for about 100 seconds as measured in two channels coming from the scalp of the patient. Electrodes were placed at the following positions: "frontal" on the forehead, "central" on top of the scalp and "temporal" at the auditory centers near the ears (positions Fp_z, Cz, A₁, A₂ according to the 10-20 system [*Spehlman, 1981*]). Event recording (administered drugs, actions of medical staff) was kept with the help of the ERDA system [*Cluitmans, 1990; De Jong, 1986*].

The level of anesthesia (see table 4.1) was assessed by an anesthesiologist. He also tried to maintain this level throughout a measurement.

Table 4.1 Anesthesia schemes

<i>Anesthesia levels</i>	<i>Clinical study</i>	<i>Cats study</i>
1	<i>baseline recording, premedicated</i>	
2	<i>sedated/responsive</i>	0.3 MAC ^{*)} N ₂ O
3	<i>motoric responses</i>	0.3 MAC N ₂ O + 0.3 MAC Isoflurane
4	<i>autonomous responses</i>	0.3 MAC N ₂ O + 0.6 MAC Isoflurane
5	<i>no responses</i>	0.3 MAC Isoflurane
6	—	0.6 MAC Isoflurane

*) see glossary

In the "cats" study, the levels 1, 2, 3, 4, and the levels 1, 5, 6, are to be considered as separate sets.

4.1.3 Data specification

EEG data were sampled at a rate of 5000 samples per second in two channels. The low pass filter with a cut-off frequency at 1.5 kHz bandlimited the EEG signal, making the sampling frequency of 5 kHz consistent with the Nyquist theorem. Sample values were encoded in 2 bytes integers, comprising of 12 bits amplitude information and 4 bits additional information. The additional 4 bits were used for indication of which channel the sample came from, and for indication if a auditory stimulus was given at the time at which that particular sample was obtained (see figure 4.1).

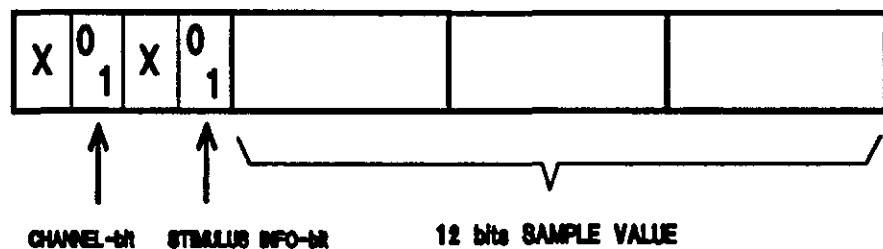


Figure 4.1 Sample encoding

The stimulus info-bit is used for triggering of the averaging process whereby evoked potentials are calculated. This bit does not need evaluation in the CCSA application, because no averaging of EEG intervals has to be applied.

Samples were obtained from one channel after another (two channels), but because of the high sampling rate, sometimes a sample was missed. Therefore, the channel indication bit was encoded in the samples, for verification in reading the data from file.

This encoding scheme implies that if we want to meet with the pre-condition of not using specific arithmetics (§ 3.2.2), the samples must be converted back to a non-specific type. This can easily be done in the programming language "C", as long as the 12 bits actual sample amplitude information was encoded in a consistent type.

In a session several measurements were made of different levels of anesthesia. One EEG data measurement of about 100 seconds produces a data file of about 2 Megabytes. The data files of the described studies were therefore stored on optical disc after each session, because of the limited space of the storage medium during a session.

Measurements of different levels of anesthesia sometimes required different settings for the calibration and offset values (i.e. multiplication factor and deviation on zero input: used for calibration of the stored sample values to proper units in micro-Volts). For this, a record was kept of these parameters for each measurement (each file).

4.2 Signal processing

The EEG data read from a file needs some processing before spectrum plots are displayed as a CSA. Pre-processing filtering techniques are necessary before any frequency transformation can be done. Specific parameters (characteristic frequencies) to be displayed in the CSA are calculated in the EEG spectra, and only after this the actual plotting on screen is performed.

4.2.1 Time domain processing: pre-filtering

Low-pass filtering. Since we are interested in evaluating EEG spectra only in the range 0 - 100 Hz, while the data on file was sampled with a pre-filtering cut-off frequency and sampling frequency f_{sample} as high as 1.5 kHz and 5 kHz respectively, a low-pass filtering algorithm is necessary.

◆ What we would actually like, is to obtain a signal that is sampled at twice (or slightly more) the maximum significant EEG frequency $f_{max,eeg}$ (which is adjustable in the CCSA program, see § 3.1.3). So we could skip $f_{sample}/2f_{max,eeg}$ samples in the input data-stream for each sample of the "modified" signal with reduced sampling frequency. But, the original signal contained frequency components above the "new" sampling frequency of $2f_{max,eeg}$, originating from the stimulus evoked responses. How small these (high) frequency components may be — a lot of averages are necessary to "lift" them above the "EEG noise" — they can influence the spectrum below an artificially reduced sampling frequency. This phenomenon is known as *aliasing*, which occurs when a signal is sampled at a too low frequency. Therefore the frequency components above the spectrum of interest should be removed *before* the sampling frequency is lowered. This is done with a finite impuls response (FIR) filter.

FIR filtering. A low-pass filter can be looked upon as a filter that "smoothes" a signal: fast changes in a signal are suppressed, while slow variations remain. This can be achieved with a "moving average" FIR filtering technique, where the resulting signal $r(n)$ is calculated from the input signal $s(n)$ by:

$$r(nT) = \frac{1}{2L+1} \sum_{k=-L}^L s((n-k)T) \quad (4.1)$$

T is the sampling interval

resulting in values of $r(n_i)$ representing the average value of $s(n)$ around n_i .

In yet another notation:

$$r(nT) = \sum_{k=-L}^L h(kT) \cdot s((n-k)T) = h(nT) \otimes s(nT) \quad (4.2)$$

impulse response $h(nT) = \frac{1}{2L+1}$, $-L \leq n \leq L$
 \otimes denotes convolution

The filter is not causal, but this problem can be solved by introducing a delay time of L samples. However, when reading stored data, we are not hampered by this problem and the delay can be implemented artificially: just read $-L$ to L samples around the desired sample n_i .

The following frequency domain formula can be given, in accordance with formula 4.2 (convolution in time domain \equiv multiplication in frequency domain, and vice versa):

$$R(e^{j\Omega}) = H(e^{j\Omega}) \cdot S(e^{j\Omega}) \quad (4.3)$$

*normalized frequency Ω corresponds
with the actual frequency f :*

$$\Omega = 0, f = 0; \rightarrow \Omega = \pi, f = \frac{f_{\text{sample}}}{2}$$

Resulting in a low pass filtered signal $r(n)$ with spectrum $R(e^{j\Omega})$, since $H(e^{j\Omega})$ can be calculated as [Verkroost, 1985]:

$$\begin{aligned} H(e^{j\Omega}) &= \sum_{n=-L}^L \frac{1}{2L+1} e^{-j\Omega n} = \frac{1}{2L+1} e^{j\Omega L} \sum_{n=0}^{2L} e^{-j\Omega n} \\ &= \frac{e^{j\Omega L}}{2L+1} \cdot \frac{e^{-j\Omega(2L+1)} - 1}{e^{-j\Omega} - 1} = \frac{1}{2L+1} \cdot \frac{e^{-j\Omega \frac{2L+1}{2}} - e^{j\Omega \frac{2L+1}{2}}}{e^{-j\frac{\Omega}{2}} - e^{j\frac{\Omega}{2}}} \\ &= \frac{1}{2L+1} \cdot \frac{\sin(\frac{2L+1}{2} \Omega)}{\sin(\frac{\Omega}{2})} \end{aligned} \quad (4.4)$$

This spectrum is given in figure 4.2 for $L = 32$. The low pass characteristic of the filter is clearly seen.

If we take the -3 dB point in this spectrum as the FIR filter cut-off frequency, we can approximate $\Omega_{\text{cut-off}}$ and $f_{\text{cut-off}}$ from formula 4.4 and figure 4.2 (see also appendix C):

$$\begin{aligned} \Omega_{\text{cut-off}} &\approx \frac{\pi}{vL} \quad \Rightarrow \\ f_{\text{cut-off}} &\approx \frac{f_{\text{sample}}}{2vL} \quad v = 2.257 \end{aligned} \quad (4.5)$$

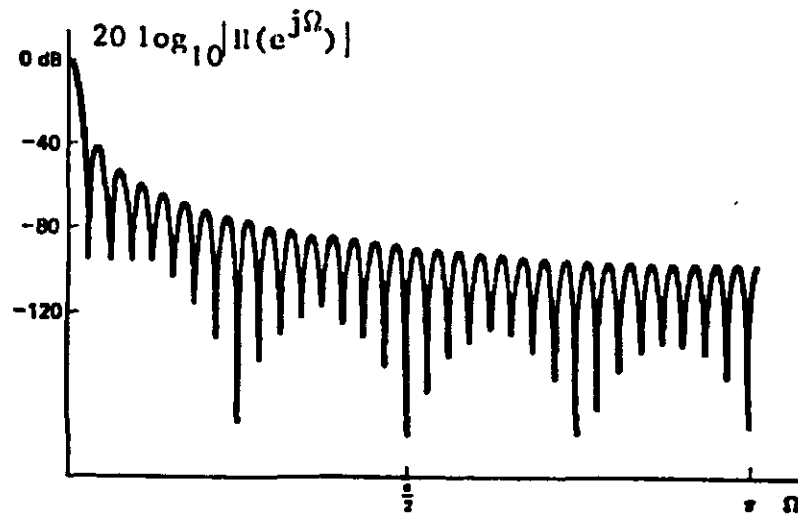


Figure 4.2 Logarithmic spectrum curve of the "moving average" filter

In the CCSA application f_{sample} and $f_{max,eeg}$ are specified by the user, and with formula C.4 (appendix C) the FIR filter parameter L can be calculated.

By applying the moving average filter we are actually able to skip a number of samples $f_{sample}/2f_{max,eeg}$, as to obtain a reduced "pseudo" sampling frequency, where the resulting spectrum is not damaged by aliasing effects below the frequency $f_{cut-off} = f_{max,eeg}$.

4.2.2 Time domain processing: windowing

Spectral leakage. Calculating the frequency transformation of an EEG signal is only feasible if short intervals are processed. Such an epoch is in fact a signal that is limited in time, which takes its effect upon the spectrum. This estimated spectrum shows "spectral leakage", which can be reduced by applying windowing functions.

If $g_0(n)$ is a (discrete) signal that is windowed with the function $w(n) = 1$, $0 \leq n \leq N - 1$; ($w(n) = 0$, elsewhere):

$$g(nT) = w(nT) \cdot g_0(nT) \quad (4.6)$$

T is the sample interval

is a time limited signal from 0 to $(N - 1)T$ seconds. The estimated spectrum is now [Verkroost, 1985]:

$$G(e^{j\Omega}) = W(e^{j\Omega}) \otimes G_0(e^{j\Omega})$$

$$\text{where } W(e^{j\Omega}) = \frac{\sin(\frac{N}{2}\Omega)}{\sin(\frac{\Omega}{2})} \cdot e^{-j\Omega \frac{N-1}{2}} \quad (4.7)$$

\otimes denotes convolution

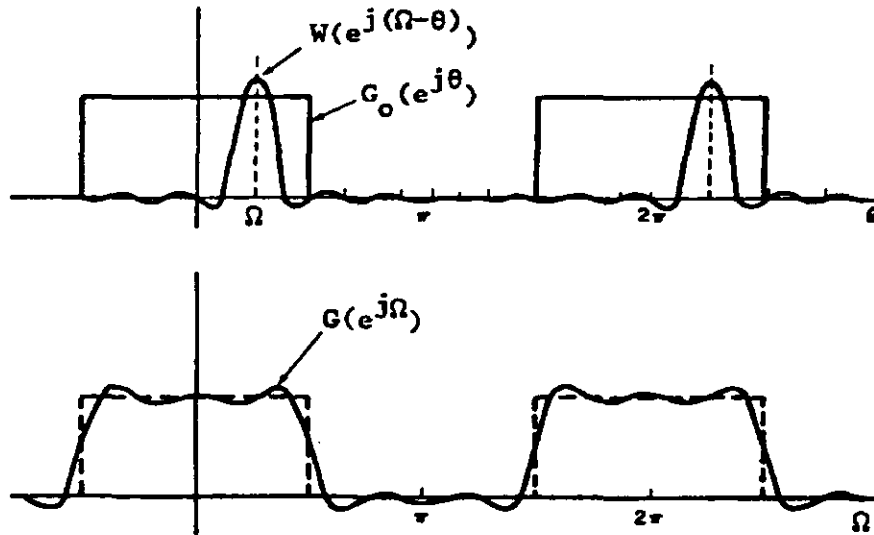


Figure 4.3 Convolution process and resulting spectrum

The “spectral leakage” is clearly visible in figure 4.3: fast changes in the original spectrum spread, and the estimated spectrum shows signal where the original did not. Therefore, the main peak in $W(e^{j\Omega})$ should be made smaller, and the side lobes should be suppressed (see figure 4.3).

Window functions. The main peak in a spectrum of a “windowing” filter will become smaller with larger N (formula 4.7), but the side lobes are only suppressed more with the use of *window* functions that go to zero towards both begin and end of the epoch. Five windows were implemented in the CCSA program, in order to be able to experiment with the different features of the windows.

In the following order these often used windows show *more* side lobe suppression and a main lobe that is *less* small (broader):

$$\text{Rectangular: } \begin{array}{ll} w(n) = 1, & 0 \leq n \leq N-1 \\ w(n) = 0, & \text{elsewhere} \end{array}$$

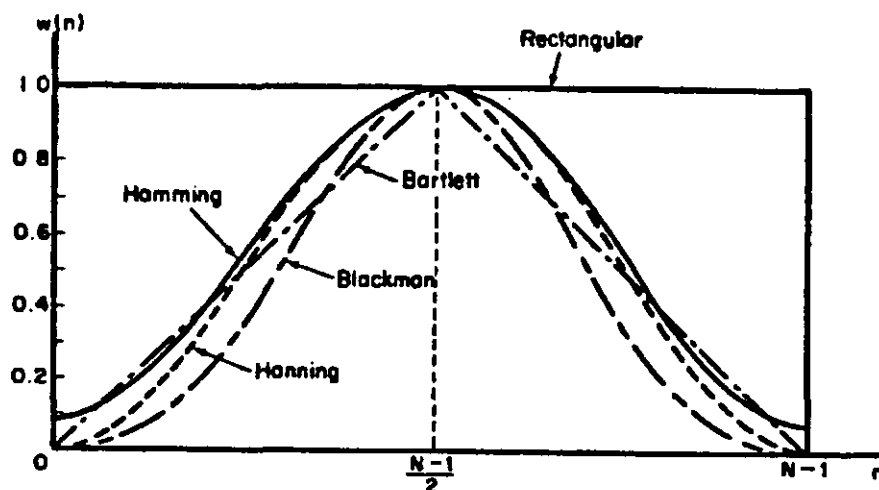


Figure 4.4 Window functions

<i>Bartlett:</i>	$w(n) = \frac{2n}{N-1}, \quad 0 \leq n \leq \frac{N-1}{2}$ $w(n) = 2 - \frac{2n}{N-1}, \quad \frac{N-1}{2} < n \leq N-1$ $w(n) = 0, \quad \text{elsewhere}$	
<i>Hanning:</i>	$w(n) = \frac{1}{2} \left(1 - \cos\left(\frac{2\pi n}{N-1}\right) \right), \quad 0 \leq n \leq N-1$ $w(n) = 0, \quad \text{elsewhere}$	
<i>Hamming:</i>	$w(n) = 0.54 - 0.46 \cos\left(\frac{2\pi n}{N-1}\right), \quad 0 \leq n \leq N-1$ $w(n) = 0, \quad \text{elsewhere}$	
<i>Blackman:</i>	$w(n) = 0.42 - 0.50 \cos\left(\frac{2\pi n}{N-1}\right) + 0.08 \cos\left(\frac{4\pi n}{N-1}\right), \quad 0 \leq n \leq N-1$ $w(n) = 0, \quad \text{elsewhere}$	

Concluding: a fairly optimal spectral leakage suppression can be obtained by choosing one of the last filters for good side lobe suppression, and a large N to obtain a small main lobe in the spectrum of the filter. For more information on the above mentioned and other windowing functions, see *Van den Enden et al. [1987]* and *Jackson [1989]*.

4.2.3 Transformation to frequency domain

Fourier transform. The most well-known way of performing time-to-frequency transformation is “Fast Fourier Transformation” (FFT — see appendix D). This is a handsome and faster way of calculating a discrete Fourier transform, which is defined by:

$$F(k) = \sum_{n=0}^{N-1} f(n) e^{-j \frac{2\pi}{N} kn}$$

$$= \sum_{n=0}^{N-1} f(n) \cos\left(\frac{2\pi}{N} kn\right) - j \sum_{n=0}^{N-1} f(n) \sin\left(\frac{2\pi}{N} kn\right) \quad (4.8)$$

$f(n)$: discrete time signal
 $F(k)$: discrete Fourier transform
 j : imaginary axis unit

For real signals $f(n)$ (not complex) however, the following properties of $F(k)$ can easily be deduced, because of the odd cosine-function and the even sine-function in 4.8:

$$\begin{aligned} \operatorname{Re}\{F(k)\} &= \operatorname{Re}\{F(N-k)\} \\ \operatorname{Im}\{F(k)\} &= -\operatorname{Im}\{F(N-k)\} \end{aligned} \quad (4.9)$$

Hartley transform. A transformation that uses the properties 4.9 is called the Hartley transform [Bracewell, 1986] after R.V.L. Hartley [1942]. This transformation in a manner of speaking “folds” the real and imaginary parts of the Fourier spectrum in one, resulting in one array containing N Hartley transform samples, instead of — in Fourier transformation — two arrays (one real and one imaginary) of together $2N$ samples. The definition of the Hartley transform is given in formula 4.10.

$$H(k) = \sum_{n=0}^{N-1} f(n) \left\{ \cos\left(\frac{2\pi}{N} kn\right) + \sin\left(\frac{2\pi}{N} kn\right) \right\} \quad (4.10)$$

$f(n)$: discrete time signal
 $H(k)$: discrete Hartley transform

From formulas 4.8 to 4.10 the following can be deduced:

$$\begin{aligned} H(k) &= \operatorname{Re}\{F(k)\} - \operatorname{Im}\{F(k)\} \\ H(N-k) &= \operatorname{Re}\{F(N-k)\} - \operatorname{Im}\{F(N-k)\} = \operatorname{Re}\{F(k)\} + \operatorname{Im}\{F(k)\} \end{aligned}$$

$$\begin{aligned}
 F(k) &= \text{Re}\{F(k)\} + j \text{Im}\{F(k)\} \\
 &= \frac{H(N-k) + H(k)}{2} + j \frac{H(N-k) - H(k)}{2} \quad (4.11)
 \end{aligned}$$

From the Hartley transform also a "fast" algorithm can be made that is approximately twice as fast as FFT (see appendix D), and with the help of formulas 4.11 a power spectrum $|F(k)|^2$ can be calculated:

$$\begin{aligned}
 |F(k)|^2 &= \{\text{Re } F(k)\}^2 + \{\text{Im } F(k)\}^2 \\
 &= \frac{1}{4} \{ [H(N-k) + H(k)]^2 + [H(N-k) - H(k)]^2 \} \\
 &= \frac{1}{2} \{ [H(k)]^2 + [H(N-k)]^2 \} \quad (4.12)
 \end{aligned}$$

Implications on parameter settings. A fast frequency transformation can only be performed on discrete time arrays that have length $N = 2^x$, $x > 0$ (a power of 2 — see appendix D). Then if an investigator chooses a particular *epoch* to be processed to a power spectrum below a particular maximum EEG frequency $f_{max, eeg}$ (corresponding with half the "pseudo" sample frequency — see § 4.2.1), these parameters need adjusting:

$$arraylength\ N = 2 f_{max, eeg} \cdot epoch \supset 2^x, \quad x > 0 \quad (4.13)$$

The epoch to be processed gets the priority of not being changed, because we do not want to change the length of the time interval to be processed, while we *can* do the following: increase $f_{max, eeg}$ to the nearest (larger) frequency $f'_{max, eeg}$, so that it meets with 4.13.

In the spectrum display, only the frequency components below the originally indicated $f_{max, eeg}$ are plotted, allowing a researcher to really customize the spectrum display (CCSA). However, to make it clear what frequency components above the visible $f_{max, eeg}$ the calculation process calculates as well (and does not display), the recalculated $f'_{max, eeg}$ is given in one of the menus.

Epoch adjusting. The frequency division $f_{sample}/2f'_{max, eeg}$ indicates the number of samples to skip in the input array (see § 4.2.1). This division however, need not be an integer value. This indicates that "pseudo" samples are to be obtained between samples: the "sample" value is obtained through interpolation.

◆ The CCSA program allows a user to choose an integer frequency division, in

order to use only actual sample values at an actual sample time. For this, the frequency division is rounded, after which $f'_{max, EEG}$ is adjusted again, to $f''_{max, EEG} = f_{sample}/2freq.division$. Now the arraylength of 2^x must be obtained by adjusting the *epoch* length (see formulas 4.13 and 4.14):

$$epoch = \frac{N}{2f''_{max, EEG}}, \quad N = 2^x, x > 0 \quad (4.14)$$

Advantages of the scheme above are:

- maximum flexibility
- only *that* arraylength of data is frequency transformed that is just needed (saving time compared to calculation with a fixed frequency of e.g. 100 Hz and then displaying only to $f_{max, EEG}$)
- *epoch* and $f_{max, EEG}$ can be customized
- *epoch* priority (*epoch* is *only* — slightly — adjusted if an integer frequency division is chosen)

4.2.4 Specific parameter calculation

In a power spectrum, several characteristic frequencies can be calculated (see § 2.2). For the calculation of these EEG parameters first the total power contents is calculated and the peak power frequency is determined. After this the median power frequency (MPF) can be calculated by comparing half the value of the total power contents to a summation of the power values of the frequency components until equation 4.15 is met:

$$\sum_{i=0}^{MPF} p_i = 0.5 P_{total} \quad (4.15)$$

In a similar way, the spectral edge frequency (SEF) can be determined:

$$\sum_{i=0}^{SEF} p_i = a P_{total} \quad (4.16)$$

a : spectral edge factor

To fasten the calculation process, the MPF and SEF are determined in the same summation $\sum p_i$. Therefore the spectral edge factor a can only be adjusted (see

§ 3.1.3) in the range $0.5 < a < 1.0$, because the calculation assumes that the MPF is smaller than the SEF.

In the source code of this characteristic frequency algorithm of the CCSA program is indicated how a user can define a "custom characteristic frequency". For the sake of simple implementation, in the first version of the program initially a choice has been made to calculate this frequency exactly inbetween the MPF and the SEF, taking into account promising results of investigations of both frequencies (see § 2.3.1). However, other calculations of custom EEG parameters can be implemented as well.

4.2.5 Display of spectra

The calculated spectra (§ 4.2.1 → .3) and the calculated characteristic frequencies from the previous sub-paragraph are to be displayed as a convex or concave CSA, with the use of "hidden line suppression" as indicated in § 3.1.1.

The hidden line suppression is implemented in the following way: first, the previously plotted spectra are shifted backward in the CCSA; second, the current spectrum is plotted in the front; third, the current spectrum is made into an enclosed display area by plotting some extra lines below the spectrum; fourth, the enclosed area is filled with the screen background color after which the extra lines are deleted.

An alternative method would have been: storing the values of a previously calculated and plotted spectrum for comparison with a newly calculated spectrum and then calculating the lines to be suppressed/hidden and deleting them on screen, and then plotting the new spectrum. However, this method takes extensive processing, especially because of the varying values of the angle of display and the number of spectra in the CCSA, and because of the possibility of convex and concave display (see § 3.1). Besides, the filling function of the graphics library used [*Media Cybernetics, 1988a*] is very fast.

Characteristic frequencies are displayed in the CCSA with different indicator signs. The signs have a color different from the color of the spectra and indicate the exact characteristic frequency positions in the spectra on screen.

4.3 Data analysis

4.3.1 Data on file

When we are going to analyze data stored on file, we should consider in advance *what* we want to observe.

In the "Anesthetic depth project" we are interested in assessment of levels of anesthesia by observing changes in spectra of the EEG. We should then reflect how a convenient and effective analyzing can be accomplished; when EEG data were stored per level (see § 4.1.2 and § 4.1.3), observing changes in relation to levels will be difficult, and also, as in our case one file of 2 Megabytes information represents only 100 seconds EEG data, the CCSA will be filled with only a few spectra (for example 10 spectra of epochs of 10 seconds).

It will therefore be more convenient to append a few measurement files containing data of different levels of anesthesia in *one* patient and then using this new, much larger file as input data stream for the CCSA program.

But now a completely new problem arises. By appending files of different measurements — maybe with different calibration and offset (see § 4.1.3) — the data in the resulting file may need a more sophisticated calibration scheme.

In the CCSA application program a possibility was made that allows users to indicate where in an input data file the calibration changes (see appendix A). We must by ourselves keep track of the time in the measurements at which the level of anesthesia changed (which can be deduced from the fileposition at which the new calibration is valid).

4.3.2 Real time adaptations

If a future version of the CCSA application has to be able to process EEG data in real time (e.g. to display spectra *during* a measurement) a few adaptations and extensions are necessary.

As the CCSA program only processes data from file, the most obvious thing to do, is to implement a separate program that obtains the data during the meas-

urement sessions and writes these data into a file that can be read by the CCSA program.

Signal and wait. The frequency transformation of an epoch can only be performed after an epoch of data was obtained. Therefore an interrupt should be signalled after the writing to file of an epoch of data (by the measurement program) to the waiting CCSA program. After this the frequency transformation and display process can be performed. The measurement program should be informed what epoch length is desired in the CCSA program. The epoch length should be chosen small (< 10 seconds) because of two things: we do not want to wait very long before a spectrum is displayed, and with increasing epoch length the dataprocessing may become too excessive.

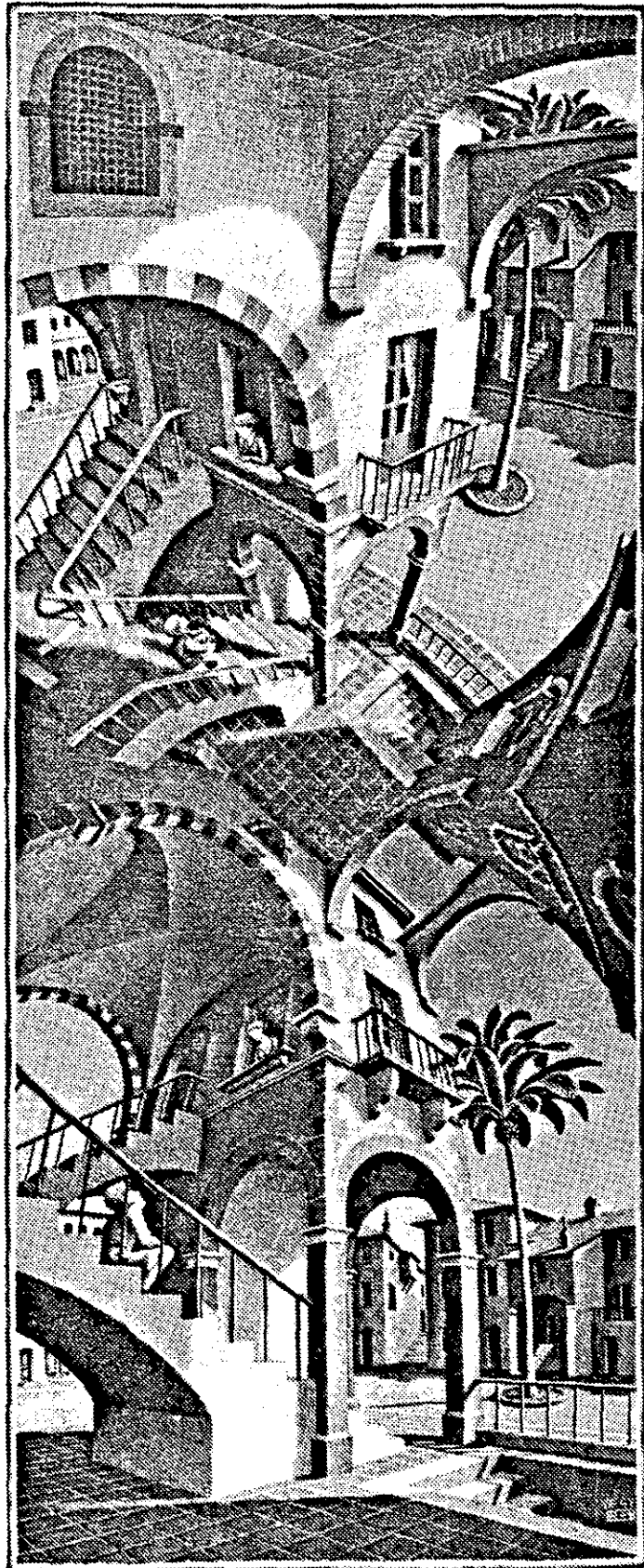
◆ These requirements, as far as the CCSA program is concerned, are already implemented, and need only slight alteration in the source code to come into execution.

Processor sharing. A process-handling routine must be implemented also, dividing the processor-time between each of the described programs. The measurement process will have the highest priority for obtaining measurement samples and writing them to file. The remainder of the processor time can be used by the CCSA program. Since the latter process uses a lot of calculation time a very fast platform has to be used.

If during a real-time measurement an adjustment in the parameter settings of the CCSA application is made, a routine within the CCSA program must take care of displaying the missed spectra (missed during the parameter changing) and then coming back in real-time mode again. If displaying the missed spectra is not feasible in terms of processing time, the data corresponding with these spectra should be skipped in the CCSA program, coming directly back in real-time mode again and therefore *really* missing some spectra.

M.C. Escher:
"Boven & Onder"
("Above & Below"),
lithograph, 1947

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Cordon Art - Baarn
- Holland



5 Testing the CCSA program

As indicated in the previous chapter, analysis of EEG data requires some reflection in advance. Therefore we will consider this data evaluation process in the next pages.

5.1 Computational aspects

"Testing" as described in this paragraph will not only concentrate so much on EEG analysis in respect to anesthetic depth, but will deal with investigating EEG processing as well.

5.1.1 Data testset

From the vast amount of stored EEG data several measurements of the "cats" pilot study (see § 4.1) were selected to be evaluated in the developed CCSA program. These files were made during sessions with well-controlled conditions where the anesthetic dosages were precisely defined (see table 4.1). Another reason for choosing measurements from the pilot study is the fact that in this study only EEG frequencies below 1.5 Hz were filtered out, while the data available from the clinical evoked potential study were high-pass filtered at 5 Hz. Therefore the selected files from the pilot study enables us to review more of the EEG spectra, and the implemented characteristic frequencies calculation will probably be more reliable.

An interesting phenomenon for EEG analysis also occurred in the selected measurements: burst suppression patterns arose during Isoflurane anesthesia (see figure 5.1) [Cluitmans, 1990]. Such signals, showing a flat signal alternated with quick fluctuations, will influence results of EEG processing algorithms to a great extent, and therefore are worth evaluating.

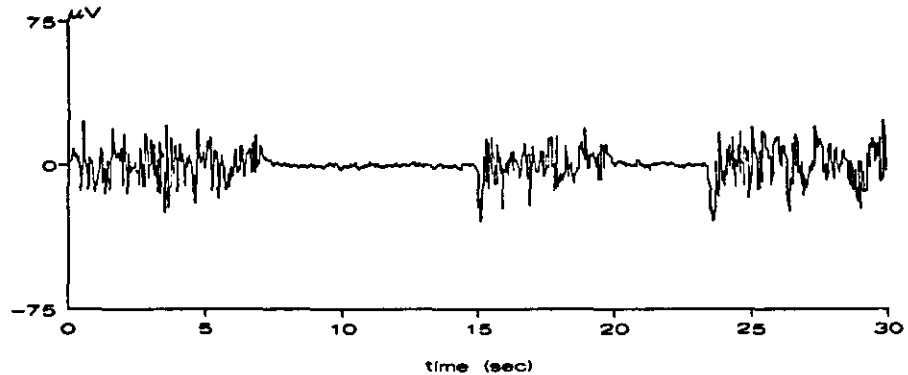


Figure 5.1 Burst suppression during 0.6 MAC Isoflurane anesthesia

The data from 7 files, each containing about 90 seconds of data of different levels in one cat "EN2", were copied into one combined file for input to the CCSA application. This enabled a convenient data analysis as described in §4.3.1.

Resuming, a brief description of the testfile of the cat "EN2", indicated with periods A to G, is given below:

period A	baseline recording, a major artifact occurred in channel 0, causing a DC EEG signal
period B	0.3 MAC N ₂ O administration
period C	0.3 MAC N ₂ O + 0.3 MAC Isoflurane
period D	0.3 MAC N ₂ O + 0.6 MAC Isoflurane
period E	0.6 MAC Isoflurane; this measurement showed burst suppression
period F	0.6 MAC Isoflurane <i>without</i> burst suppression patterns
period G	0.3 MAC Isoflurane

5.1.2 Testing procedure

After some introductory testing for verification of elementary program functioning (proper data reading, filter characteristics, etc.), which will not be described in this report, we are to contemplate precisely *what* effects of adjusting *which* EEG

processing parameters we want to evaluate, besides the obvious interpretation of changes in the spectra in relation to administered drugs ("level" of anesthesia).

Practical restrictions. As the separate levels in the testfile were only measured for 90 seconds, we will not be able to obtain a lot of spectrum parameters if we choose large epoch lengths. Therefore the epoch lengths used in the testing were kept small (see below).

◆ EEG spectra as calculated in this study are the transformation of EEG time signals that were obtained during high-frequency auditory stimulation. The effects on the EEG data are small, but to ensure proper spectrum calculation, the FIR filtering setting was used.

◆ The maximum EEG spectrum frequency has to be chosen high enough to ensure the calculation of the *entire* spectrum, since the FIR filter cuts off all frequency components higher than the chosen $f_{max, EEG}$. After some pre-evaluation of spectra of the data, this $f_{max, EEG}$ was set at 50 Hz.

We will investigate the differences between the time windows that were implemented in the program (see § 4.2.2). This will be evaluated briefly in chapter 6. For the evaluation of using different epoch lengths the Blackman window was used, because this window is believed to give good reduction of spectral leakage (see *Van der Enden et al. [1987]*).

Measurements. The testdata were subjected to the following processing settings:

- maximum EEG frequency 50 Hz
- windowing with the Blackman window
(and brief evaluation of other implemented windows — see § 6.1.2)
- FIR filtering on
- epoch length 2 seconds, 5 seconds and 10 seconds
- ◆ All implemented characteristic frequencies will be calculated and recorded in a file for quantitative evaluation of correlations with anesthetic depth and influence of the different epoch lengths.

Settings of other parameters in the CCSA program will be discussed briefly in § 5.2.

5.1.3 Processing accuracy

In order to obtain an indication of the processing accuracy of the CCSA program, a simple accuracy estimation is performed below. The EEG data as measured during the previously performed studies were written to files in 12 bits precision. As the data process is implemented in high-precision calculation (esp. compared with 12 bits data), the noise in the input signal as a result of this quantisation in 12 bits is taken as a starting point.

For a uniformly distributed error function of the quantisation process the quantisation noise power P_e can be calculated as [Verkroost, 1985]:

$$P_e = 10 \log \frac{\Delta^2}{12} \text{ (dB)} \quad (5.1)$$

Δ : 2^{-b}
where b : number of bits in sample

In our input signal the number of bits b is 12, so 5.1 results in:

$$P_e = 10 \log \frac{2^{-24}}{12} = -83 \text{ dB} \quad (5.2)$$

The frequency transformation process is implemented in calculation with 8 byte precision (64 bits), so we may state that the processing of the EEG data will only add to the quantisation noise power in algorithms that calculate new values out of two or more samples from the *input* array.

The frequency transformation algorithm is the only calculation in the CCSA program that uses several stages where the intermediate results consist of terms of sub-results (i.e. the input array). In the derivation of the Hartley transformation, esp. formulas D.4 (appendix D), we see that there are *three* sub-terms. If we assume that each term is afflicted with a white noise term $n_i(t)$ and that these processes are ergodic and not correlated, we can calculate the noise power after each stage as:

$$\{n_1(t) + n_2(t) + n_3(t)\}^2 = n_1^2(t) + n_2^2(t) + n_3^2(t) = 3n_1^2(t) \quad (5.3)$$

(the cross-terms $n_i(t) \cdot n_j(t)$ are zero)

The calculation 5.3 models the *worst case* noise power in the result (the separate terms add up). We can now calculate the noise contribution of each stage in the Hartley transformation:

$$\delta P_{e, n} = 3 P_{e, n-1} \quad (5.4)$$

$\delta P_{e, n}$: increase of P in stage n
 n : stage number in the Hartley transform ($n \geq 2$)
 $(P_{e, 1} = P_e$: see 5.1)

There are several stages that contribute to the total noise power:

$$\begin{aligned}
 P_{e, S} &= P_{e, 1} + \delta P_{e, 2} + \delta P_{e, 3} + \dots + \delta P_{e, S-1} \\
 &= \frac{\Delta^2}{12} + 3 \frac{\Delta^2}{12} + 9 \frac{\Delta^2}{12} + \dots + 3^{S-1} \frac{\Delta^2}{12} = \frac{\Delta^2}{12} \sum_{n=0}^{S-1} 3^n \quad (5.5)
 \end{aligned}$$

After the last stage S , the Hartley spectrum samples are raised to a square and summated for making a power spectrum (formula 4.12), whereby the noise again is doubled:

$$P_{e, \text{proc.}(S)} = 2 \frac{\Delta^2}{12} \sum_{n=0}^{S-1} 3^n \quad (5.6)$$

S : $\log_2 N$, N is the length of input array

In the first implementation of the CCSA application, maximally 11 stages can occur ($S = 11$):

$$P_{e, \text{proc.}(11)} = -31 \text{ dB} \quad (5.7)$$

From 5.2 and 5.7 we see that the data processing adds 52 dB to the input quantisation noise power in this worst case modelling. If we approximate the normalized ($0 \leq P_u \leq 1$) average input power by $P_u = 1/16$ (stochastic characterisation of an EEG signal, normal distribution [Verkroost, 1985]) we can calculate the resulting information contents I :

$$I_{\text{input}} = 10 \log \frac{P_u}{P_e} = 10 \log 1/16 + 83 = 71 \text{ dB} \quad (5.8)$$

$$I_{\text{total}} = I_{\text{input}} - 52 = 19 \text{ dB} \quad (5.9)$$

This is the information contents of the calculated power spectrum in the worst case model, where all noise terms add up, and where the frequency transformation is performed in the maximum number of 11 stages (whereby the noise is forwarded 11 times in the calculation process — see form. 5.5).

Screen resolution. As we have calculated the (worst case) accuracy of the spectrum calculation, we will assess the accuracy of the spectrum display. This will concern the number of pixels that are available in vertical direction for the display of the power value on a monitor screen.

◆ Only a part of the total available pixels in the y-direction are used for the display of power values (see figure A.1, appendix A). In the CCSA program $\frac{1}{5}$ of the height of the screen is reserved for the power-axis. This implicates that for example in VGA display mode 96 pixels are available for the range of the power values. Logarithmically, this "power resolution" is:

$$R_{display} = 10 \log 96 \cong 20 \text{ dB} \quad (5.10)$$

Comparing 5.10 with 5.9, we see that the resolution on screen is almost the same as the *worst case* modelling of the calculation process.

5.2 Testing the usage of the application

When the development of a new tool is done, one is interested in how users will work with the application. In short, we want to know whether the user-friendliness in the design is good and practical.

In the CCSA application, several features are of interest when considering the usage of this EEG analysis tool:

- options that were implemented for improvement of the ability to see details in the EEG spectra such as the convex/concave display, color display and changing the angle of view of the CSA, should be evaluated on their usefulness.
- the menus that were designed to enable users to adjust parameters such as epoch length and EEG spectrum frequency range and also settings like channel or time window should be easy to use.
- the designed function keys should enable short-cuts for changing parameters and as such, should be useful.

These features are considered again in the next chapter.

6 EEG analysis

EEG data were used for evaluation of the developed CCSA spectrum analysis tool. The first part of this chapter however, also deals with relations with anesthetic levels of the investigated data.

6.1 Anesthetic depth assessment

This paragraph will evaluate characteristic frequencies in the EEG data as measured from the cat "EN2", where we will go into some (technical) details in the first sub-paragraph and consider customized parameters in the second. As the evaluation was concerned with data from only one subject, the observations described in this paragraph should be considered as a case study. No general conclusions can be given.

6.1.1 Quantitative correlations

The measurement of quantitative EEG parameters from the data testset (see § 5.1.1) consisted of letting the CCSA program calculate the characteristic frequencies in the EEG spectra, and recording of these parameters into a file. The results were plotted in several graphs, of which two are printed below. Please refer to § 5.1.1 for information about the anesthesia levels in the seven periods.

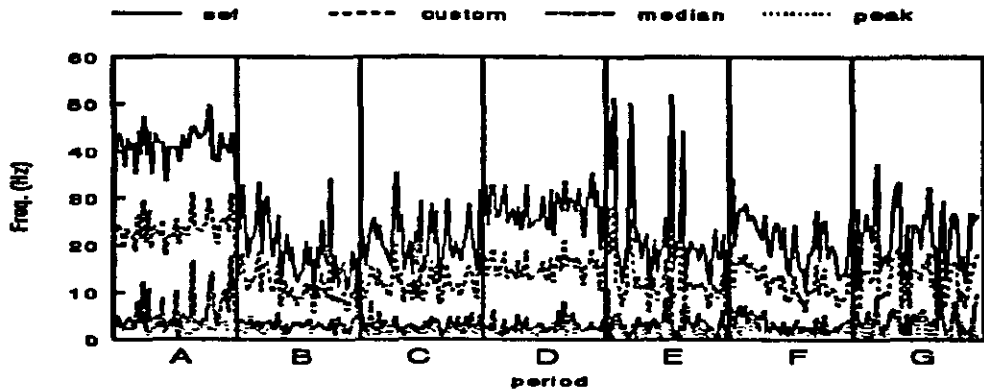


Figure 6.1 Characteristic frequencies, calculated in channel 1, with epoch 2 seconds (Blackman window)

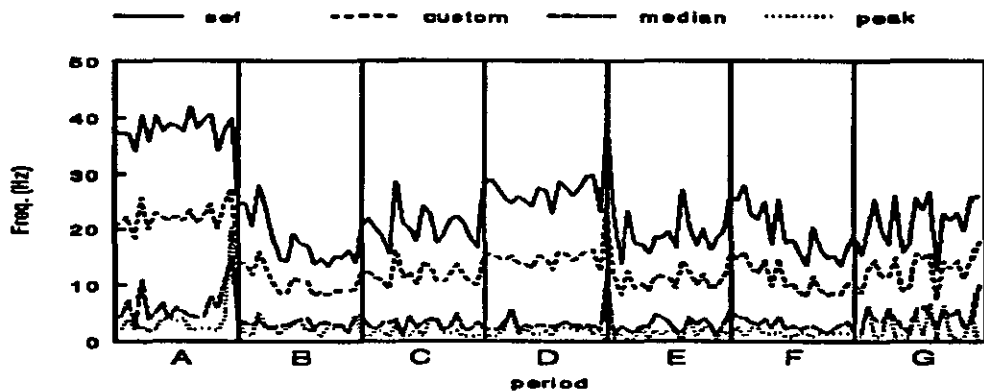


Figure 6.2 Characteristic frequencies, calculated in channel 1, with epoch 5 seconds (Blackman window)

In figures 6.1 and 6.2, the periods A to G in the horizontal axis represent the different levels of anesthesia (separately measured files were put in one combined file), where the duration of each period with constant level is 90 seconds.

In these figures we see that only the spectral edge frequency SEF and the custom frequency show clear variations. The custom frequency will be discussed in the next paragraph 6.1.2, so we will now concentrate on the SEF only. However, we can state for sure that, when considering all measurements in this one subject, generally the baseline recording (period A) showed higher characteristic frequencies (especially the spectral edge and median frequencies).

Burst suppression. Figure 6.1 clearly shows the influence of burst suppression in level 6 (period E). From the extreme variations in the SEF we may conclude that such measurements do not provide reliable results. For verification, see also the other figures in this chapter (with other epoch lengths).

Sequences. There are two sequences of anesthesia levels to be considered in the figures 6.1 and 6.2. The first sequence is given from periods A to D, where after the baseline recording first N₂O was administered, and thereafter N₂O was used together with 0.3 MAC Isoflurane and with 0.6 MAC Isoflurane as anesthetic. We see that the use of *these combinations* of drugs *excites* the EEG.

◆ The second sequence of data is given by period A: baseline, period G: low Isoflurane, period F: high Isoflurane. From the channel 1 recording of this sequence the following tables were made:

Table 6.1 Statistics of spectral edge freq., period A (level 1)

<i>epoch</i>	<i>(sec.)</i>	<i>mean</i>	<i>(Hz)</i>	<i>standard dev.</i>	<i>(Hz)</i>
2		41.36		3.36	
5		38.20		2.13	
10		37.53		1.24	

Table 6.2 Statistics of spectral edge freq., period G (level 5)

<i>epoch</i>	<i>(sec.)</i>	<i>mean</i>	<i>(Hz)</i>	<i>standard dev.</i>	<i>(Hz)</i>
2		21.73		6.74	
5		21.10		4.14	
10		21.15		3.03	

Table 6.3 Statistics of spectral edge freq., period F (level 6)

<i>epoch</i>	<i>(sec.)</i>	<i>mean</i>	<i>(Hz)</i>	<i>standard dev.</i>	<i>(Hz)</i>
2		20.89		5.13	
5		19.52		4.65	
10		19.81		4.15	

We see from these tables that the mean value of the SEF is lower for deeper anesthesia, although the differences between levels 5 and 6 are small.

Another observation of the tables 6.1 → 6.3 indicates the higher standard deviation values for shorter epoch lengths. A conclusion is therefore that when processing EEG data, the epoch length should not be chosen too short. Resulting EEG parameters should be considered together with the standard deviation. Further, quantitative analysis of implications of processing relatively short epochs is to be performed.

6.1.2 Custom parameters

The custom characteristic frequency that was implemented in the CCSA program, is defined as the mean value of the spectral edge frequency SEF and the median power frequency MPF. But as can be seen in the figures in this chapter, the MPF does not change very much in different levels of anesthesia; therefore, the customized parameter shows the same variations as the SEF. In future versions of the program, this custom EEG parameter may be used for other calculations, since this can be changed easily in the source code.

Windows. In figures 6.3 and 6.4 measurements with different time windows (see § 4.2.2) are presented. The usefulness of being able to choose different time windows can be seen in the figures: the influence of the burst suppression patterns, present in period E, is more clearly seen in figure 6.3, calculation with the Blackman window. The “dip” in the characteristic frequencies, caused by an artifact in the baseline recording — period A, is more dramatic in using the Bartlett time window, and therefore perhaps easier to detect.

◆ However, generally speaking the implemented time windows give the same results. The only two, major, differences are: one, the Rectangle and Bartlett

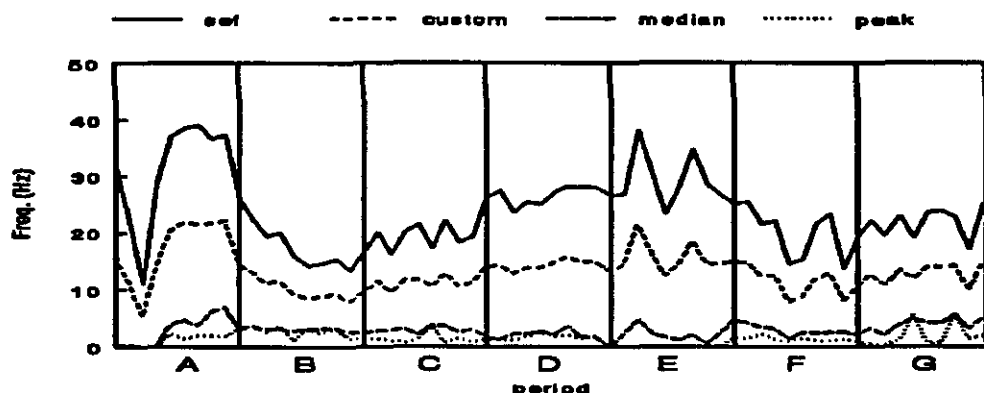


Figure 6.3 Characteristic frequencies, calculated in channel 0, with epoch 10 seconds, using the Blackman window

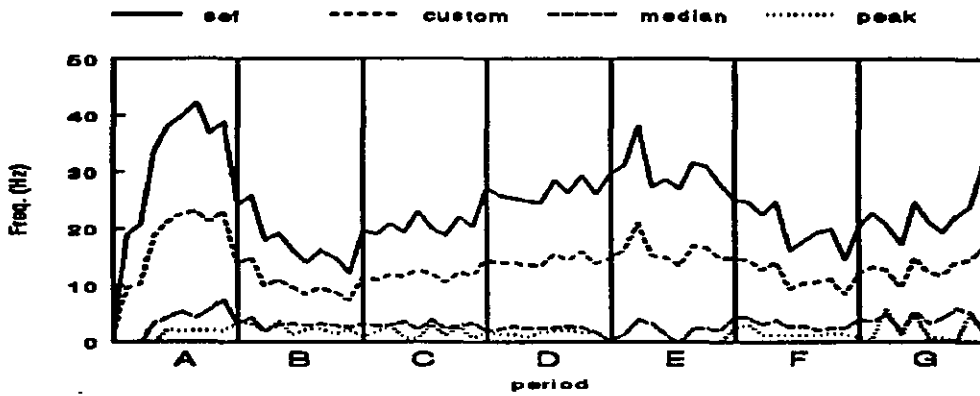


Figure 6.4 Characteristic frequencies, calculated in channel 0, with epoch 10 seconds, using the Bartlett window

windows do not reduce power contents of the original EEG signal as much as other windows, and two, the Hanning, Hamming and Blackman windows use more processing time (see § 4.2.2). So for large arrays (large *epochs*, $f_{max, eeg}$) the use of the latter windows can be dissuaded, the more so as processing *large* arrays of EEG data *already* reduces the spectral leakage phenomenon (see chapter 4).

6.2 Using the CCSA application

6.2.1 Overall performance

In general, I think I may state that the performance of the developed EEG spectrum analysis tool is good. A few researchers already experimented with the program and indicated some minor alterations. About the usage, the following remarks can be made:

- Of the improvements that were made on the CSA technique, the use of different colors for the successive spectra and an angle of view different from 90 degrees (compare for instance figure 2.2 – chapter 2, to the CCSA in figure 3.2) are pleasant to use, and really make the display of

spectra more clear. The concave CSA option is not frequently used, but this may be different with different data.

- The menus provide easy-to-change parameter settings, although users in the beginning can not easily remember what to change in which menu (see appendix A). Changing a few settings/options in different menus at the same time is sometimes wanted, but this is not possible in the current design.
- Shortcut keys for changing e.g. the channel in a file to be processed are not frequently used. The most useful function keys are those that enable the "stepping" through a file (next/previous CCSA, F4 and F5, see appendices A and B).

6.2.2 Completeness of analysis options

The CCSA application program proved to be fairly complete, as to the display of data and possibilities in changing parameters, but only one major extension may be very useful: the display of the time data that is processed. With this extension, investigators of EEG spectra are able to detect major artifacts in the EEG, and are then "on-line" able to assess the reliability of the resulting spectra.

The parameter settings that are displayed on screen as well as in the menus (see figure A.1, appendix A) are sufficient. Other settings are visible in the CCSA display or are easily remembered.

6.3 Summary

This chapter presented results of a case study of EEG data as measured in one cat. Because of this small testset, general conclusions cannot be given. However, in the measured characteristic frequencies PPF, MPF and SEF we observed only significant changes in relation to anesthetic depth in the SEF parameter. Furthermore, the processing of not too short epoch lengths (> 2 seconds) can be recommended.

The data were particularly used for evaluation of the developed CCSA tool, and from the use of this application by several people we can conclude that the tool

provides a useful extension for the Anesthetic depth project. From now on the work in this project is not only concerned with the auditory evoked potential studies in subjects under anesthesia, but the assessment and design of "direct" EEG parameters will also be part of the research.

7 Conclusions

7.1 General evaluation

Reflecting on the development and testing as described in the previous chapters, this study comes to a conclusion by giving the overall results and achievements below.

The main purpose of this study was to extend the Anesthetic depth project of the division of Medical Electrical Engineering at the Eindhoven University of Technology into the field of EEG monitoring of anesthetic depth. As a result of this study, the analysis of EEG spectra and parameters in these spectra can be performed with the developed CCSA application in a flexible manner, where new, customized EEG parameters can be easily implemented by researchers with some programming experience.

A brief case study was performed on EEG data in one subject as measured during previous studies. Technical details of this study indicate that different properties of data used for evaluation in the frequency domain influence the usefulness of EEG spectrum analysis. Conclusions should be drawn with caution.

In this case study, we have also tried to assess anesthesia levels, through analysis of characteristic frequencies calculated in the EEG spectra. The only major conclusion to be stated here, is the observation that the "spectral edge frequency" seems to be a promising EEG parameter for assessment of anesthetic depth.

Further research is necessary to analyze the EEG data available within the Anesthetic depth project. New designed EEG parameters can be investigated with the developed EEG analysis tool.

7.2 Annotations

7.2.1 Future use of the CCSA program

Within the Anesthetic depth project the developed CCSA program shall be used for evaluation of EEG measurements, and as a tool for trying to define and investigate (new) parameters that have definite correlations with anesthetic depth. This will be part of evoked potential studies (already two EP studies were performed — see *Cluitmans [1990]*), where the incorporation of the EEG parameters should help in the assessment of the level of anesthesia and especially awareness.

I want to state very clearly here that the CCSA program is a research-tool; we do not mean to impose a new, additional anesthesia monitoring screen on the anesthetist, for he or she already has an extensive task of interpreting all kinds of patient-signals during an operation. If any EEG (spectrum) parameter as mentioned above has been found, further research is necessary to investigate the possible future use in an automatic anesthesia monitoring and control system.

7.2.2 Development of extensions

In future usage of the developed CCSA program users (researchers) may come to think of some useful additions they would like to see implemented. Easy implementation depends in the first place on the complexity of the problem and of course also on the experience of the programmer.

Some possible extensions that I have thought of are:

- display of the processed time signal simultaneously with the power spectrum plots, enabling investigators to “see what’s going on” in the original signal, for example for detection of “burst suppression” patterns. For this, use could be made again of the display-area of the “messages/function-keys” bar at the bottom of the designed screen (see appendix A).

- display on screen of exact values of characteristic frequencies. These values can only be reviewed exactly now in a recorded file. Plotting them on screen for instance as floating point numbers may prove to be useful when the accuracy of the visual screen evaluation is too limited (see also § 5.1.3).
- printing to file of the values of the spectrum arrays of a selected portion of the CCSA spectra, thus enabling to review spectra with the exact values of the frequency components. Again, accuracy on screen limits this during the *display* of spectra. A convenient format must be defined for this writing to file of a lot of (floating point) numbers.
- extending the program for more (new) EEG spectrum parameters. Implementation of this will probably be simple, as already some example parameters were implemented (characteristic frequencies).
- real-time processing for on-line spectrum evaluation during measurement sessions. The on-line calculation of spectra could be used for previewing derivations of the measured data, and therefore might be used as an indication for the information contents and maybe for the "usefulness" of the measurement. Real-time adaptations are already (briefly) described in § 4.3.2.

The above mentioned possibilities could provide an even more flexible CCSA application, but implementation is only meaningful if there really is a need for these extensions.

7.3 Final remarks

In this report, EEG data evaluation is brief. Although some general observations of anesthetic depth correlates were made, the data evaluation particularly focussed on the use of the newly developed EEG spectrum analysis tool. Implications of changes in the spectrum calculation process on the usefulness and quality of the resulting EEG derivatives or possible anesthetic depth parameters were investigated.

Therefore, the Anesthetic depth project of the division of Medical Electrical Engineering at the TUE will evaluate extensively all available data previously

measured or measured in the future. The auditory evoked potential studies can then be extended by taking into account the new found EEG parameters and a more reliable (automatic) anesthetic depth assessment should come within reach.

Glossary

ADC	analog to digital conversion
AEP	auditory evoked potential
aliasing	distortion in a signal as a result of sampling the original signal with a too low sample frequency
alpha (α)	(in EEG:) main frequency distribution in the range 8 Hz - 12 Hz (approx.)
amnesia	loss of memory (in this report especially:) induced by anesthesia [<i>Merriam-Webster Inc., 1986</i>]
analgesia	insensibility to pain without loss of consciousness [<i>Merriam-Webster Inc., 1986</i>]
anesthesia	loss of sensation and usually of consciousness without loss of vital functions, artificially produced by the administration of one or more agents that block the passage of pain impulses along nerve pathways to the brain [<i>Merriam-Webster Inc., 1986</i>]
anesthesiologist	a physician specializing in <i>anesthesiology</i> < : branch of medical science dealing with anesthesia and anesthetics> [<i>Merriam-Webster Inc., 1986</i>]
anesthetist	one who administers anesthetics [<i>Merriam-Webster Inc., 1986</i>]
ANSI	American National Standards Institute
beta (β)	(in EEG:) main frequency distribution in the range 12 Hz - 30 Hz (approx.)

<i>brain waves</i>	rhythmic fluctuations of voltage between parts of the brain resulting in the flow of electric current [<i>Merriam-Webster Inc., 1986</i>]
<i>CCSA</i>	convex/concave compressed spectral array
<i>CFAM</i>	cerebral functioning analyzing monitor
<i>cortex</i>	the outer layer of grey matter of the cerebrum and cerebellum that contains most of the higher nervous centers [<i>Merriam-Webster Inc., 1986</i>]
<i>CNS</i>	central nervous system
<i>CSA</i>	compressed spectral array
<i>DC</i>	direct current
<i>delta (δ)</i>	(in EEG:) main frequency distribution in the range 0 Hz - 4 Hz (approx.)
<i>DFT</i>	discrete Fourier transform
<i>DHT</i>	discrete Hartley transform
<i>DSA</i>	density spectral array
<i>EEG</i>	electroencephalogram: the tracing of brain waves made by an <i>electroencephalograph</i> < : an apparatus for detecting and recording brain waves > [<i>Merriam- Webster Inc., 1986</i>]
<i>EMDABS</i>	electrophysiologic monitoring database system
<i>EP</i>	evoked potential
<i>epoch</i>	time interval to be frequency transformed
<i>ERDA</i>	event recording and data acquisition
<i>ergodic</i>	of or relating to a process in which every sequence or sizeable sample is the same statistically and therefore equally representative of the whole [<i>Merriam-Webster Inc., 1986</i>]
<i>FFT</i>	fast Fourier transformation
<i>FHT</i>	fast Hartley transformation
<i>FIR</i>	finite impuls response

<i>hypoxia</i>	deficiency of oxygen reaching the tissues of the body whether due to environmental deficiency or impaired respiratory and circulatory organs [Merriam-Webster Inc., 1986]
<i>ischemia</i>	localized tissue <i>anemia</i> < : a condition in which the blood is deficient in red blood cells, hemoglobin, or both or deficient in total volume due to obstruction of the inflow of arterial blood > [Merriam-Webster Inc., 1986]
MAC	minimal alveolar concentration < : the concentration of an inhalation anesthetic drug at 1 atmosphere equilibrium required to abolish movement in response to a noxious stimulus in 50 percent of a test population >
MPF	median power frequency
NLA	non-linear analysis
<i>Nyquist's theorem</i>	(also called <i>sampling theorem</i>) a signal may be uniquely represented by discrete samples spaced no more than half the bandwidth apart
PPF	peak power frequency
SEF	spectral edge frequency
SNR	signal to noise ratio
<i>theta</i> (θ)	(in EEG:) main frequency distribution in the range 4 Hz - 8 Hz (approx.)
VGA	Video Graphics Array

References

Bart, A.J. and J. Homi, H.W. Linde (1971)

Changes in power spectra of electroencephalograms during anesthesia with fluoroxene, methoxyflurane and ethrane.

Anesth. and Analg., Vol. 50 (1971), No. 1, p. 53-63.

Basar, E. (1980)

EEG-Brain dynamics: relation between EEG and brain evoked potentials.

Amsterdam: Elsevier, 1980.

Berezowskyj, J.L. and J.A. McEwen, G.B. Anderson, L.C. Jenkins (1976)

A study of anaesthesia depth by power spectral analysis of the electroencephalogram (EEG).

Can. Anaesth. Soc. J., Vol. 23 (1976), No. 1, p. 1-8.

Bickford, R.G. and T.W. Billinger, N.I. Flemming, L. Stewart (1972)

The compressed spectral array (CSA): a pictorial EEG.

Proc. San Diego Biomedical Symposium, San Diego, February 2-4, 1972. San Diego: San Diego Biomedical Symposium, 1972. Vol. 11. P. 365-370.

Bickford, R.G. and J. Brimm, L. Berger, M. Aung (1973)

Application of compressed spectral array in clinical EEG. In: Automation of clinical electroencephalography.

Ed. by P. Kellaway and I. Petersén. New York: Raven Press, 1973. P. 55 - 64.

Bickford, R.G. (1979)

Newer methods of recording and analyzing EEGs.

In: Current practice of clinical electroencephalography. Ed. by D.W. Klass and D.D. Daly. New York: Raven Press, 1979. P. 451-480.

Blacher, R.S. (1984)

Awareness during surgery.
Anesthesiology, Vol. 61 (1984), p. 1-2.

Blom, J.A. (1990)

The SIMPLEXYS experiment: real time expert systems in patient monitoring.
Ph. D. Thesis. Eindhoven University of Technology, 1990.

Booij, L.H.D.J. (1989)

Bewust van bewustzijn. (Aware of awareness. In Dutch).
Nijmegen: Nijmegen Catholic University, 1989.

Bogetz, M.S. and J.A. Katz (1984)

Recall of surgery for major trauma.
Anesthesiology, Vol. 61 (1984), p. 6-9.

Bovill, J.G. and P.S. Sebel, A. Wauquier, P. Rog (1982)

Electroencephalographic effects of sufentanil anaesthesia in man.
Br. J. Anaesth., Vol. 54 (1982), p. 45-52.

Bracewell, R.N. (1986)

The Hartley transform.
New York: Oxford University Press, 1986.

Clark, D.L. and E.C. Hosick, B.S. Rosner (1971)

Neurophysiological effects of different anesthetics in unconscious man.
J. Appl. Phys., Vol. 31 (1971), p. 884-891.

Cluitmans, P.J.M. (1990)

Neurophysiological monitoring of anesthetic depth.
Ph. D. Thesis. Eindhoven University of Technology, 1990.

Collins, V.J. (1976)

Principles of anesthesiology.
2nd ed.. Philadelphia: Lea & Febiger, 1976.

De Jong, P.G.M. (1986)

Ontwikkeling van een event recording module voor een event recording en data
acquisitie systeem. (Development of an event recording module for an event
recording and data acquisition system. In Dutch).
M. Sc. Thesis. Division of Medical Electrical Engineering, Faculty of Electrical
Engineering, Eindhoven University of Technology, 1986.

Eger, E.I. (1984)

Monitoring the depth of anesthesia.

In: *Monitoring in anesthesia*. 2nd ed.. Ed. by L.J. Saidman and N.T. Smith.
Boston: Butterworth, 1984. P. 1-17.

Faulconer, A. and R.G. Bickford (1960)

Electroencephalography in anaesthesiology.

Springfield, ILL.: Charles C. Thomas, 1960.

Findeiss, J.C. and G.A. Kien, K.O.W. Huse, H.W. Linde (1969)

Power spectral density of the electroencephalogram during halothane and cyclopropane anesthesia in man.

Anesth. and Analg., Vol. 48 (1969), p. 1018-1023.

Grundy, B.L. (1985)

Selecting an EEG machine for your practice, if, when, and what machine, EEG monitoring in the operating room and critical care unit.

In: *EEG monitoring in anesthesia & critical care: state of the art: 1985*, March 8, 9 & 10 (Course in Houston). Betty Grundy, M.D., Course Director, Department of Anesthesiology, University of Florida, J. Hillis Miller Health Center, Gainesville, FLA.

Course book.

Hartley, R.V.L. (1942)

A more symmetrical Fourier analysis applied to transmission problems.

Proc. IRE, Vol. 30 (1942), p. 144-150.

Interspec Inc. (1985)

EEG and evoked potential monitoring: during and after surgery.

Interspec Inc., 1100 E. Hector St., Conshohocken, PA, 1985.

Monograph, revision 3.

Jackson, L.B. (1989)

Digital filters and signal processing.

2nd ed.. Boston: Kluwer, 1989.

Jansen, J.W. (1990)

Artefact detectie en verwijdering in auditiële evoked potentials. (Artefact detection and removal in auditory evoked potentials. In Dutch).

M. Sc. Thesis. Division of Medical Electrical Engineering, Faculty of Electrical Engineering, Eindhoven University of Technology, 1990.

Kernighan, B.W. and D.M. Ritchie (1988)

The C programming language.

2nd ed.. Englewood Cliffs: Prentice Hall, 1988.

Kuipers, H. (1991)

Ontwerp en formele definitie van het 'Study/Subject/Session' gedeelte van het data model voor het klinische informatie systeem EMDABS. (Design and formal definition of the 'Study/Subject/Session' part of the data model for the clinical information system EMDABS. In Dutch).

Division of Medical Electrical Engineering, Faculty of Electrical Engineering, Eindhoven University of Technology, 1991.

Internal report 91EME01.

Levy, W.J. and H.M. Shapiro, G. Marushak, E. Meathe (1980)

Automated EEG processing for intraoperative monitoring.

Anesthesiology, Vol. 53 (1980), p. 223-236.

Levy, W.J. and B.L. Grundy, N.T. Smith (1984)

Monitoring the electroencephalogram and evoked potentials during anesthesia.

In: Monitoring in anesthesia. 2nd ed.. Ed. by L.J. Saidman and N.T. Smith.

Boston: Butterworth, 1984. P. 227-267.

Levy, W.J. (1986)

Power spectrum correlates of changes in consciousness during anesthetic induction with enflurane.

Anesthesiology, Vol. 64 (1986), p. 688-693.

Levy, W.J. (1987)

Effect of epoch length on power spectrum analysis of the EEG.

Anesthesiology, Vol. 66 (1987), p. 489-495.

McCallum, W.C. (1989)

Attention.

In: Encyclopædia Britannica, 15th ed., Vol. 14. Chicago: Encyclopædia Britannica, 1989. P. 380-386.

Media Cybernetics (1988a)

HALO '88™ Graphics kernel system: library reference.

Silver Spring, MD: Media Cybernetics, 1988.

Reference manual.

Media Cybernetics (1988b)

HALO '88™ Graphics kernel system: language and device reference.
Silver Spring, MD: Media Cybernetics, 1988.

Reference manual.*Merriam-Webster Inc. (1986)*

Webster's third new international dictionary of the English language - unabridged.

Chicago: Encyclopædia Britannica, 1986.

Microsoft® Corporation (1990)

Writing portable programs.

In: Microsoft® C: advanced programming techniques. Redmond, WA: Microsoft® Corporation, 1990. P. 317-342.

Programmers manual.*Pfaffenhöfer, F.M. and P.J.M. Cluitmans, H.M. Kuipers (1991)*

EMDABS: design and formal specification of a datamodel for a clinical research database system.

Eindhoven: Faculty of Electrical Engineering, Eindhoven University of Technology, 1991.

EUT report 91-E-250.*Pronk, R.A.F. (1986)*

Peri-operative monitoring.

In: Handbook of electroencephalography and clinical neurophysiology. Revised series. Vol. 2: Clinical applications of computer analysis of EEG and other neurophysiological signals. Ed. by F.H. Lopes da Silva and W. Storm van Leeuwen, A. Remond. Amsterdam: Elsevier, 1986.

Pryse-Phillips, W.E.M. (1989)

Nervous system diseases and disorders.

In: Nerves and nervous systems, In: Encyclopædia Britannica. 15th ed., Vol. 24. Chicago: Encyclopædia Britannica, 1989. P. 836-858.

Rampil, I.J. and F.J. Sasse, N.T. Smith, B.H. Hoff, D.C. Flemming (1980)

Spectral edge frequency: a new correlate of anesthetic depth.

Anesthesiology, Vol. 53 (suppl.) (1980), No. 3, p. S12 (abstract).

Rampil, I.J. and N.T. Smith (1984)

Computers in anesthesiology.

In: Monitoring in anesthesia. 2nd ed.. Ed. by L.J. Saidman and N.T. Smith. Boston: Butterworth, 1984. P. 441-496.

Schwilden, H. and J. Schüttler, H. Stoeckel (1987a)

Closed-loop feedback control of methohexital anesthesia by quantitative EEG analysis in humans.

Anesthesiology, Vol. 67 (1987), p. 341-347.

Schwilden, H. and H. Stoeckel (1987b)

Quantitative EEG analysis during anaesthesia with isoflurane in nitrous oxide at 1.3 and 1.5 MAC.

Br. J. Anaesth., Vol. 59 (1987), p. 738-745.

Schwilden, H. and H. Stoeckel, J. Schüttler (1989)

Closed-loop feedback control of propofol anaesthesia by quantitative EEG analysis in humans.

Br. J. Anaesth., Vol. 62 (1989), p. 290-296.

Sebel, P.S. and J.G. Bovill, A. Wauquier, P. Rog (1981)

Effects of high-dose fentanyl anesthesia on the electroencephalogram.

Anesthesiology, Vol. 55 (1981), p. 203-211.

Sebel, P.S. and D.E. Maynard, E. Mauor, M. Frank (1983)

The cerebral function analyzing monitor (CFAM).

Br. J. Anaesth., Vol. 55 (1983), p. 1265-1270.

Sebel, P.S. (1985)

Effects of anesthetics on the EEG.

In: EEG monitoring in anesthesia & critical care: state of the art: 1985, March 8, 9 & 10 (Course in Houston). Betty Grundy, M.D., Course Director, Department of Anesthesiology, University of Florida, J. Hillis Miller Health Center, Gainesville, FLA.

Course book.

Simons, A.J.R. and E.H.J.F. Boezeman, R.A.F. Pronk (1989)

Automatic EEG monitoring of anaesthesia.

Baillière's Clin. Anaesth., Vol. 3 (1989), No. 3, p. 623-646.

Smith, N.T. and I.J. Rampil, F.J. Sasse, B.H. Hoff, D.C. Flemming (1979)
EEG during rapidly changing halothane or enflurane.
Anesthesiology, Vol. 51 (suppl.) (1979), No. 3, p. S4 (abstract).

Spehlman, R. (1981)
EEG Primer.
Amsterdam: Elsevier, 1981.

Van den Enden, A.W.M. and N.A.M. Verhoeckx (1987)
Digitale signaalbewerking (Digital signalprocessing. In Dutch).
Amerongen, The Netherlands: Delta Press, 1987.

Van der Aa, J.J. (1990)
Intelligent alarms in anesthesia: a real time expert system application.
Ph. D. Thesis. Eindhoven University of Technology, 1990.

Van der Ende, N. and E.H.J.F. Boezeman, S.J. Hengeveld, A.J.R. Simons (1990)
Is sound-related desynchronization of the alpha-rhythm in the
electroencephalogram a useful criterion for the detection of awareness?
In: Memory and Awareness in Anaesthesia. Ed. by B. Bonke and W. Fitch, K.
Millar. Amsterdam: Swets & Zeitlinger, 1990. P. 362-364.

Värri, A. (1988)
Digital processing of the EEG in epilepsy.
Licentiate Thesis. Tampere University of Technology, Finland, 1988.

Verkroost, G. (1985)
Signalen III (Signals III. In Dutch).
Faculty of Electrical Engineering, Eindhoven University of Technology, 1985.
Lecture notes, code 5625.

Withington, P.S. and J. Morton, R. Arnold, P.S. Sebel, R. Moberg (1986)
Assesment of power spectral edge for monitoring depth of anaesthesia using
low methohexitone infusion.
Int. J. Clin. Monit. Comput., Vol. 3 (1986), p. 117-122.

A. Description of the CCSA program & display layout

Description

The CCSA program processes EEG data for analysis of the power spectra of an EEG recording (one channel at a time). The chronological spectra are displayed as a CCSA: "Convex/concave (color) Compressed Spectral Array".

For starting the program, the following arguments are valid:

ccsa <timedata file> <calibration file> <settings file>

These files are checked on accessibility at startup time.

If the third argument is left out, a default settings file is used. If the first and second names are not given, the program starts up normally (loading the default settings file), and then first asks for the filename of the timedata file to be analyzed, and after this asks for the filename of the calibration file.

A *calibration* file contains the calibration and offset values for each of the channels (encoded in the samples — see § 4.1.3) and the filepositions (in bytes) in the timedata file between which the calibration values are valid. Also a "comment"-string can be specified, which is displayed during the plotting of the corresponding data.

A *settings* file contains information on how spectra are to be calculated and displayed.

Four menus are available: "options", "characteristic frequencies", "settings" and "function keys". The last menu only gives a brief description of the use of the function/shortcut keys (see appendix B).

- The **options** menu enables to change:
fsample, fmax, eeg, epoch length, adjusting of epoch (yes/no), normalized/squared voltage CCSA spectra, rescaling of CCSA (yes/no), time interval begin of CCSA, opening of the characteristic frequencies menu.
- The **characteristic frequencies** menu enables to choose/adjust:
plotting of MPF, PPF, SEF, custom frequency (yes/no), spectral edge factor, recording of the char. frequencies (yes/no).

- The **settings** menu enables to choose/change:
 - convex/concave display, color/nocolor, number of lines in the CCSA, angle of view, Time window (Rectangle / Bartlett / Hanning / Hamming / Blackman), FIR filtering (yes/no), channel (0/1/...), Saving of settings file, Loading of time-data file (& calibration file), Restoring of default settings, Loading of a new settings file.*

Messages are displayed when a user tries to adjust a parameter to a wrong value (e.g. f_{sample} must always be larger than twice $f_{max, eeg}$).

Display layout

A simplified representation (black & white) of the CCSA display layout on a monitor screen is printed in figure A.1

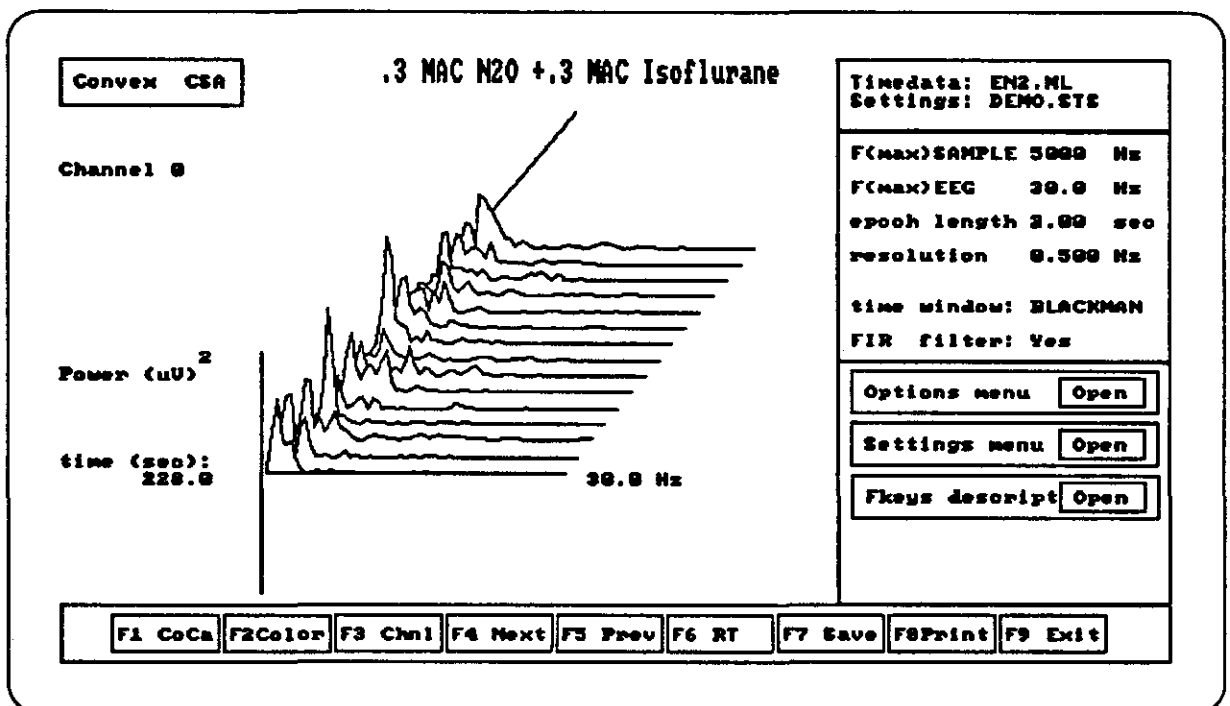


Figure A.1 Display layout of the CCSA program

B. Flow chart of the CCSA menu structure

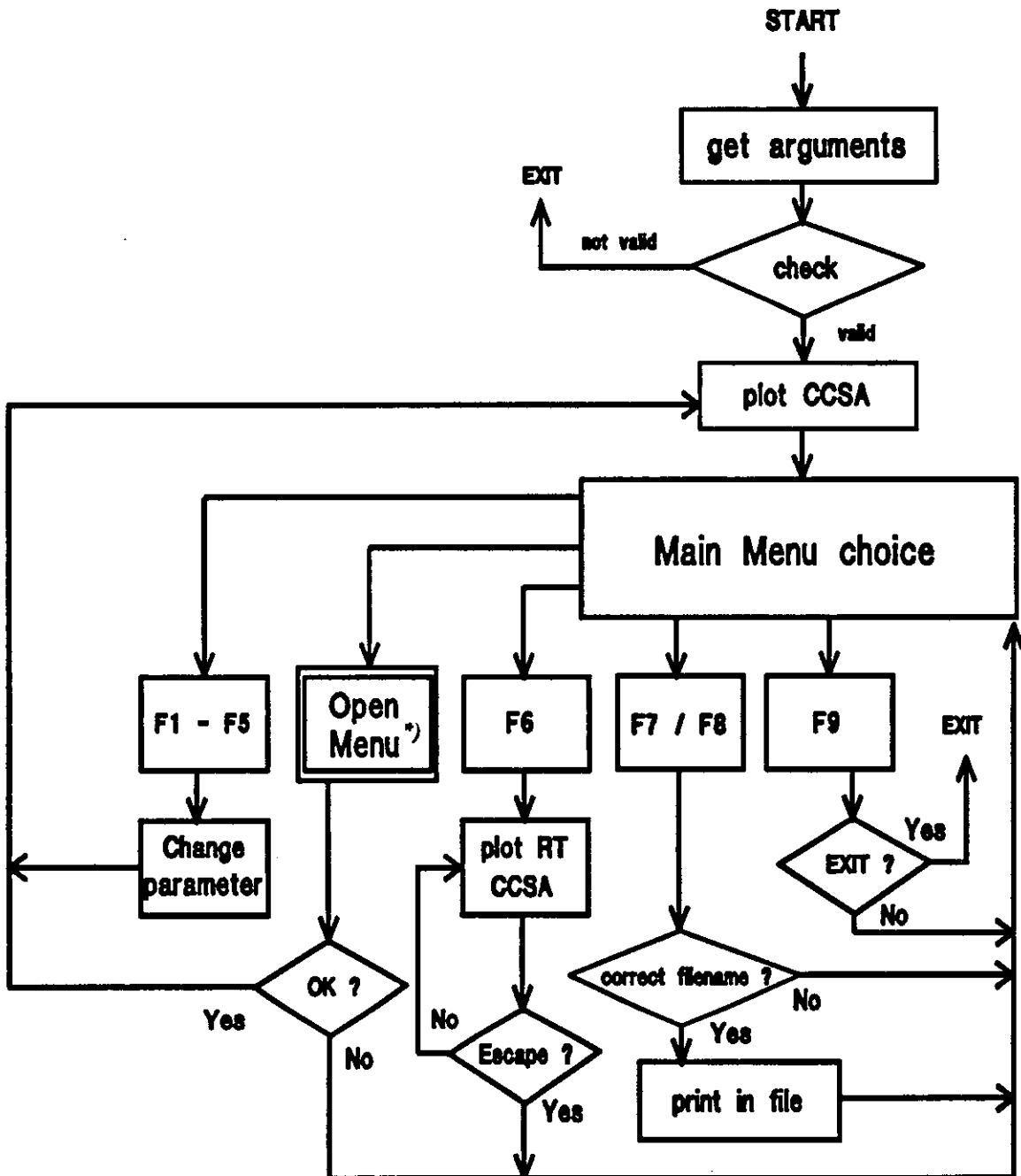


Figure B.1 Main CCSA flow chart

*) see figure B.2

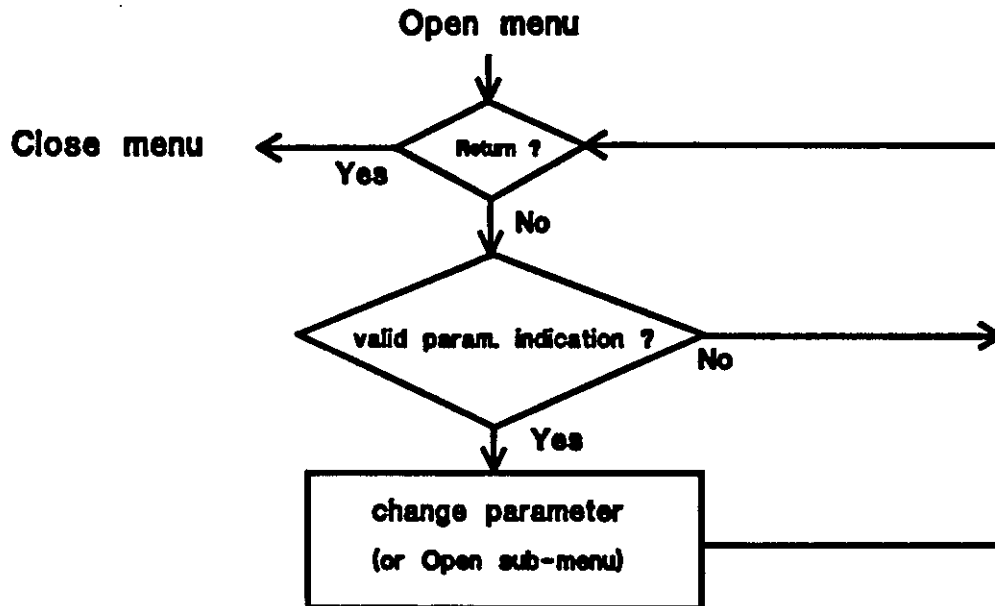


Figure B.2 Chart of flow in a menu

Explanatory notes:**arguments :**

timedata, calibration, settings files

F1 : convex / concave

F2 : color / nocolor

F3 : next channel

F4 : next CCSA (time shift in timedata file)

F5 : previous CCSA (time shift in timedata file)

Menus :

Options, Settings, Function keys menu

Sub-menu :

Characteristic frequencies menu

F6 : plot Real Time (simulation) till Escape key is hit

F7 : save current parameters settings to a file

F8 : print current CCSA screen to a file

F9 : exit the program

C. Calculation of the FIR filter transfer value

The FIR filter transfer function (formula 4.4 — chapter 4) does not have a definite mathematical solution. Its value depends on two variables, L and Ω , and therefore we can only approximate Ω as a function of L .

In low-pass filtering transfer functions, we are interested in the cut-off frequency $\Omega_{cut-off}$, which is the -3 dB point in logarithmic power spectrum plots: at this point the power of the input signal is halved, which implies that the amplitude has diminished with the factor $\sqrt{0.5}$. From figure 4.2 we can deduce that $\Omega_{cut-off}$ will be approximately proportional to π/L , and therefore we will derive the value of $H(e^{j\Omega'_{cut-off}})$ for:

$$\Omega'_{cut-off} = \frac{\pi}{vL}, \quad v > 0 \quad (C.1)$$

With this formula we obtain an estimation $\Omega'_{cut-off}$ for the precise cut-off frequency $\Omega_{cut-off}$. Below, we will show how well $\Omega_{cut-off}$ is estimated, and what value of v should be chosen.

With C.1 the FIR filter transfer function becomes (compare to form. 4.4):

$$H(e^{j\Omega'_{cut-off}}) = \frac{1}{2L+1} \frac{\sin(\frac{2L+1}{2} \frac{\pi}{vL})}{\sin(\frac{\pi}{2vL})} \quad (C.2)$$

We can now calculate the limit:

$$\begin{aligned} \lim_{L \rightarrow \infty} H(e^{j\Omega'_{cut-off}}) &= \lim_{L \rightarrow \infty} \frac{1}{2L+1} \frac{\sin(\frac{2L+1}{2} \frac{\pi}{vL})}{\sin(\frac{\pi}{2vL})} \\ &= \lim_{L \rightarrow \infty} \frac{1}{2L} \frac{\sin(\frac{2L}{2} \frac{\pi}{vL})}{\sin(\frac{\pi}{2vL})} = \lim_{L \rightarrow \infty} \frac{\sin(\frac{\pi}{v})}{2L(\frac{\pi}{2vL})} = \frac{\sin(\frac{\pi}{v})}{(\frac{\pi}{v})} = \text{sinc}(\frac{1}{v}) \end{aligned} \quad (C.3)$$

This resulting "sinc"-function should have the value $\sqrt{0.5}$ for $\Omega_{cut-off}$. In a "sinc"-table we find:

$$H(e^{j\Omega'_{cut-off}}) = \text{sinc}\left(\frac{1}{v}\right) = \sqrt{0.5} = 0.7071$$

$$\Rightarrow v = 2.257$$

But, while we have only calculated an *estimation* for the cut-off frequency $\Omega_{cut-off}$, the actual FIR filter transfer value (formula C.2) is verified below for the calculated value $v = 2.257$.

Table C.1 FIR filter transfer value for different L

L	$H(e^{j\Omega'_{cut-off}})$
1	0.452
2	0.578
5	0.655
10	0.681
20	0.694
50	0.702
100	0.704

In table C.1 we see that the FIR transfer value at our estimated $\Omega_{cut-off}$ is smaller than the desired value of $\sqrt{0.5}$ for small L , but while we will have fairly large L this is acceptable; for example if $f_{sample} = 5000$ Hz, $f_{max, EEG} = 50$ Hz:

$$L = \frac{f_{sample}}{2 f_{max, EEG} 2.257} = 22.15 \quad (C.4)$$

Concluding we can say that the FIR filter transfer value at the chosen cut-off frequency $f_{max, EEG} \Leftrightarrow \Omega'_{cut-off}$ (see § 4.2.1) is not exactly the -3 dB point $\Omega_{cut-off}$, but one should keep in mind the fact that any aliasing-effects will influence the spectrum *only close* to the $\Omega_{cut-off}$, because the transfer value rapidly diminishes to -40 dB anyway for increasing Ω (see figure 4.2), which implies that only $1/100$ (1 percent) of a signal passes through the filter.

D. Frequency transformation: Fourier versus Hartley

Fast Fourier transformation

A handsome way of calculating a power spectrum is called *Fast Fourier Transformation* (FFT). In this technique the original Discrete Fourier Transform (DFT — see form. 4.8, chapter 4) is splitted up into a part with the even indexes in an array and a part with the odd indexes:

$$\begin{aligned}
 F(k)_N &= \sum_{n=0}^{N-1} f(n) \left\{ \cos\left(\frac{2\pi}{N} kn\right) - j \sin\left(\frac{2\pi}{N} kn\right) \right\} \\
 &= \sum_{n=0}^{\frac{N}{2}-1} f(2n) \left\{ \cos\left(\frac{2\pi}{N} 2kn\right) - j \sin\left(\frac{2\pi}{N} 2kn\right) \right\} \\
 &\quad + \sum_{n=0}^{\frac{N}{2}-1} f(2n+1) \left\{ \cos\left(\frac{2\pi}{N} (2n+1)k\right) - j \sin\left(\frac{2\pi}{N} (2n+1)k\right) \right\} \\
 &= A(k)_{N/2} + \cos\left(\frac{2\pi}{N} k\right) B(k)_{N/2} - j \sin\left(\frac{2\pi}{N} k\right) B(k)_{N/2} \tag{D.1}
 \end{aligned}$$

$A(k)_{N/2}$ and $B(k)_{N/2}$ are the $(N/2)$ -point DFT of the even and odd indexes k of $F(k)_N$

The resulting $A(k)_{N/2}$ and $B(k)_{N/2}$ are again Fourier transforms that can be calculated the same way as in D.1. When doing so, a recursive algorithm or butterfly arises (D.2) where we can start calculating $N/2$ 2-points DFT's, then $N/4$ 4-points DFT's, etc., to eventually 1 N -points DFT. This algorithm is $O(N/2 \log_2 N)$, while the original discrete Fourier transformation (formula 4.8) is $O(N^2)$, in case of $N = 256$ already a factor 64 better!

$$\begin{aligned}
 \textcircled{1} \quad F(k)_N &= F(k)_{N/2} + \cos\left(\frac{2\pi}{N} k\right) F\left(\frac{N}{2} + k\right)_{N/2} - j \sin\left(\frac{2\pi}{N} k\right) F\left(\frac{N}{2} + k\right)_{N/2} \\
 \textcircled{2} \quad F\left(\frac{N}{2} + k\right)_N &= F(k)_{N/2} - \cos\left(\frac{2\pi}{N} k\right) F\left(\frac{N}{2} + k\right)_{N/2} + j \sin\left(\frac{2\pi}{N} k\right) F\left(\frac{N}{2} + k\right)_{N/2} \tag{D.2}
 \end{aligned}$$

$F(k)_{N/2}$ indicates $A(k)_{N/2}$

and $F\left(\frac{N}{2} + k\right)_{N/2}$ indicates $B(k)_{N/2}$ in form. D.1

These resulting formulas can be repeated for the transforms of $A(k)_{N/2}$ and $B(k)_{N/2}$, resulting again in a recursive algorithm. This algorithm is however somewhat different from the algorithm given by D.2. This is because each stage of the Hartley transform depends on three different terms of a previous stage (see D.3), instead of two in the case of Fast Fourier Transformation (D.1). Because of this, each next stage of the Hartley spectrum can not simply overwrite the previous stage values the same way as is done in FFT algorithms.

Therefore, a new set of calculations was designed for the Hartley spectrum stages ($N/2$ 2-points DHT's to 1 N -points DHT), in order to be able to perform the overwriting of the Hartley array in each stage. This will save memory space that would have been necessary for storing the intermediate results of the calculations.

①

$$H(k)_N = H(k)_{N/2} + \left\{ \cos\left(\frac{2\pi}{N}k\right) H\left(\frac{N}{2} + k\right)_{N/2} + \sin\left(\frac{2\pi}{N}k\right) H(N - k)_{N/2} \right\}$$

②

$$H\left(\frac{N}{2} + k\right)_N = H(k)_{N/2} - \left\{ \cos\left(\frac{2\pi}{N}k\right) H\left(\frac{N}{2} + k\right)_{N/2} + \sin\left(\frac{2\pi}{N}k\right) H(N - k)_{N/2} \right\}$$

③

$$H(N - k)_N = H\left(\frac{N}{2} - k\right)_{N/2} + \left\{ \cos\left(\frac{2\pi}{N}k\right) H\left(\frac{N}{2} + k\right)_{N/2} - \sin\left(\frac{2\pi}{N}k\right) H(N - k)_{N/2} \right\}$$

④

$$H\left(\frac{N}{2} - k\right)_N = H\left(\frac{N}{2} - k\right)_{N/2} - \left\{ \cos\left(\frac{2\pi}{N}k\right) H\left(\frac{N}{2} + k\right)_{N/2} - \sin\left(\frac{2\pi}{N}k\right) H(N - k)_{N/2} \right\}$$

(D.4)

$H(k)_{N/2}$ indicates $A(k)_{N/2}$

and $H\left(\frac{N}{2} + k\right)_{N/2}$ indicates $B(k)_{N/2}$

and $H(N - k)_{N/2}$ indicates $B\left(\frac{N}{2} - k\right)_{N/2}$ in form. D.3

This algorithm is not valid for two index values: $k = 0$ and $k = N/4$. When $k = 0$ equations ② and ④ are the same, so one is redundant. A more serious problem is that equation ③ is not valid for $k = 0$, because these sub-transformations go from zero only to $(N - 1)$. When $k = N/4$ the four equations are valid, but in this case the equations ① and ④ are the same, and ② and ③ are the same.

The following is a smart way of solving these problems:

When performing the transformation, test the array-index for being zero or $N/4$, and if so, perform the next algorithm:

$$\begin{aligned} \textcircled{1} \quad H(k)_N &= H(k)_{N/2} + H\left(\frac{N}{2} + k\right)_{N/2} \\ \textcircled{2} \quad H\left(\frac{N}{2} + k\right)_N &= H(k)_{N/2} - H\left(\frac{N}{2} + k\right)_{N/2} \end{aligned} \quad (D.5)$$

This also saves the calculation of the multiplications in D.4. The input array to the algorithm must again be in bitreversed order.

The recursive algorithm defined by D.4 $\textcircled{1}$ - $\textcircled{2}$ and D.5 $\textcircled{1}$ - $\textcircled{2}$ may seem a bit more intricate than the FFT algorithm D.2, but one must keep the following in mind:

- The FFT recursive algorithm works with 2 calculations, and may thus seem simpler and faster. The FHT recursive algorithm on the other hand must indeed calculate 4 equations each pass, but this means also that the array will be processed in half the number of passes of the FFT, resulting in a processing time that will approximately be the same, as far as this goes. In this context a *pass* means: performing the recursive algorithm once.
- When looking more closely at D.2 and D.4 we can see that for each newly calculated transformation sample one multiplication is necessary. That is, two by two the new samples use the same terms (consisting of a cosine and a sine function multiplied by a sample) as well in FFT as FHT. However, the multiplications needed by the FFT are complex multiplications, meaning two actual multiplications, while the FHT multiplications are only real.

Therefore, one can state that the Fast Hartley Transformation will need approximately only half of the time of Fast Fourier Transformation.

- (224) Book of abstracts of the first Benelux-Japan Workshop on Information and Communication Theory, Eindhoven, The Netherlands, 3-5 September 1989.
Ed. by Han Vinck.
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A POSSIBILITY TO INCORPORATE SATURATION IN THE SIMPLE, GLOBAL MODEL OF A SYNCHRONOUS MACHINE WITH RECTIFIER.
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