Finding a needle in Auditory Brainstem Responses

Christopher Jonsson

November 4, 2013

Abstract

In this thesis we look at data where sedated patients have been pinpricked with a needle during an Auditory Brainstem Response recording. By looking at this data set with different statistical methods some butterfly pattern emerged and peaks appeared in the spectrum around the time where the needle pinpricking should have occurred. With this results a model was developed and evaluated. Future investigations is needed to interpret the results.

Acknowledgement

I would like to thank my helpful and patient mentor Professor Maria Sandsten.

I would also like to thank my family for supporting me during my time as student at Lunds University and my year abroad in Australia as a student at RMIT.

Thanks also to Associate Professor Xiadong Li and Dr Dean Cvetkovic for inspiring me to follow my passion in neural science.

A thank you to Professor Anders Heyden at Department of Mathematics at Lund University.

At last thank you to SensoDetect for providing this interesting research topic and Johan Källstrand from SensoDetect for his guidance.

Contents

1 Purpose

1.1 Introduction

A thought or maybe just a feeling? Where do they come from?

Where does consciousness start and where does it end? What kind of information do we apprehend and how do we transform it to a thought? These are some of the questions that science have not been able to pinpoint yet but things we do know is that with and within the brain we are able to process and react to changes in our environment. An interesting question is if we can get access to some of the information flowing through our brains.

Every day billions of neurons in the brain fire off millions of signals just to comprehend all the impressions we encounter in daily life. This system is built up of a gigantic network of neurons which is grown through our young years by constantly feeding the network with impressions from our environment. It is fascinating how a group of simple cells like neurons can build up an amazing system and organ like the brain. The brain makes it possible for us to feel feelings, sense sensations and our consciousness. With the brain we steer our body into great motorical intense movements to effect our surroundings [7].

The brain is in the center of this great system, handling information from all of our surroundings going through our neural network. Information like what temperature it is outside, if there is any danger from outer environment we have to evade. But there are much more information than that flowing through the the brain [2]. The body itself have through the evolution become amazingly adaptive to the environment but can sometimes need some help.

Say that we somehow where able to access just a portion of the information flowing through our neural network. That would just be amazing and that is actually what this thesis is trying to do to some extent. To find something significant from data recorded from the brainstem and try to interpret it into something happening in the outer world. Is there a way to get access to information flowing in the neural system in our brain? And how can we interpret this information?

In this thesis we will look at the Auditory Brainstem Response (ABR) and see what new information can be extracted from the brainstem.

1.2 Aim

The aim of this thesis is to see if the pain of pinpricking a patient with a needle can be detected in the Auditory Brainstem Responses (ABR). This will be investigated by looking at data with spectral analysis methods and other statistical methods. The data set is provided by the Swedish company SensoDetect AB which conducted all of the experiments. To get out information about the activity in the brain the Auditory Brainstem Response is used. The ABR is a method which looks at the electrical potential on the scalp while stimulating a patient with sound.

1.3 Research Questions

- Is it possible to detect the pain of a needle in ABR?
- What information is lost during the processing of the data?
- How can we model the ABR signal?
- How can we model the ABR signal with the pain of the needle?

2 The Auditory Brainstem Response

The brain is one of our most complex organs which have caught the humans fascination in several decades. Even if we have been able to chart the smallest components of the brain anatomically, it is still a great challenge to understand how it works and extracting this information. To understand what we see using statistical methods I need to present what is known about the brain today.

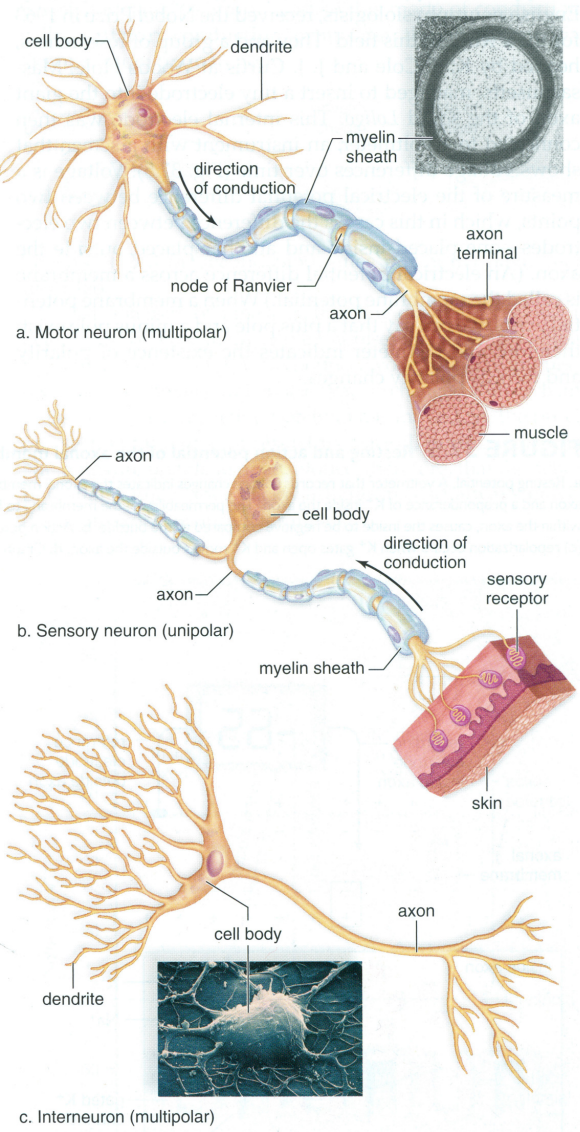

Figure 1: Shows a sketch of the different kinds of neurons [7]

The neural system is composed of neurons and neuroglia which serves as a support for the neurons. As we can see in figure 1 the neuron has nucleus as all other cells. But what's special with the neurons is how it builds up a greater system by connecting their dendrites and axones coated in myelin sheaths [7].

In figure 1 we see sketches of the different kinds of neurons in the neural system. The motor neuron conduct the signal out to axon terminals which activates muscles and glands in the body. Where the sensory neurons signal instead starts to conduct from its sensory receptors giving the neural system information about the outer world. To connect and process this the information is sent to the interneuron to sort out the information to new neurons [7].

Through these dendrites and axones the neurons communicate with other neurons. The difference between the dendrites and axons is in which direction they transfer the signal. The dendrites receives the signal to the neuron and the axon sends signal out neuron's cell body.

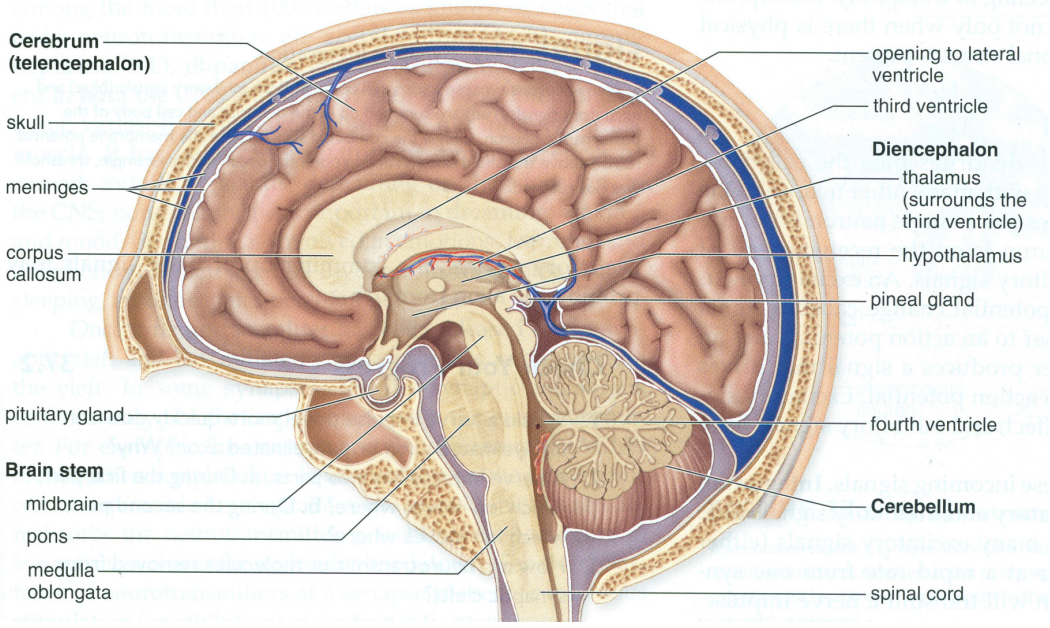

Figure 2: Shows a cross section of the human brain [7]

The structure of the brainstem consist of the midbrain, the pons and the medulla oblongata which can be seen in figure 2. The Midbrain works as a relay station between the cerebrum, cerebellum and the spinal chord. The tracts cross in the brainstem so that the right and the left cerebral hemisphere can control the opposite side of the body. The brainstem is also the reflex

center for neural information of visual, auditory and tactile responses [7].

The cerebrum is the largest part in the brain divided into right and left cerebral hemispheres which is connected with tracts in corpus callosum which lies above the thalamus. The thalamus can be seen as an information sorter routing the information from the body's sensors to the correct part in the cerebrum. It is then in the cerebrum we gather all the information from the body's sensors. By integrating all this input the brain then makes a decision which leads to the body being put into action [7].

We find the cerebellum under the occipital lobe of the cerebrum in the back of the head. The cerebellum take information and correct the body's muscles accordingly, letting us keep our posture and balance. To learn new motor skills the cerebellum ensures the coordination of the body's muscles so they can create a smooth and steady movement. The pon is bundles of axons and the medulla oblongata contains reflex center regulating the body's respiration, vomiting, heartbeat and blood pressure [7].

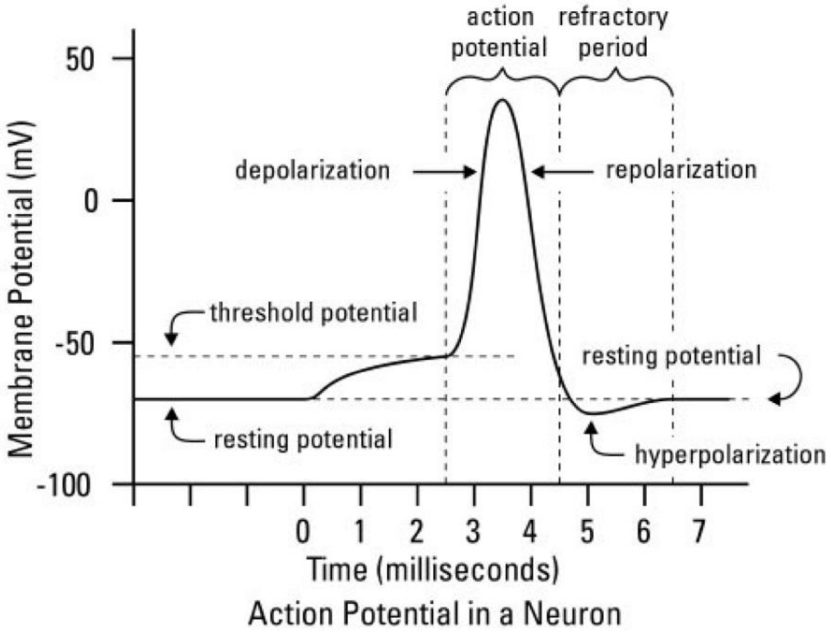

Figure 3: Shows how the potential change of the membrane during an impulse

As all other cells in the body the neurons need oxygen and nutrition. The brain use 40% of the oxygen of the body which in many methods has been used to see brain activity by looking at the oxygen consumption. The oxygen is also negatively charged and the changes in the charge distribution creates an electrical field which we see in the ABR potential.

There are a lot of different exchanges of different compounds flowing back and forth.To send a signal through an axon the potential difference between the inner and outer cell wall of the axon changes and then gets restored which can be seen in figure 3.

When the membrane starts in its resting potential the concentration of potassium (K+) and sodium (Na+) is higher outside the membrane and the negative charged anions inside. When the potential threshold gets breached the potassium (K+) and the sodium (N+) rush trough the cell membrane due to electrical force and diffusion which creates the potential spike. The cell membrane then pumps out the potassium and sodium again so the membrane returns to its resting potential.

In figure 4 we see the potassium (K+) gets pumped out to the extracellular medium to create the starting potential so the membrane is ready to transfer a new signal. With this process the impulse transcends through the axon over a quite large distance to the new neuron or receptor. Figure 3 shows how this process changes the potential over the cell membrane.

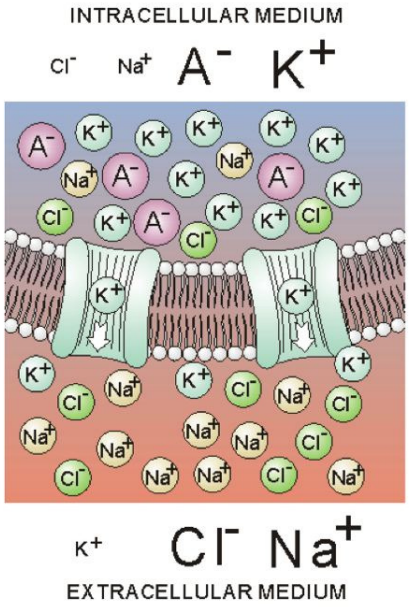

Figure 4: The Axons cell membrane and the compounds creating the electrical potential [8].

2.1 Measuring Electrical Potentials

The ABR shows the potential between two points at the scalp and is defined as the following

Definition 1 *The definition of the potential is*

$$V(a) - V(b) = -\int_a^b E_f(z) \cdot dz$$

where a and b are the different the location in the room. $E_f(z)$ is the electric field at point z in the room.

In the ABR we will see the potential change during 15 ms after an auditory stimulation. The change in the ABR then comes from the change in the electric field which depends on the change in the charge distribution.

Definition 2 *The potential can also be defined at point p with the charge distribution $q(z)$ as*

$$V(p) = \frac{1}{4\pi\varepsilon_0} \int \frac{q(z)}{d} dz$$

where ε_0 is permittivity of space and d is the distance to charge $q(z)$.

Anatomically speaking these charges are the compounds and ions which flows back and forth during the process of the neurons in the brain. Some of the major indicator for brain activity is local oxygen consumption and the neurons firing of signals through their axons to the connecting neurons.

What the potential really show is an integration of the changes in the electric field caused by the billion neurons. And the change itself comes from the range in the charge distribution caused by a simple thought firing signal through the brain. We lose the precision of brain activity but instead get a more general view over the response. In this case the pathway is the one connected with processing of the auditory stimulation in the brain.

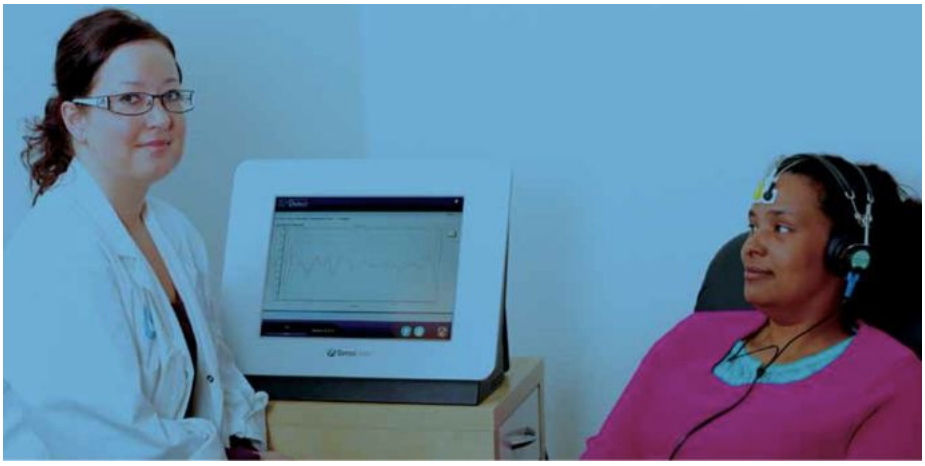

Figure 5: Picture of the setup during an ABR recording from SensoDetect

2.2 Method Auditory Brainstem Response

In this thesis we will look at the auditory brainstem responses (ABR) which is a potential difference on the scalp which occur due to sound stimulation. When measuring the ABR the patient are applied with electrodes according to figure 5. With this setup the potential between the forehead and beneath the ear can be measured. As can be seen in figure 5 this is done on both the right and left side of the patient which give us an ABR signal from both brain halves. In this thesis the focus will be on the ABR from the left side of the brain. Mostly because this is where the majority of the analysis have been applied [4][5][6].

When the brain gets stimulated the nerve signals travels through certain areas in the brain to be processed. The ABR consist of seven positive (waves I-VII) peaks 10 ms after the auditory stimulation (see figure 6) [5]. By applying the same stimulation a similar response appears and by doing this several times a statistical significant amount of data is gathered. In this master thesis 1300 ABR is collected from each patient.

In these ABR waves different peaks have been shown to connect to different parts in the brain.Wave I are produced by the auditory nerve stimulation which then travels down to the medulla oblogata (wave II) and then up through the pons (wave III) to the midbrain (wave IV and V). From the midbrain the nerve signals then travel up to the thalamus (wave VI) and then out to rest of the brain (wave VII). So if we follow this path in figure 2 the ABR path goes down to medulla oblongata and then continue to transcend up through the brain.

A profile is created for the patient which can then be compared to other profiles by looking at the slopes and amplitudes of the different waves [6]. With these profiles SensoDetect has been able to differentiate and diagnose schizophrenic patients and patients with Asper syndrome [4][5][6].

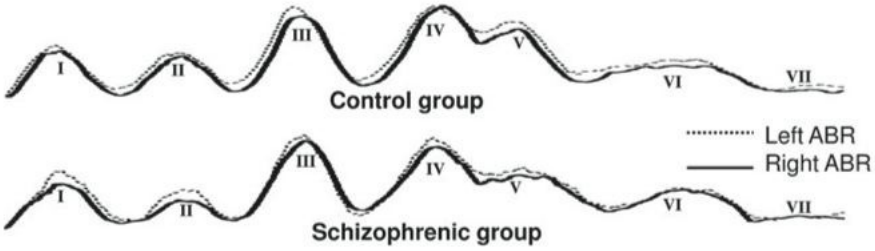

Figure 6: Shows the profiles from two different groups in a research from SensoDetect [5]. Here we see a good example of ABR where all the waves have been identified in each profile.

3 Theory - the Methods

To familiarize with a new dataset there are different approaches you can take. To look into the mathematical methods used in this thesis, we need to introduce some definitions.

Definition 3 *An observation is denoted as $x(t)$, $t \in [1, t_{end}]$ where t is the sample at time t in observation $x(t)$ and n is the number of observations .*

By observing the same process several times, sufficient amount of statistical amount is collected.

3.1 Spectral density

When looking at these kinds of signals an usual approach is to look at the frequency content of the signals by estimating the spectral density, which basically is the Fourier transform of the covariance function. By looking at the frequency content, the signals components can be extracted and further analyzed.

Definition 4 *The definition of the spectral density is*

$$\hat{S}(w) = \sum_{\tau=-\infty}^{\infty} e^{-iw\tau} r(\tau)$$

where $w = 2\pi f$ and $r(\tau)$ is the covariance function.

Definition 5 *The covariance function is defined*

$$r(\tau) = C[X_k, X_l] = E[X_k X_l] - m_{X_k} m_{X_l},$$

with $\tau = k - l$. The covariance $r(\tau)$ is a measure of the dependence between x_l and x_k where $E[x]$ is the expectation and m is the mean of observation x.

Other interesting properties when looking at a series of observations is how the different observations depend of each other. By looking at the correlation matrix you can access some of this information.

To increase the accuracy of spectrum we have chosen two different methods, the multitaper and MUSIC. The multitaper is a non-parametric method which does not need any further information to extract the amplitude and frequencies. To get a better approximation of the frequency we will use the parametric method MUSIC where we will make a qualified guess on the number of peaks in the spectrum.

3.2 Multitaper Method

The idea behind the multitaper method is to create several periodograms over the same data set and average them which decreases the variance. Welch introduced this method and by using the Welch window with a 50% overlap, the result can be seen in figure 7 [10]. Thomson later found that this methods could be reformulated using using the total data length as long as the windows are uncorrelated (which they are in the Welch method) [9].

Definition 6 *With the multitaper method the spectrum is defined as the average of K periodograms,*

$$\hat{S}_t(w) = \sum_{k=1}^{K} \alpha_k \hat{S}_k(w)$$

where α_k is the weight of the k:th window and

$$\hat{S}_k(w) = |\sum_{t=1}^{N} y(t) h_k(t) e^{-iwt}|^2$$

and h_k is a window estimating the spectrum from N samples.

For our case we will use the Welch as a reference method and multipeak window which is good at estimating the true amplitude of the spectrum [3]. The two different types of multitapers can be seen in figure 7, where we can see eight periodogram windows.

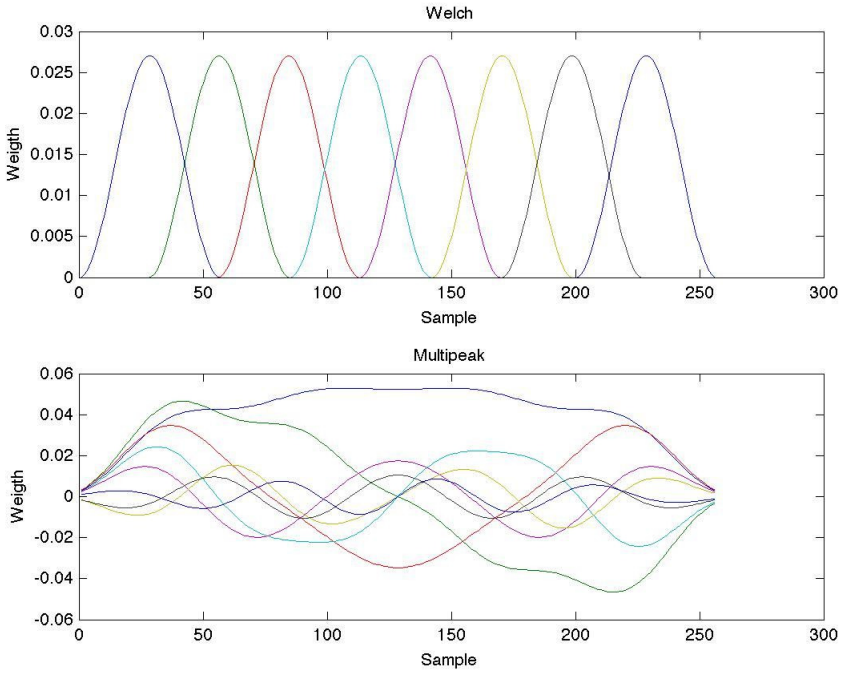

Figure 7: The figures show the multitapers for $K = 8$ that builds up the spectrum over 256 sample.

3.3 MUSIC- MUltiple SIgnal Classification

To get a greater resolution in the frequency domain the spectral density will be estimated with the method MUSIC. MUSIC is a method which optimize over the spectrum to find the highest peaks in the spectrum, which is possible if the number is known or estimated with a good reliability.

Definition 7 *The MUSIC algorithm does the following steps*

1. The covariance matrix is calculated according to

$$\hat{R} = \frac{1}{N}\sum_{t=m}^{N} \tilde{y}(t)\tilde{y}^*(t)$$

where

$$\tilde{y}(t) = \begin{pmatrix} y(t) \\ y(t-1) \\ \vdots \\ y(t-m+1) \end{pmatrix}$$

and m is a positive integer.

2. Find L highest peaks of the pseudo-Spectrum

$$\frac{1}{a^*(w)\hat{G}\hat{G}^* a(w)},\ w \in [-\pi, \pi]$$

where

$$a(w) = [1 \ \ e^{-iw} \cdots e^{-iw(m-1)}]^T$$

and $\hat{G}$ comes from the eigendecomposition

$$\hat{R}_y = \begin{pmatrix} \hat{F} & \hat{G} \end{pmatrix} \begin{pmatrix} \lambda_1 & & 0 \\ & \ddots & \\ 0 & & \lambda_N \end{pmatrix} \begin{pmatrix} \hat{F}^* \\ \hat{G}^* \end{pmatrix}$$

where $\hat{F}$ are eigenvector belonging to $m-1$ first eigenvalues of $\hat{R}_y$ and $\hat{G}$ are the eigenvectors to eigenvalue m to N.

3.4 Correlation and Coherence

Each observation usually have something in common, so the question is what is similar and what is different. By looking at the covariance and the correlation one can get a measure how they depend on each other.

Definition 8 *If we have the two observations X_i and X_j, then the correlation is*

$$\rho_{j,k} = \frac{C[X_j, X_k]}{\sqrt{C[X_j, X_j]C[X_k, X_k]}} = \frac{E[(X_j - m_{x_j})(X_k - m_{x_k})]}{\sqrt{C[X_j, X_j]C[X_k, X_k]}}.$$

where m is the mean of observation X. A correlation matrix is defined as

$$\begin{pmatrix} \rho_{1,1} & \cdots & \rho_{N,1} \\ \vdots & \ddots & \vdots \\ \rho_{1,N} & \cdots & \rho_{N,N} \end{pmatrix}$$

where N is the number of observations.

Looking at the correlation matrix helps one grasp the dependencies, although it might be better to study the coherence when comparing the two signals if we want to grasp what frequencies they have in common. By doing this through the series in ascending order we get a relative measure of the change in frequencies between the following observations.

Definition 9 *The cross-spectral density is defined as*

$$\hat{S}_{X_j,X_k}(w) = A_{X_j,X_k}(w)e^{i\phi_{X_j,X_k}(w)}$$

where

$$A_{X_j,X_k}(w) = |\hat{S}_{X_j,X_k}(w)|$$

and $\phi_{X_j,X_k}(w)$ is the shared frequency components between observation X_j and X_k.

In this master thesis we will use two different definitions for the coherence. The coherence spectrum can give different results depending of where in the calculation you remove the imaginary part from the spectrum estimate or what kind of window you use [1].

Definition 10 *The squared coherence spectrum can be defined as either*

$$\psi^2_{X_a,X_b} = \frac{\sum_{k=1}^{K} \mid \hat{S}_{X_a,X_b}(w)_k \mid^2}{\sum_{k=1}^{K} \hat{S}_{X_a,X_a}(w)_k \cdot \sum_{k=1}^{K} \hat{S}_{X_b,X_b}(w)_k} \tag{1}$$

or

$$\psi^2_{X_a,X_b} = \frac{\mid \sum_{k=1}^{K} \hat{S}_{X_a,X_b}(w)_k \mid^2}{\sum_{k=1}^{K} \hat{S}_{X_a,X_a}(w)_k \cdot \sum_{k=1}^{K} \hat{S}_{X_b,X_b}(w)_k}. \tag{2}$$

where $\hat{S}_{X_a,X_b}(w)$ is cross-spectral density of observation X_a and X_b weighted with window k. $\hat{S}_{X_a,X_a}(w)$ and $\hat{S}_{X_b,X_b}(w)$ are the corresponding spectra for X_a and X_b.

The different definitions are good at extracting information in different fields and because there are no information of how the ABR should behave we test which definition should be used for the ABR.

4 The Data

To arrange the data we need to introduce some definitions.

Definition 11 *An observation $x_i(t)$ is 256 samples of potential with the sample interval of 0.06 ms. The data is then arranged in chronicle order according to figure 8.*

For each patient several series of 1300 observations were recorded where the patient was in different states. The series this thesis will look at are the series where the patients was pinpricked with a needle in the right ring finger somewhere in the middle of the series while being sedated. Each observation was collected 15 ms after a click which occur every 100ms ±7ms. The random time between each pair of clicks is there to avoid interference noise.

The measured data is then filtered by removing all artificial peaks and the 50 Hz frequency noise from the power outlet. Then a trimmean is taken over all the observations before a total mean is applied.

4.1 The "Third" Dimension

By organizing the observation in this manner an additional time dimension has been introduced and to address this the following denotation will be used. For each observation, t_s will be the time given by the certain sample and t_o will be the time shown in the observation axis. After the preprocessing, t_o will become t_c which stands for the clusters which the data will be compressed to with trim mean.

It is quite an intuitive way the data has been structured but the added complexity of the time dimensions means that even simple operations has to be taken with care. The trimmean function is set to take the mean of the 50% median of 30 observations and this is done over the t_o domain with an overlap of 15 clusters (50%) giving us about 90 cluster. A cluster is defined as trimmean of 30 observations.

Definition 12 *Trimmean is defined as*

$$Trimmean = mean(median(N, \alpha))$$

where N is the the number of observations and α is the percentage of values kept by the median.

With the trimmean function the artificial peaks are removed and at same time only true data affect the end result. Only the measured data will affect the value in the cluster due to extreme values and samples with no value will be sorted out with the median.

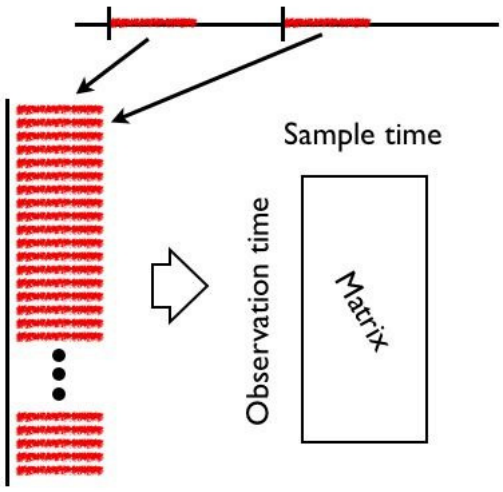

Figure 8: The structuring of the data. In the top of the figure we see timeline from which 256 samples are recorded and then ordered into a matrix.

5 Pre-Analysis of Data

To get a grip on this complex data set, a number of different methods was used to get an idea of the data sets behavior. To showcase certain behaviors patients have been handpicked to show common but distinct results. In figure 9 we see the data arranged according to figure 8 with the cluster time t_c at the y-axis and the sample time t_s at the x-axis. To remove high frequencies like the one seen for patient A in figure 9 around cluster 50 can be removed with a moving average.

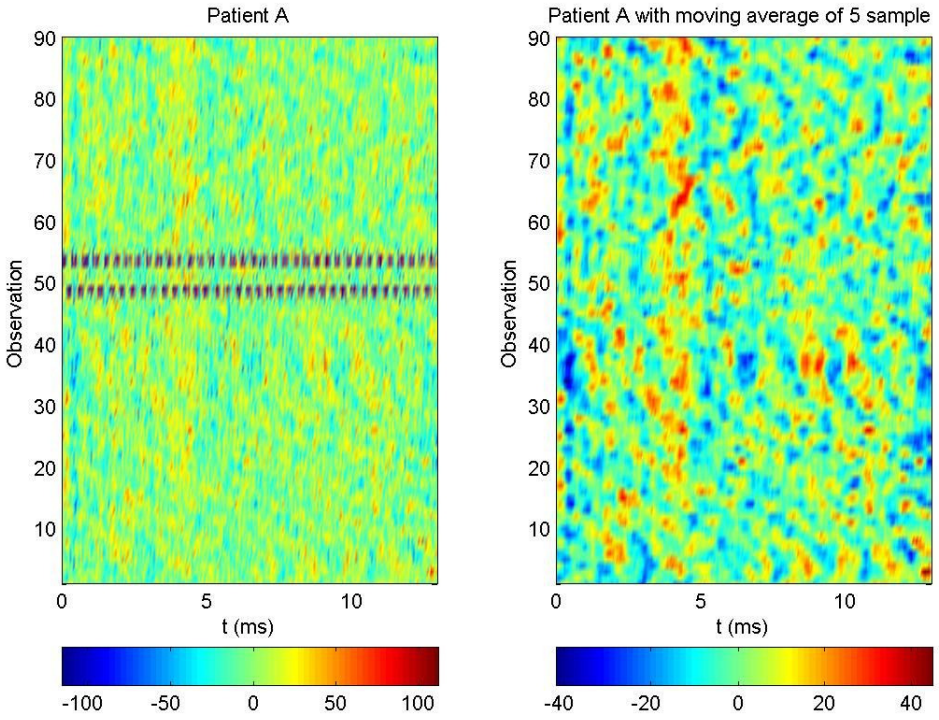

Figure 9: Data from patient A where the higher frequencies is removed.

The number of samples averaged is decided individually for each patient by looking at a single cluster. In figure 10 we see how the ABR change depends on the number of samples we average and the average is on this patient chosen to be 5 which is the first case where the peaks starts to appear. The aim is to extract the seven ABR waves without losing information. The moving average will enhance the waves but also remove noise like the one around cluster 50 in figure 9.

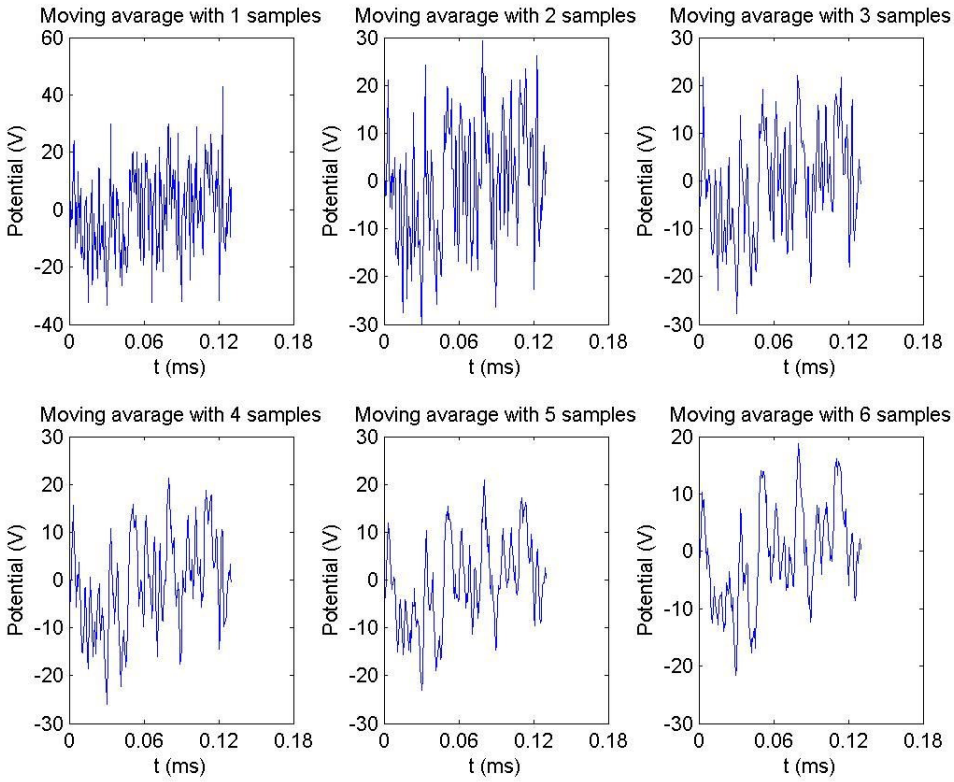

Figure 10: Moving average on a cluster from patient A

By looking at the spectrum created by the multitaper, MUSIC and Welch methods we can see the spectrum with high resolution in either frequency or amplitude. The MUSIC method will in our case look for two peaks and the multitapers will use $K = 8$ windows to estimate the spectral density describing the frequency components in each cluster.

In figure 11 we see that there is some kind of activity in the area around 50% of the clusters had occurred, which should be somewhere between cluster 40 and 50. This peak is exactly what we are looking for and want to see around the time of the needle pinpricking. Some indication helping us to decide at what time the pinpricking should have occurred. The only worry is the peak at the end of the ABR recording which make one wonder what happens at that point in time because there should only be one single needle pinpricking. Maybe it is noise but if it also occurs in other patients the peak could have another significant meaning.

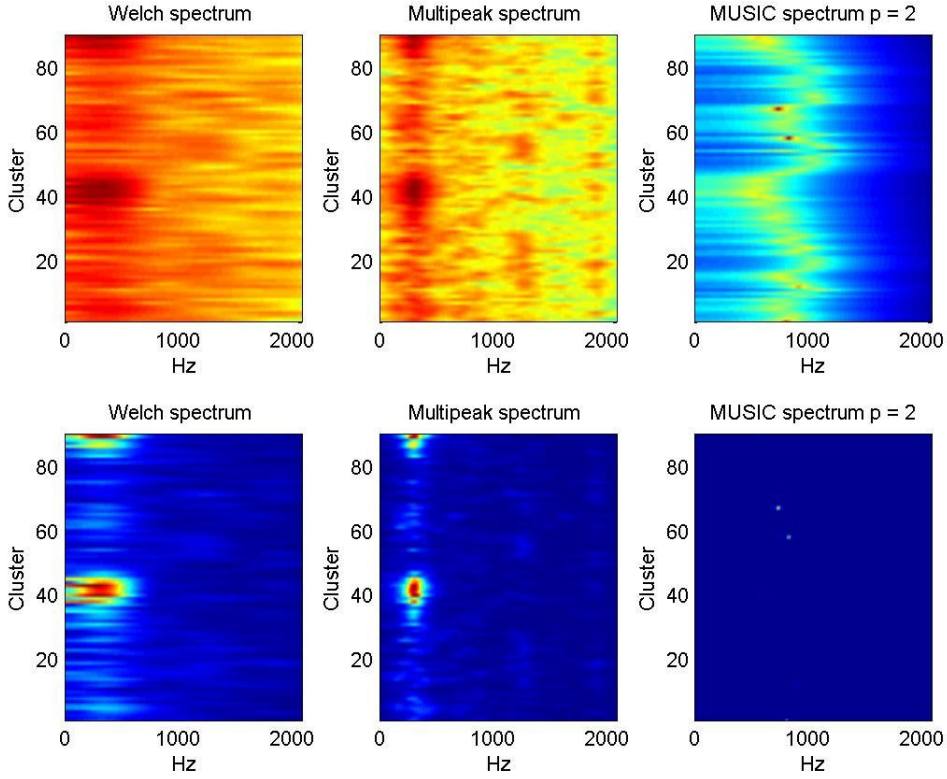

Figure 11: The spectrum of patient B where the pinpricking happened at 47% into 1300 click series which should be cluster 40-45. The upper row of plots is plotted in dB scale to increase amplitude resolution and the lower row is the regular spectrum for each method.

In the case of the patient in figure 11 we see a patient which has been pinpricked with the needle when 47% of the clicks had occurred. The peak is quite smeared out which is due to overlap between the cluster and the trim-mean of the observations in each cluster. This makes it harder to pinpoint the exact time for the needle pinpricking.

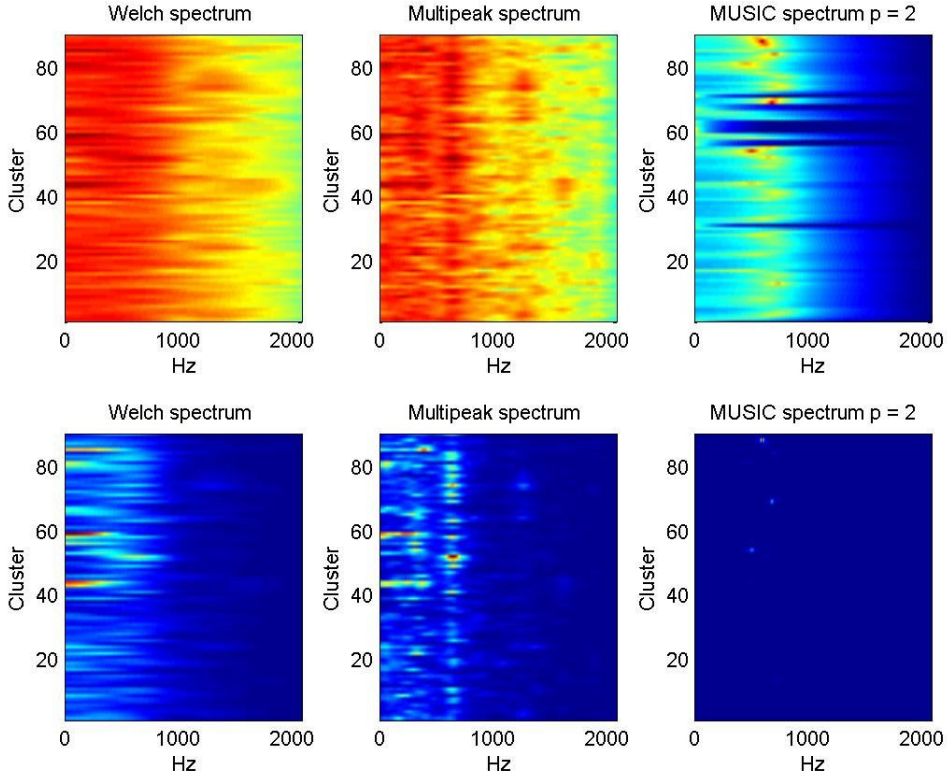

Figure 12: The spectrum of patient G where the pinpricking happened at 58% into 1300 click series which should be cluster 55-60. The upper row of plots is plotted in dB scale to increase amplitude resolution and the lower row is the regular spectrum for each method.

In figure 12 we see the high intensity is at later than 50% of the clicks which leads us to a possible connection of the needle pinpricking and high intensity. In this case the patient actually was pinpricking when 58% of the series of clicks had occurred which strongly indicate that there exists a connection between the intensity and the needle.

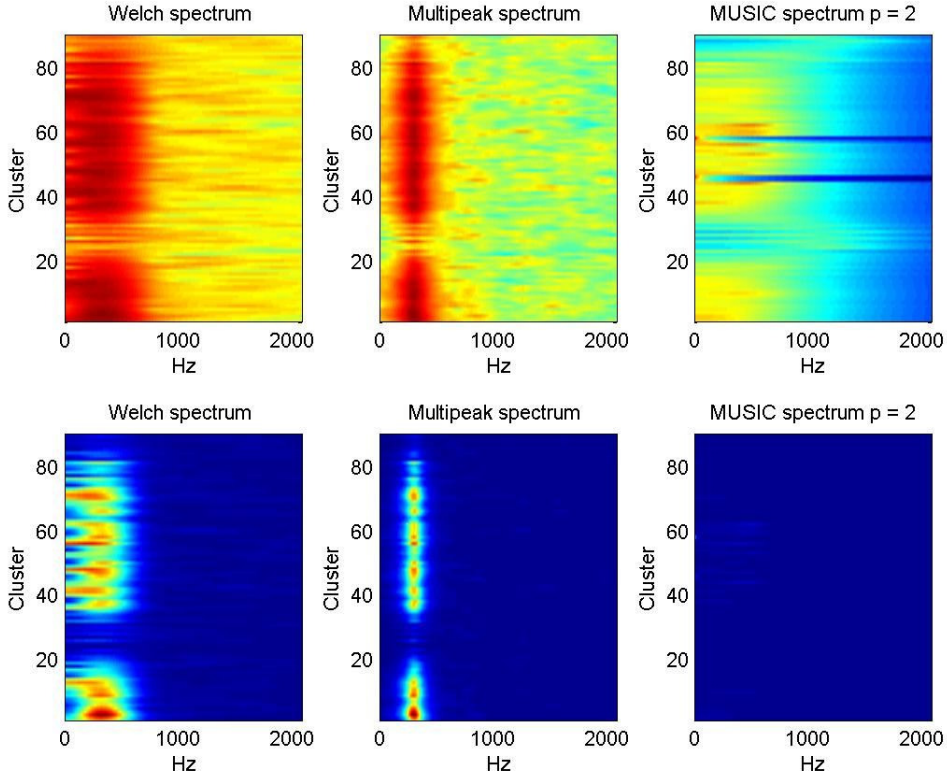

Figure 13: The spectrum of patient C where the pinpricking happened at 51% into 1300 click series which should be cluster 45-50. The upper row of plots is plotted in dB scale to increase amplitude resolution and the lower row is the regular spectrum for each method.

But also in these result there is an indications of a "needle" which seems to appear several times during the same session. For example see figure 13 where this increase in intensity can be seen several times during the measurement. In this case we would be forced to guess at several points in time where the pinpricking could have occurred. This indicates that the intensity in the spectrum at these frequencies is not only connected with the needle pain but the overall brainstem activity or nerve traffic. These intensities can only be interpreted to be connected to something that have happened at that point in time but does not tell what actually happened. Peaks where found in 7 of the 10 patients at the known time of the needle pinpricking, but it was not always the highest value for the whole spectrum.

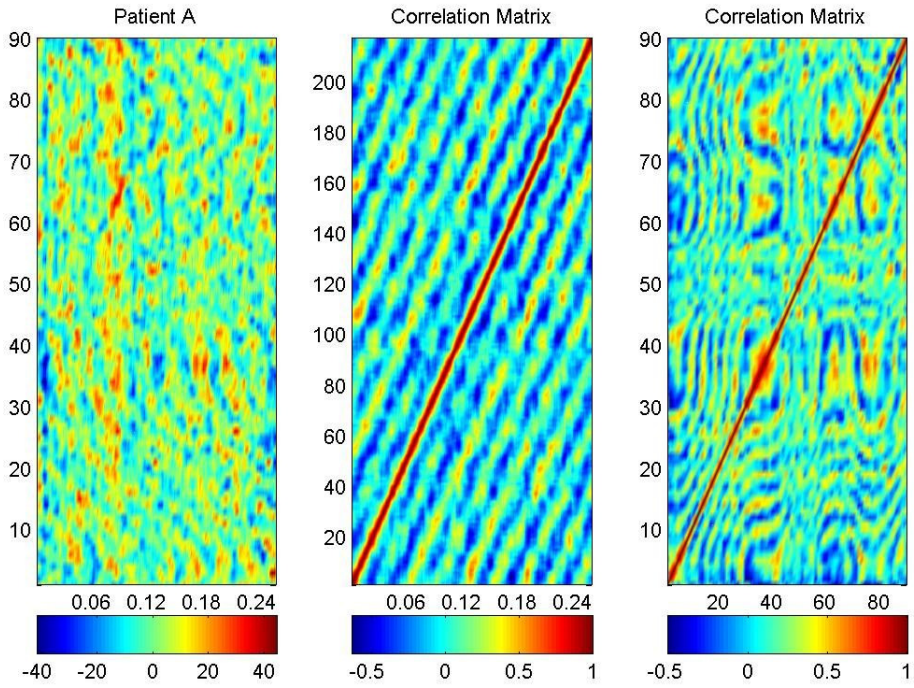

Figure 14: Data for patient A with correlation matrices for samples and clusters.

Other interesting properties to look at is the correlation which shows the dependency between different clusters. The pattern that are descending from the correlation matrix can be seen in figure 14. These butterfly patterns actually show up in several patients as can be seen in figure 15. Between the samples we also see the linear tendencies that are usual for sinusoids. To extract more information from the data we will look into how a sinusoidal model with similar properties behaves.

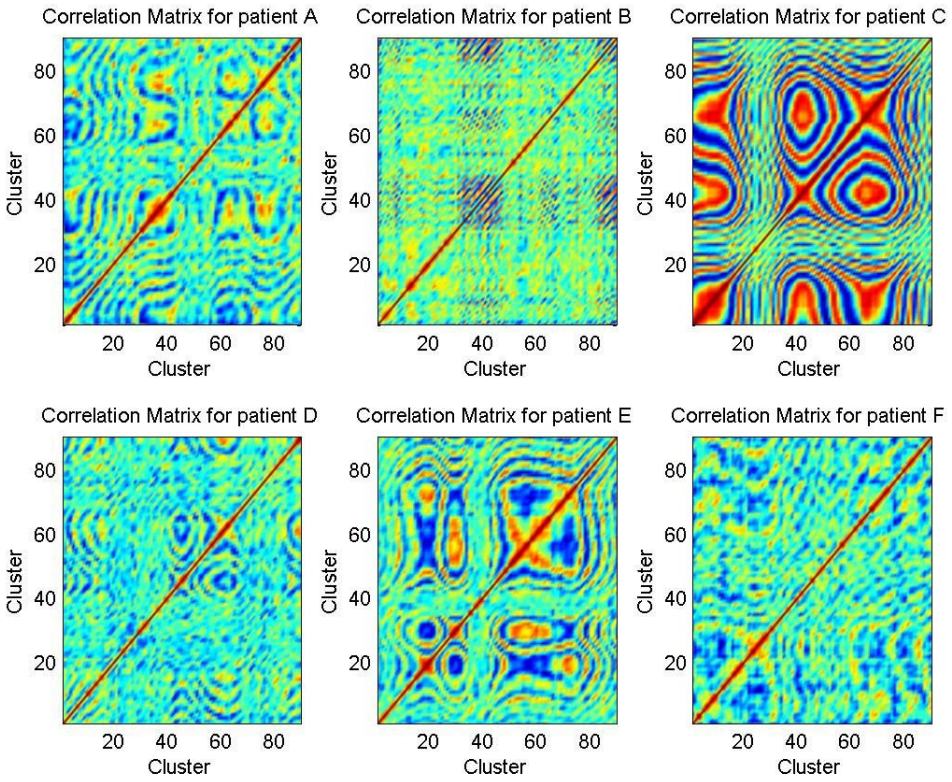

Figure 15: Correlation matrices from patient A-F describing the correlation between the clusters.

5.1 Analysis of findings

To understand what we see in our findings we will look at a simple model of the ABR signal and its behavior to the methods that have been used in this master thesis. In the following section a simple but quite effective model will be presented.

6 A Simple Sinusoidal model

Lets look at the ABR data again in figure 10 where we see the sinusoidal like behavior which can also be seen as the linear behavior in the correlation between the samples. So the first model will just be a single sinusoidal with some noise.

Definition 13 *The first ABR model will be defined as*

$$y_i(t) = sin(w_0 t + \phi_i) + e_i(t)$$

for observation i, where $\phi \in [0, 2\pi]$ *is a random phase shift with uniform distribution, and* $e_i(t)$ *is a colored noise.*

To simulate a patient a series with 1300 observations are created on which we then apply the same techniques, that are used to extract the information from the patients. In figure 16 we see the plot of the simulated data with a correlation plot between both the clusters and the samples which is a behavior we want our model to reproduce. But we also want the simulated data to look like an ABR signal at the observation level in the model.

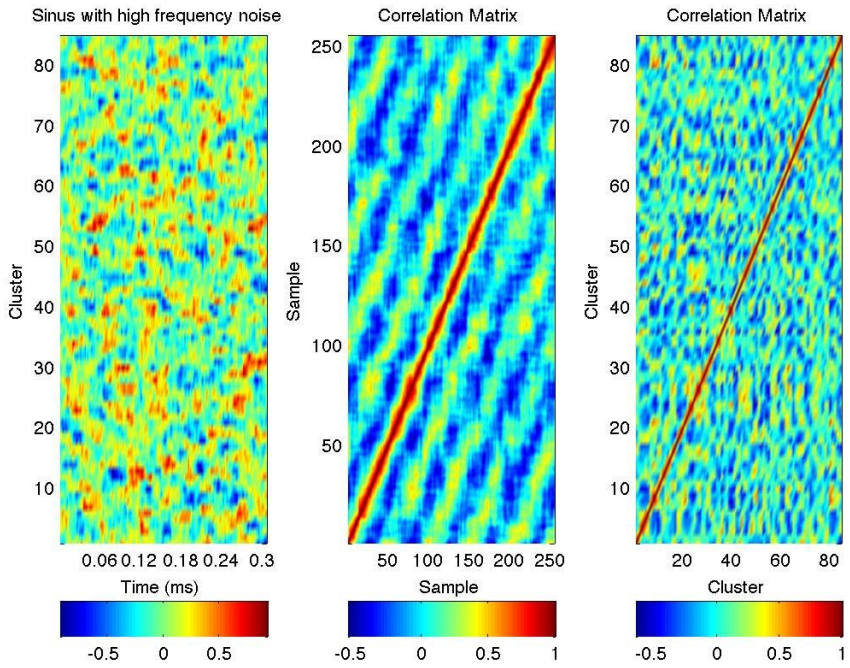

Figure 16: Data for a simulated patient with correlation for samples and clusters.

With the moving average the high frequencies are removed from the ABR which tells us the noise have a high frequency component. In figure 16 we see how the model behave by plotting the same plots as we used at the patients. As we can see the butterfly patterns that showed in several patients are not there (see figure 15) but otherwise it seems to be quite a good match with the expected behaviors we observed in the patients. So by looking at this simple model we can try to see which parameters are important. In this case we are interested in finding a parameter which influence the correlation between the clusters so we hopefully can recreate the butterfly pattern.

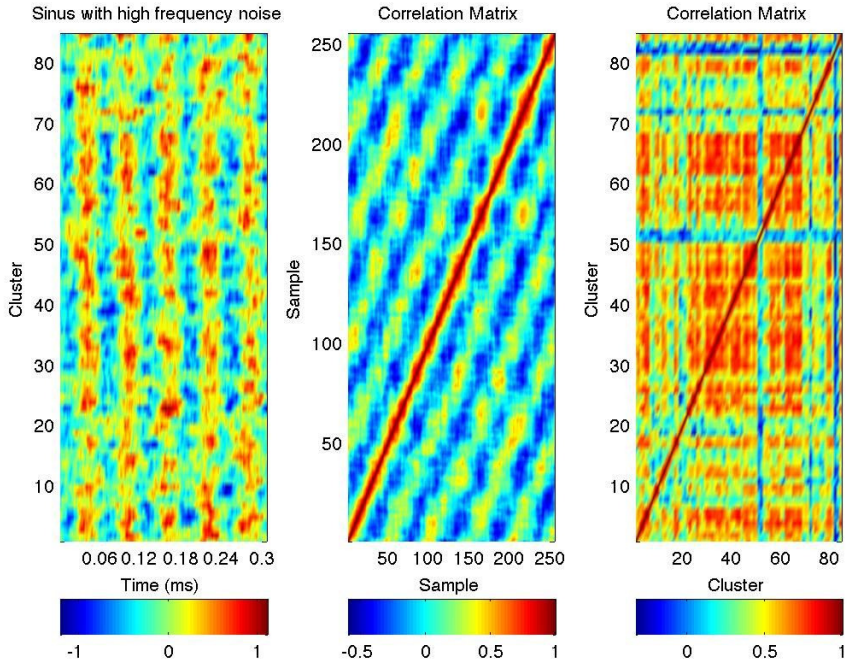

Figure 17: Data for a simulated patient where the phase function has been changed. We also see the correlation matrix for the samples and clusters for the simulated patient.

By changing the parameters in the model the major contributor to the butterfly pattern seems to be the change in phase. In figure 17 we can see how the models characteristics can change when you put in another function than uniformed noise as the phase function (compare with figure 16).

Extracting the phase is a challenge because of the non-linear behavior of the phase. That is why we look at the coherence spectrum to try to extract information about how the phase behave. In this thesis two definitions of coherence (see definition 10) will be used because the different outcome they can give to a data set with unknown properties [1].

6.1 Evaluate the Model

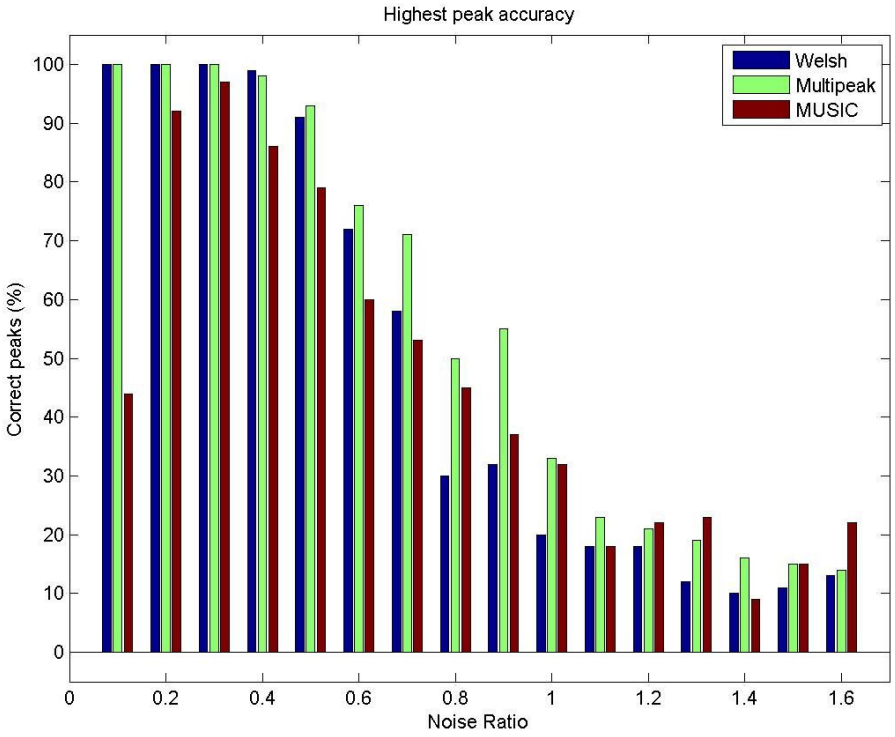

Figure 18: The figure shows the different methods accuracy of the highest peak ability to distinguish a simulated needle pinpricking in a simulated patient. The pinpricking was simulated to happen after 50% of the simulated data, the highest peak was found between cluster 40 and 50 according to the figure with the specific noise ratio.

To evaluate the model and to test if the highest peak in the spectrum indicates the time of the needle pinpricking the following simulation was done. A sinusoid model was used to simulate 1300 observations for 100 patients. The phase shift $\phi \in [-\frac{\pi}{2}, \frac{\pi}{2}]$ was uniformly distributed and a high frequency noise was added to the sinusoid to create the observation. A simulated needle is applied (added) to the observation at observation 625-675 (after about 50% of the simulated observation had occurred). A similar sinusoidal model with 500 Hz frequency was used to simulate the needle. As the pinpricking was simulated to happen after 50% of the simulation, the highest peak should be found between cluster 40 and 50. This assumption makes the peak distribution becoming a binomial distribution with two outcomes. In figure 18 we see how many times the needle is found between cluster 40 and 50, for the different spectral density estimate methods. The methods could not find the needle when the bound of the phase distribution increased.

With no noise in the signal the MUSIC method behaves a bit strange and gives a low accuracy. The reason for this is that the MUSIC method is looking for two peaks in the spectrum while the model only consist of one sinusoid which should give only one peak in the spectrum. So there appear spurious peaks when different model assumptions collide which shows in the accuracy.

7 Further Investigation

Coherence spectrum is a measure of shared frequencies between two general processes with something in common which usually is the source. In our case, the coherence spectrum have been calculated for each cluster and the chronological ordered observation to give us information about the change between clusters close in time t_c.

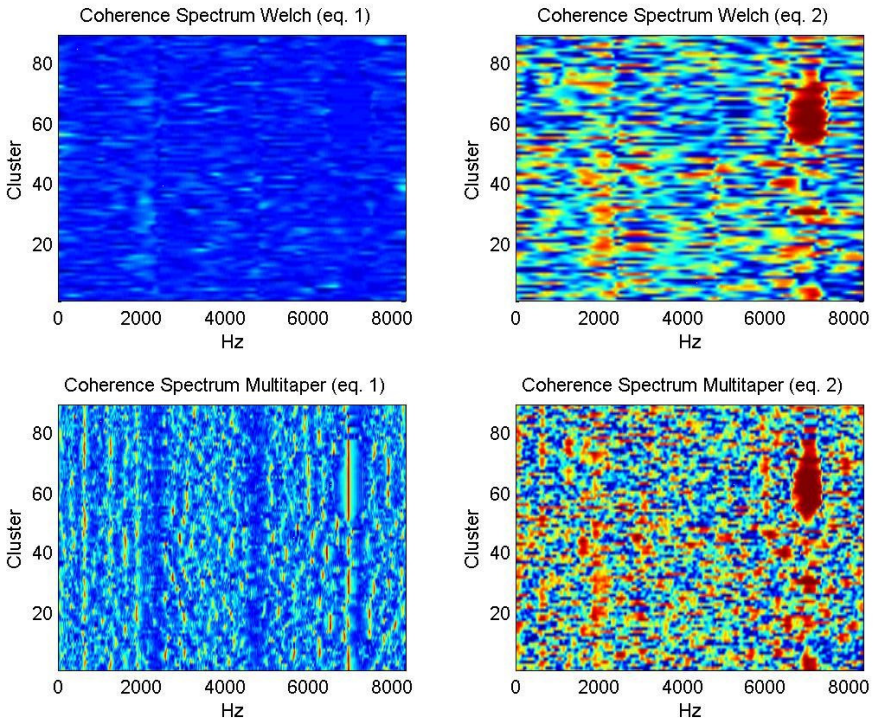

Figure 19: The coherence spectrum of a patient G where the pinpricking happened at 58% into 1300 click series. The 1 and 2 indicate which equation which was used in definition 10. The difference between the equations lies in which order the summation and the imaginary part was removed.

In figure 19 we look at the coherence spectrum for patient G (see figure 12 for the spectral density) where we can see a clear indication of the brain activity in the higher frequencies at cluster 60 over several cluster pairs. In the plots with the spectral densities for the patients the higher frequencies was removed due to the lack of information in that area which increased the resolution in the lower frequencies. What is also quite surprising is that the resolution of the lower left coherence spectrum have an unexpectedly high resolution.

To interpret the coherence in the lower left graph a straight line can be assumed to share the same frequency. But two separated lines which is differentiated by a gap on the same frequency should not be assumed to share the same frequency to the same degree. This is due to the relative measurement which have been used to make this analysis. These assumptions and interpretations needs further investigation to become more certain.

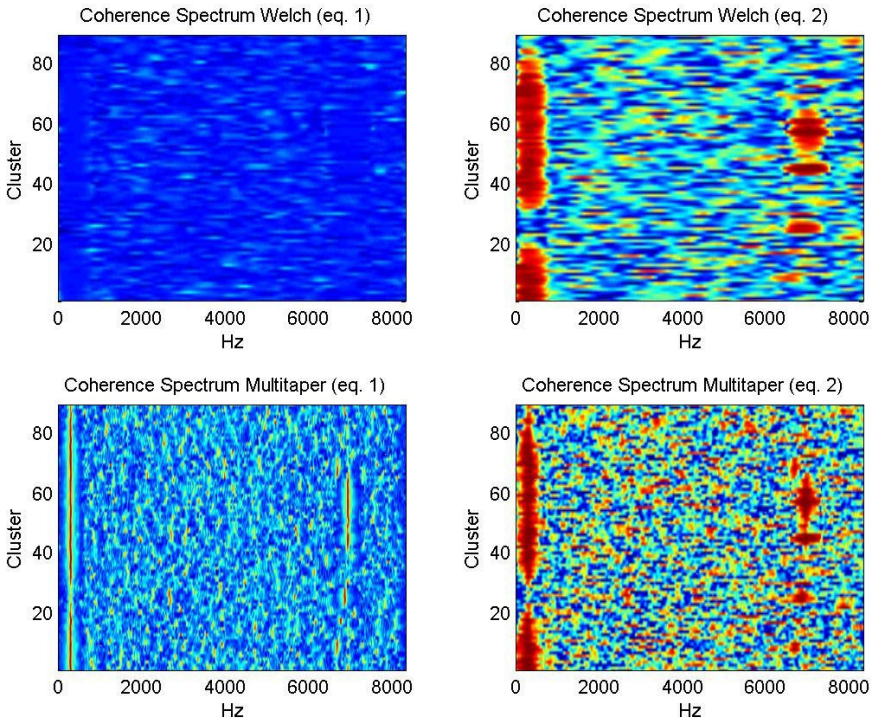

Figure 20: The coherence spectrum of a patient C where the pinpricking happened at 51% into 1300 click series. The 1 and 2 indicate which equation which was used in definition 10. The difference between the equations lies in which order the summation and the imaginary part was removed.

If we take a look at coherence for patient C again in figure 20 we see that something happens around 50% at about 7000 Hz and that there is a lingering peak. Compared to the spectrum for patient C the coherence plot shows the needle pinpricking much clearer (see figure 13 and 20).

8 Conclusion

As expected there is a lot of information hidden in the auditory brainstem responses which can actually be extracted with common statistical methods. Surprisingly there also occurred a quite distinctive butterfly pattern which was easy to recognize even if the interpretation of the patterns still needs to be explored a bit more. It is more unexpected that a such distinctive and easy recognizable pattern occurred in the data which combined with the sinusoidal model led to new and interesting results.

To address the purpose of this thesis I think the spectrums shows that a needle can be detected by the ABR method. But to distinguish the peaks connected to the needle pinpricking from other brainstem activity in the brain is hard with the spectrum. By using the coherence combined with the spectrum density etiolate methods may shed some light over the different brain activity peaks but further investigation is needed.

In the ideal situation each peak in the spectrum would be matched to an outer physical activity. In several figures there is indication to brain activity at several times and to connect these peaks more data needs to be collected about movements or other interferences which may have occurred during the measurement.

The information we gained is everything outside the profiles from the mean of the clusters that SensoDetect use in their research. All the other information is something we have gained compared to before. So the model, spectrum, covariance and the coherence plots all tell us something new. A lot of this information need further investigations as mentioned before but there is also strong indications of different methods can extract the needle pinpricking from real data.

When I look at the ABR analysis method the greatest loss seems to be in the time dimension due to the averaging of all the clusters. But this also removes a lot of resolution from the information you can get out from the ABR method.

The model shows promise but I am aware of that further investigation is needed to decide how well the model describes the ABR signal. I think the model miss some elements to describe the ABR signal. The model is not stable enough when the phase shift distribution changes. By looking at the phase and the coherence some of the mystery around the butterfly pattern lifted. There is some connection between the phase and butterfly pattern but it is hard to pinpoint.

Other areas that would need to be studied are stability and reliability of the coherence method using equation 1 from definition 10. A discussion and investigation of the interpretation for real world problems would also be useful.

The methods advantage of resolution in frequency would make it a great tool to both the neuroscience but also other areas. Another important point of the coherence is that you can get a relative measure in time just by comparing the observation to the following observation. This can lead to that information can be extracted in real time.

It is possible that the coherence plots indicate that the model is to simple which is not that surprising. The model should probably be the sum of sinusoids. The model should carefully be expanded to ensure the stability. To simulate the needle pinpricking an additional high frequency sinusoid component seems like a good model according to the coherence plots.

References

[1] G. D. Brushe and J. R. Waller. On the computation of an averaged coherence function. *Digital Signal Processing*, 11(2):110–119, 2001.

[2] D. Cvetkovic and I. Cosic. *States of Consciousness: Experimental Insights into Meditation, Waking, Sleep and Dreams*. Frontiers collection. Springer, 2011.

[3] M. Hansson and G. Salomonsson. A multiple window method for estimation of peaked spectra. *IEEE Transactions on Signal Processing*, 45(3):778–781, 1997.

[4] J. Källstrand, P. Montnémery, S. Nielzén, and O. Olsson. Auditory masking experiments in schizophrenia. *Psychiatry Res*, 113(1-2):115–25, 2002.

[5] J. Källstrand, S.F. Nehlstedt, M.L. Sköld, and S. Nielzén. Lateral asymmetry and reduced forward masking effect in early brainstem auditory evoked responses in schizophrenia. *Psychiatry Res*, 2012.

[6] J. Källstrand, O. Olsson, S.F. Nehlstedt, M.L. Sköld, and S. Nielzén. Abnormal auditory forward masking pattern in the brainstem response of individuals with asperger syndrome. *Neuropsychiatr Dis Treat*, 6, 2010.

[7] S. S. Mader. *Biology*. McGraw-Hill, New York, NY 10020, 10th international edition, 2010.

[8] J. Malmivuo and R. Plonsey. *Bioelectromagnetism-Principles and Applications of Bioelectric and Biomagnetic Fields*. Oxford University Press, New York, 1995, 1995.

[9] D. J. Thomson. Spectrum estimation and harmonic analysis. *Proceedings of the IEEE*, 70(9):1055–1096, 1982.

[10] P. Welch. The use of fast fourier transform for the estimation of power spectra: a method based on time averaging over short, modified periodograms. *Audio and Electroacoustics, IEEE Transactions on*, 15(2):70–73, 1967.