SIMULATION AND EXTRCATION OF SINGLE TRIAL EVOKED POTENTIALS

by

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Evoked potentials (EPs) are defined as potentials that are caused by the electrical activity in the central nervous system after stimulation. In analysis of evoked potentials the main problem is to extract the EP waveform from the measurements that also contain on-going background electroencephalogram (EEG).

The most conventional tool for the analysis of evoked potentials has been the averaging of the measurements over an ensemble of trials. This is the optimal way to improve the signal-to-noise ratio when the evoked potential is a deterministic signal independent of and additive to background noise of zero mean. However it is evident that the evoked potential can vary with repetitions of the stimuli.

There are two aims of this thesis. The first is to develop a new simulation method for evoked potentials with slow variations among different trials. The second aim is to develop a new method to extract the variations occurring in a number of time-aligned trials. These variations are then added to the mean of the measurements to reconstruct the single trial evoked potentials.

The extraction method has been evaluated using both simulated data and real measurements with satisfactory results.

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1.0 INTRODUCTION

1.1 BACKGROUND AND NATURE OF PROBLEM

Evoked potentials (EPs) or event related potentials (ERPs) result from the electrical activity of the central nervous system in response to an external stimulus. There are two types of evoked potentials, *exogenous* EPs and *endogenous* EPs [3]. Exogenous EPs are determined by the physical characteristics of the stimuli only whereas endogenous EPs are determined by the psychological significance of the stimuli. An example for endogenous EP is cognitive EPs.

The evoked potentials are usually measured from the scalp of the human head. The measured potential is a superposition of various electrical activities of the brain. These activities include those from muscles, eye movements, and spontaneous background electroencephalographic (EEG) waves. The background EEG is usually thought to be uncorrelated with the evoked potentials as well as with the stimulus. The origin of EPs has been investigated, see for example [4], however it will not be discussed in this thesis.

Amplitude and latency are two important characteristics of EPs. The delay time between a stimulus and a corresponding EP component is referred as the component's latency. Normally the latency can range from 2 milliseconds to over 300 milliseconds. However, under some pathological conditions the latency as well as the amplitude and the shape of the EP may change considerably. As a result, the EPs have become very useful clinically and it is important to detect the time varying evoked potentials quickly. A fundamental problem in EP analysis is to extract the waveform of EP from measurements that contain on-going background EEG. The most

widely used tool for EP extraction has been the averaging of the measurements over an ensemble of trials. This is the optimum way to improve the signal-to-noise ratio (SNR) when the EP is a deterministic signal independent of the additive, zero mean background noise and the waveform of the EP in different trials do not change. However, it is evident that EPs vary in different trials. In particular, the latencies and the amplitudes of the peaks in the potentials can vary between the repetitions of the stimulus [5]. The information about the variation of EPs vanishes when EP trials are averaged.

Currently, the goal in the analysis of the EPs is to obtain information about single potentials, e.g., obtain the best possible estimate for each trial. The notion of single trial analysis can be used in this context. The most common way to perform single trial analysis is to form a filter with which the unwanted on-going background activity can be filtered out from the measured data. A major difficulty in this task is the very low signal-to-noise (SNR) ratio which is often less than -10 dB. As we will see in subsequent chapters, there are several methods of detecting time varying single trial EPs. However, each method has some drawbacks.

1.2 THE AIMS AND CONTENTS OF THE THESIS

There are two specific aims of this thesis .The first is to provide a simulation method for single trial potential. The second aim is to develop a method that effectively extracts single trial EPs.

In order to accomplish these two tasks, this thesis is divided into five chapters including this introduction. Chapter 2 provides a literature review on simulation methods of EPs and EEG. The different existing methods for estimation of EPs are analyzed in Chapter 3. Chapter 4 contains the novel part of the thesis. In this chapter we introduce a new method for simulation and extraction of EPs. Chapter 5 contains the overall discussion and conclusion of the thesis.

2.0 SIMULATION OF EVOKED POTENTIALS

2.1 INTRODUCTION

Simulation is an important part of the evaluation of any estimation method before applying it to real measurements. By simulation we mean a method with which one can create artificial observations whose properties match in some sense with the properties of real measurements. These properties can be controlled in the simulated data to evaluate the performance of the estimation method in different situations. One can then calculate the true estimation errors and try to form estimators that minimize the errors. In the case of real measurements one can only access the residual.

2.2 SIMULATION OF THE BACKGROUND EEG

In evoked potential estimation it is usually assumed that the background EEG is a stationary process. This is a reasonable assumption because the background EEG is by definition independent of the stimulus. It is then easy to simulate the EEG with some time-independent parametric model. The AR-model approach is used e.g. in [6, 7 ,8].

Let $E_i^{(j)}(t)$ be the background EEG. As a stationary process it can be approximated with the sum

$$\hat{E}_i^{(j)}(t) = \sum_{k=1}^{N} \phi(k)\, \hat{E}_i^{(j)}(t-k) + v_i^{(j)}(t) \qquad (2.1)$$

that is, with an AR(p) model. The constant N is the model order, Φ(k) are the so called prediction coefficient (AR parameters) and $v_i^{(j)}(t)$ *is* white noise. There are several methods for the

estimation of AR parameters. The most common methods are Yule-Walker method and least square method.

2.3 SIMULATION OF EVOKED POTENTIAL

Evoked potentials are commonly simulated by making linear combination of sine and cosine wave [7, 8]. Simulation of evoked potentials depends upon the method of estimation used to estimate evoked potentials. In this section we review two different methods presented in [9] for simulation of evoked potentials.

COMPONENT BASED SIMULATION

In some cases the goal of evoked potential analysis is to get information about the location of peaks and their amplitudes. In this case we need a simulation method in which we can use peak locations as parameters.

In this method a set of evoked potentials are measured and their average is calculated .From the averaged evoked potential the number and locations of the peaks are determined. By using non-linear least square scheme a Gaussian shape function is fitted to the averaged evoked potential. Limits of desired location and amplitude variation of the peaks are set .These locations and the amplitudes can then be selected by some joint density like Gaussian or uniform densities. These simulated evoked potentials with varying peaks are then added to the simulated EEG to get the data.

This method is not consistent with the real data in a strict sense and is suitable for evaluating the performance of latency estimation methods.

PRINCIPAL COMPONENT BASED SIMULATION

This method is based on the interpretation of the evoked potentials as random vectors. The second-order statistics of a prototype set of real measurement is first extracted.

Then from a set of evoked potentials $z_{1(j)},\ldots.z_N^{(j)}$ the mean η_j and the centered covariance $\hat{C}_z^{(j)}$ can be estimated .

$$\hat{C}_z^{(j)} = \frac{1}{N}\sum_{i=1}^{N}\left(z_i^{(j)} - \eta_j\right)\left(z_i^{(j)} - \eta_j\right)^T \tag{2.2}$$

From the eigen decomposition

$$\hat{C}_z^{(j)}\ U_j\ =\ U_j\Lambda_j \tag{2.3}$$

where $U_j\ =(u_1^{(j)},.....u_T^{(j)})$ and $\Lambda_j = diag(\lambda_1^{(j)},...\lambda_T^{(j)}).U_{j,p}$ matrix can be formed from the eigen vectors .Usually p eigenvectors correspond to p largest eigen values. The idea is that the eigenvectors should correspond to evoked potential part and not to the background EEG.

Evoked potentials are then simulated using

$$\hat{s}^{(j)} = U_j\Lambda_j^{1/2}x\ +\eta_j \tag{2.3}$$

where x is jointly Gaussian random vector with zero mean and covariance C_x=I. The density of $\hat{s}^{(j)}$ is jointly Gaussian with mean η_j and covariance $U_{j,p}\Lambda_j U^T_{j,p}$ .These simulations are then added with the simulated EEG to get simulated measurement. This method gives more realistic result as compared to the component simulation method as the first and second moment of the measured and simulated data are almost same by construction.

3.0 ESTIMATION OF EVOKED POTENTIAL

3.1 INTRODUCTION

Evoked potentials represent the time-varying potentials ***s*** in some location of the scalp. The potential is caused by stimulation of the somatosensory system. We assume that the measurements ***z*** of these potentials also contain noise ***v***. The source of *v* is the spontaneous brain activity which is called the background EEG. Background EEG is thought to be independent of the stimulation and additive to the evoked potential. This is called the additive noise model for observations

$$z = s + v \tag{3.1}$$

The methods that are used to estimate the evoked potentials are sometimes divided into deterministic and stochastic methods. In the deterministic approach, ***s*** is thought to be fixed between repetitions of the test. Although it has been evident [5] that this is not always a proper assumption, it is commonly used in estimation of evoked potentials. In the stochastic approach the evoked potential ***s*** is assumed to be random vector with some probability density *p(s)*.

3.2 IMPORTANT ISSUES IN EVOKED POTENTIAL ESTIMATION

There are some important issues which have to be considered in estimation of evoked potentials. A review of the current literature shows that these can be summarized as follows.

- *Assumption* is one of the most crucial issues as the nature of estimation itself ensures that there will be assumptions being made. The trick is to make justifiable assumptions about the data's nature. Sometimes, people make such assumptions

which make the estimation method easy but jeopardize the accuracy of the estimated evoked potentials.

- *Signal to Noise Ratio (SNR):* In dealing with evoked potentials, one of the most difficult problems is dealing with the background EEG. Other than EEG there are some other noise sources like amplification artifacts, scalp conductance noise, and external electrical interference. As the SNR is usually very low in these kinds of problems the estimation method should be efficient enough to increase it to an optimum level.
- *Detection of Time-Varying behavior*: It is now evident that the evoked potential is a non-stationary signal. It is important that the estimation method should be able to determine whether the evoked potential is changing in terms of latency, amplitude or shape. Some estimation methods are dedicated only to find time-varying changes.
- *Evoked Potential Waveform:* We want to determine the changes occurring in evoked potential but simultaneously we want to have an idea as to what the evoked potential looks like.

3.3 OVERVIEW OF CURRENT EVOKED POTENTIAL ESTIMATION METHODS

In this chapter we review the existing methods for the estimation of evoked potentials. The different methods can be categorized into *ensemble analysis* methods and *single trial* methods.

- *Ensemble Analysis* methods are those that give the information about the first or second order statistics of set of evoked potentials.
- *Single Trial* methods are those that give information about single responses.

It has been suggested that the use of average waveform is not a proper approach in source localization. The use of single trials in topographic estimates also gives temporal information about adaptation and habituation as underlined in [10].

Most of the methods that are reviewed here are applicable for analysis of several kinds of evoked potentials. The potentials that are used in the evaluation of the methods include e.g. the somatosensory evoked potentials (SEP), visual evoked potentials (VEP) and auditive evoked potentials (AEP).

ENSEMBLE ANALYSIS

In this section we review in detail some of the ensemble analysis methods used in evoked potential analysis.

Averaging

The most conventional method of estimating evoked potential is ensemble averaging. The following are the assumptions made in this scheme

- The noise is random and stationary.
- The noise is uncorrelated to the signal and has zero mean.
- The response of the nervous system is stable over the measurement interval i.e. the evoked potential is stationary.

The measurement vectors $\mathbf{z_i}$ *are* averaged to increase the SNR ratio. If $\boldsymbol{s}$ does not vary between the repetitions, the measurements can be written in the form.

$$z = s + v = H\theta + v \tag{3.2}$$

where $H = (I|....|I)^T$, $\theta = s$, $z = (z_1^T, ..., z_N^T)^T$ and , $v = (v_1^T, ..., v_N^T)^T$ .The least squares solution for s can then be written in the form

$$\hat{s} = \left(H^T H\right)^{-1} H^T z \tag{3.3}$$

$$= \left(NI\right)^{-1} \sum_{i=1}^{N} z_i \tag{3.4}$$

$$= \frac{1}{N} \sum_{i=1}^{N} z_i \tag{3.5}$$

$$= \bar{z} \tag{3.6}$$

Thus we conclude that the average of the measurements is the best estimator in least squares sense for deterministic signal s and additive model. The minimization of the least squares criterion is equivalent to the assumption v ~ $N(0,\sigma^2 I)$

If s is not deterministic, we can obtain for expectation of $\hat{s}$

$$E\left(\hat{s}\right) = \frac{1}{N} \sum_{i=1}^{N} E\left(z_i\right) \tag{3.7}$$

$$E\left(\hat{s}\right) = \frac{1}{N} \sum_{i=1}^{N} E\left(s_i\right) + \frac{1}{N} \sum_{i=1}^{N} E\left(v_i\right) \tag{3.8}$$

As v_i is zero mean,

$$E\left(\hat{s}\right) = \frac{1}{N} \sum_{i=1}^{N} \eta_s = \eta \tag{3.9}$$

so that with the stochastic assumption for the evoked potentials, the average of the observations is an unbiased estimator of the expected value of the evoked potential.

Weighted Averaging

In conventional averaging all the measurements are treated with the same weights. An approach to reduce the effect of noisy waveform is to take into account the covariance of the background EEG.

$$C_v=E\{(v_1^T,\ldots\ldots v_N^T)^T(v_1^T,\ldots\ldots v_N^T)\} \tag{3.10}$$

Usually we can assume that the noise vectors v_i are mutually independent. In this case the covariance of the EEG is of the block diagonal form

$$C_v=diag(C_{v1},\ldots\ldots C_{vN}) \tag{3.11}$$

The estimated evoked potential is

$$\hat{s}=\left(\sum_{i=1}^{N}C_{v_i}^{-1}\right)^{-1}\sum_{i=1}^{N}C_{v_i}^{-1}z_i \tag{3.12}$$

Peak Component Latency-Corrected Average Method (PC-LCA)

Most of the authors seem to agree that latency is the most important characteristic of evoked potentials. Part of the explanation for this is, that latency corresponds to conduction delay along the neural pathways. PC-LCA method introduced in [8] is based upon LCA [11].This method consists of three main steps. The observed response trials are first preprocessed by a time-varying adaptive filter so as to eliminate the ongoing EEG from single trial. Then, the peak components are detected, and those having similar latency are grouped and averaged to get the estimates of the mean amplitude and latency. In doing so, a peak component distribution function (PCDF) is computed to determine validated intervals over which the detected peak components should be grouped. The resulting discontinuous evoked potential is superimposed on the

background waveform obtained from conventional ensemble averaging and then smoothed by fitting a truncated Fourier series to get the final estimate.

SINGLE TRIAL METHODS

In this section we review the most common method proposed for single trial estimation.

Wavelet Denoising

Wavelet denoising is comparatively a new method proposed in [12] for estimation of single trial evoked potentials. It provides time-frequency decomposition for the analysis of evoked potentials. This method assumes that the evoked potential is non-stationary. In this method the activity of the averaged evoked potential is decomposed in different frequency bands and times using the wavelet multiresolution decomposition. Wavelet coefficients correlated with evoked potentials are identified and the remaining ones are set to zero. The chosen coefficients cover a time range in which the single-trial evoked potentials are expected to occur and then the inverse transform is calculated to obtain the denoised averaged evoked potential. The above found coefficients are used to denoise the single trial evoked potential. This method used prior information about the peaks of evoked potential to identify the coefficients. These coefficients are identified manually which is a very tedious task. This method uses a time range in which single trials evoked potentials are expected but does not mention how to calculate the time range.

Adaptive Filtering

The use of adaptive filtering in analysis of evoked potentials has been studied intensively during the last ten years. Most of the methods implement LMS algorithm for filtering as done in [13].

In this method the authors model the evoked potentials with dynamic Fourier series and apply adaptive filtering using LMS algorithm to find the Fourier coefficients which minimizes the

MSE between the successive sweeps and the model, thus adapting to the time-varying changes in evoked potentials. This method needs to know the frequencies of the evoked potentials. The method does not work well when two peaks are present in the evoked potentials .Since it is required that the evoked potential is coherent, stimulus artifacts can not be dealt with noise which has any of the evoked potential frequencies.

4.0 NEW METHOD FOR SIMULATION AND EXTRACTION OF EVOKED POTENTIALS

4.1 SIMULATION OF EVOKED POTENTIAL

Simulation is an important part of the evaluation of any estimation method before applying to real measurements. By simulation we mean a method with which one can create artificial observations whose properties match in some sense, as closely as possible with the properties of real measurements. One can then calculate the true estimation errors and try to form estimators that minimize the errors. In the case of real measurements one can only access the residual. In this section we present a new method for simulation of single trial evoked potentials which we call as *variation-based single trial simulation*.

VARIATION-BASED SINGLE TRIAL SIMULATION

It is now well established that the evoked potential is not a stationary signal and it varies from trial to trial, it is important to consider these variations while simulating the evoked potentials. The following are the assumptions made for the simulation of single trial evoked potentials

- The variations occurring in single trial EPs have low frequencies which means that the waveform of EPs changes slowly with the stimulus..
- The background EEG is uncorrelated with the evoked potential as well as with the stimulus.
- The background EEG is a stationary signal and has a zero mean.
- The background EEG segments are random and uncorrelated with each other.

- The background EEG is additive to the evoked potential i.e. it follows the additive noise model z = $s + v$ where z is the measurements, s is the evoked potential and v is the EEG.

In this simulation method we used a prototype of real measurements. This ensures that the properties of the simulations are comparable with the real measurements. For this purpose we used real auditory evoked potential data from channel Cz.

The proposed method is as follows

1. Measure a set of evoked potentials single trial data $z = (z_1,...,z_N)$. In our case we used auditory EP in which each trial is 770 data points long as shown in Fig 1

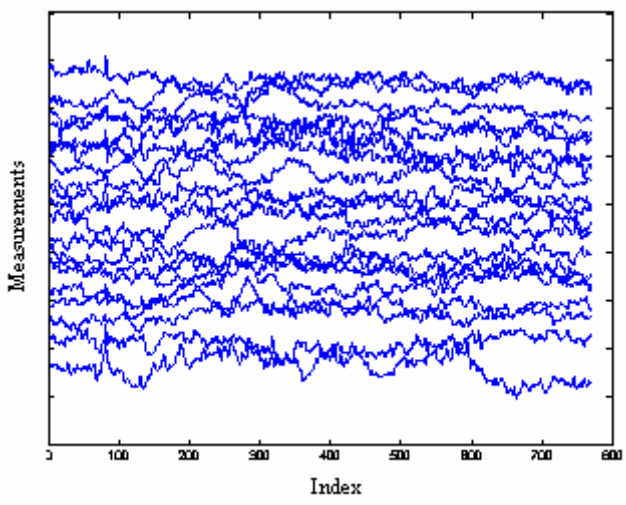

Figure 1: First 20 trials of real auditory data

2. By classical method compute the average m of the data z .As the EEG is uncorrelated with EP, random and zero mean, the average noise will converge to zero and a single EP waveform will be left as shown in Fig 2.

$$m = \frac{1}{N}\sum_{i=1}^{N} z_i \qquad (4.1)$$

3. By doing averaging we lose the variations occurring in the EPs and are left with one waveform. To make more EP trials create a mask Q of size N x M where N is the number

of trials and *M* is the number of data point in each trial. This mask can be created by using random Gaussian noise with zero mean and unit variance. A 770 x770 mask is shown in Fig 3.

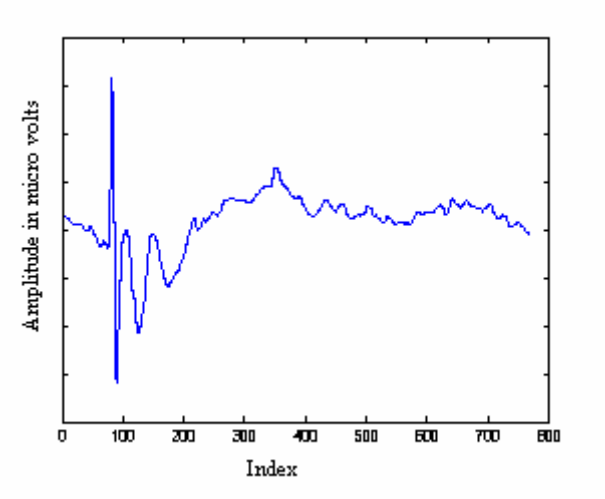

Figure 2: Averaged evoked potential waveform

4. The purpose of making this mask is to simulate the variations that occur in single trials. The noise present in *Q* is white and the spectrum of white noise has all the frequencies. We have assumed that the variations occurring in single trial EPs have low frequencies and change very slowly with the stimulus. To make low frequencies variations, filter the high frequencies present in mask *Q* using *a 2*-dimensional filter.

White Noise

A white noise is a random wide-sense stationary process *x(n).* A process is said to be white if the covariance function is zero for all k except zero.

$$c_x(k) = \sigma_x^2 \delta(k) \tag{4.2}$$

Therefore, the covariance function of one-dimensional white noise is an impulse function while for a two-dimensional white noise it is a diagonal matrix. White noise is a sequence of uncorrelated random variable, each having a variance of σ_x^2 .

The autocorrelation sequence of a WSS process provides a time-domain description of the second-order moment of the process. The discrete-time Fourier transform of $c_x(k)$,

$$P_x\left(e^{jw}\right) = \sum_{k=-\infty}^{k=\infty} c_x(k) e^{-jkw} \tag{4.3}$$

is called the *power spectrum* or *power spectral density* of the process. It provides the frequency domain description of the second-order moment of the process. Power spectrum is a real and even function. The power spectrum of a zero mean white noise is a constant over all the frequencies.

$$P_x(e^{jw}) = \sigma_x^2 \tag{4.4}$$

The *Q* matrix has 2-dimensional white noise whose power spectrum has a constant value across all the frequencies. To simulate the variations we have to filter out the high frequencies from the matrix *Q*.

Filtering White Noise

x(n) is white noise with zero mean , σ_x^2 variance and autocorrelation $r_x(k)$.If *x(n)* is filtered with a stable linear shift-invariant filter having a unit sample response *h(n)*, then the output *y(n),* is a random process that is related to *x(n)* by the convolution sum.

$$y(n) = x(n) * h(n) = \sum_{k=-\infty}^{\infty} h(k) x(n-k) \tag{4.5}$$

The mean of *y(n)* is zero and its autocorrelation is given by

$$r_y(k) = r_x(k) * h(k) * h(-k) \tag{4.6}$$

The power spectrum of y(n) is given by

$$P_y(e^{jw}) = \sigma_x^2 \ | H(e^{jw})^2 | \tag{4.7}$$

If *h(n)* is a low pass filter then the high frequencies present in *x(n)* will be filtered out.

As the noise in Q matrix is 2-dimensional and isotropic in nature, we use a 2-dimensional filter to filter out high frequencies. Gaussian filter would be the best filter for this purpose due to the following properties of it.

- In two dimensions, Gaussian functions are rotationally symmetric. This means that the amount of smoothing performed by the filter will be the same in all the directions.
- Gaussian function has a single lobe. This means a Gaussian filter smoothes by replacing each image pixel with a weighted average of the neighboring pixel such that the weight given to the neighbor decreases monotonically with distance from the central pixel.
- Fourier transform of a Gaussian is itself a Gaussian. The single lobe in the Fourier transform means that the unwanted high frequency signal will be cancelled out.
- The width, and hence the degree of smoothing, of a Gaussian filter is parameterized by σ (standard deviation), and the relationship between σ and the degree of smoothing is very simple. A larger σ implies a wider Gaussian filter and greater smoothing.

$$G[i, j] = Ke^{-\left(\frac{i^2+j^2}{2\sigma^2}\right)} \tag{4.8}$$

Where *G[i,j]* is the 2-dimensional Gaussian filter and *k* is a constant. The low frequency mask *F* can be computed by doing the convolution of *G* over *Q*

$$F = G * Q \tag{4.8}$$

We call *F* matrix as variation matrix. The filter and the variation mask are shown in Fig 4 and Fig 5 .The power spectrum and the autocovariance matrix of the F matrix are shown in Fig 6 and Fig 7

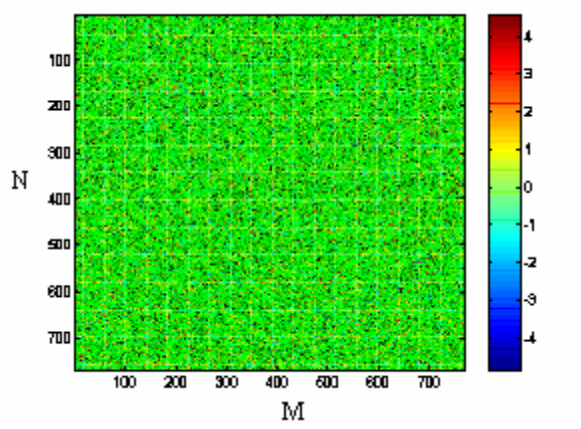

Figure 3 : Gaussian white noise mask of size 770 x 770

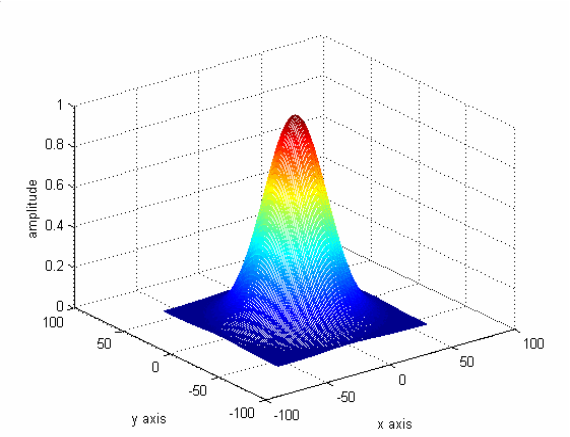

Figure 4: Two dimensional Gaussian filter of size 120x120 with standard deviation of 20

5. Add the averaged waveform *m* to each row of the variation mask *F* to get *N* single trial EPs of *M* data length denoted as $(s_1, \ldots s_N)$. The simulated single trials are shown in Fig 8 and Fig 9

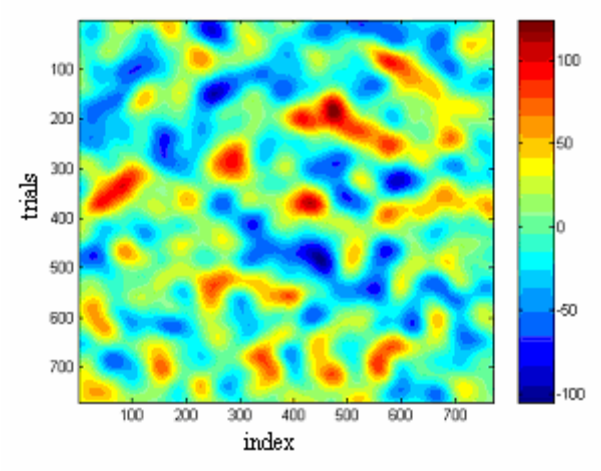

Figure 5 : Variation mask of size 770x770

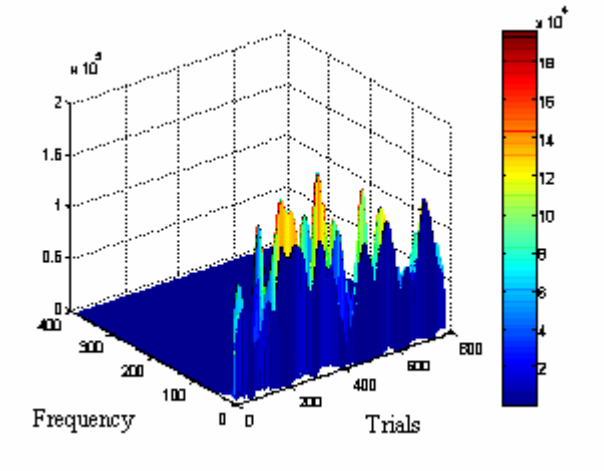

Figure 6 : Power spectrum of the variation matrix

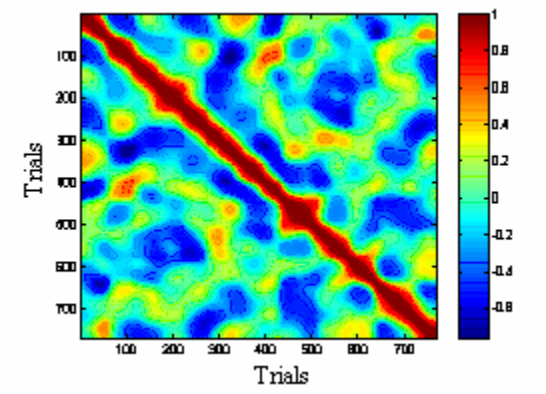

Figure 7 : Autocovariance matrix of the variation matrix

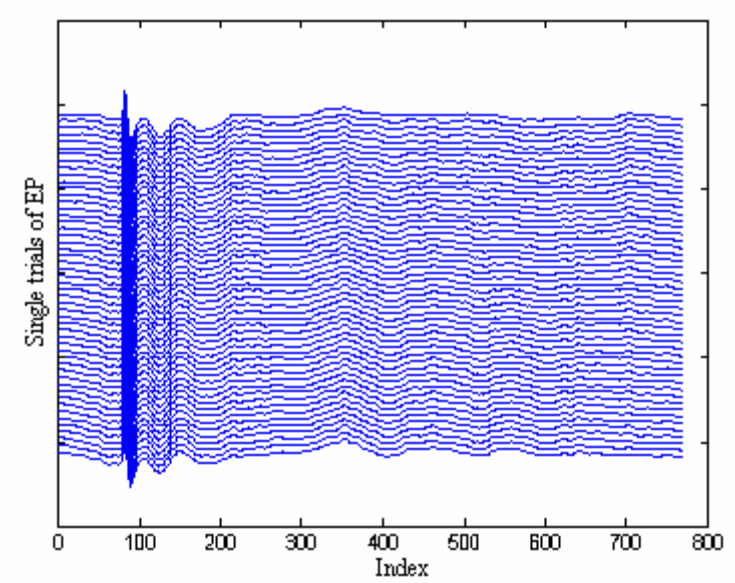

Figure 8 : First 50 simulated single trial evoked potentials

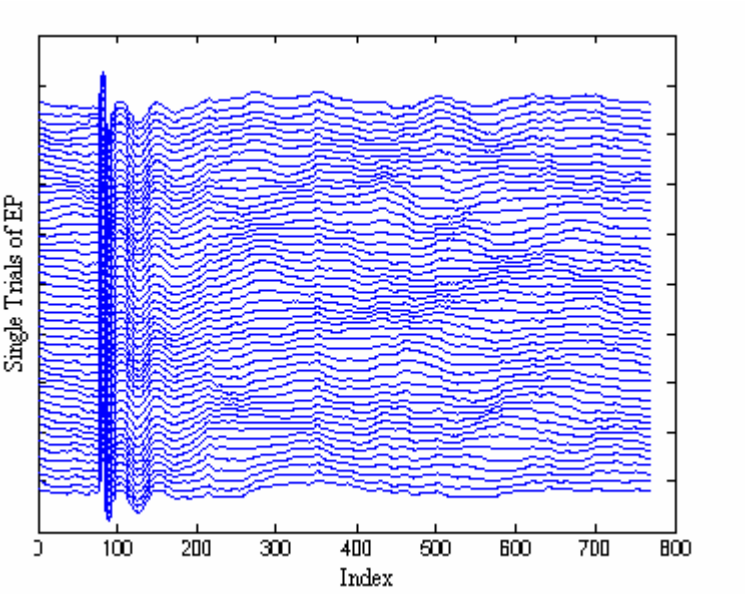

Figure 9 : Every tenth simulated evoked potential

6. To simulate the data *z* we also need to simulate the background EEG. Compared to the approach of AR modeling for simulation of EEG as done in [6, 7, 8], which uses a white noise, it is more accurate and realistic to use real EEG data. For this purpose we used a real EEG signal that does not have any EP embedded inside it and divided that signal in

N equal segments ,each of length M to create EEG data $(v_1, \ldots v_N)$ .The EEG data we used in our simulations is shown in Fig 10.

7. Using the additive model of noise we added the real EEG data to the simulated single trial EPs to get the simulated data:

$$z = s + v$$

The simulated data with a SNR of -17.17 where, $SNR = 20\log_{10}\left(\frac{\sigma(f)}{\sigma(v)}\right)$ is shown in Fig.11

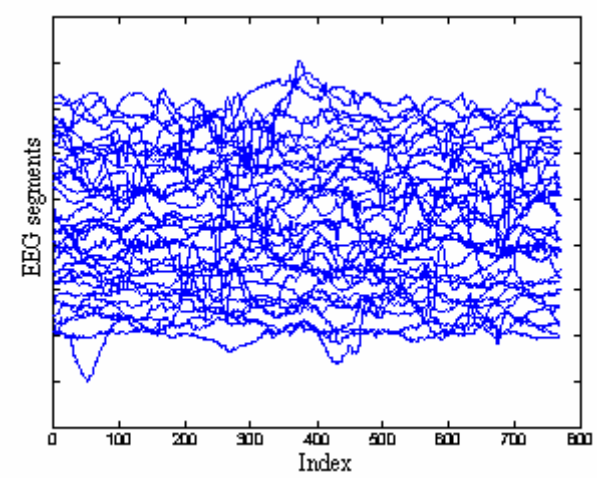

Figure 10 : First fifty segments of EEG data

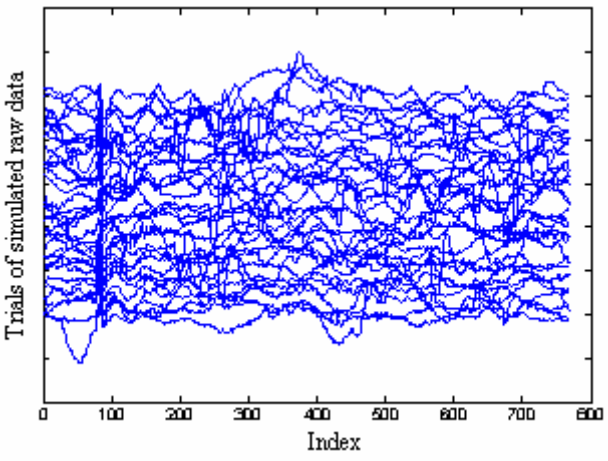

Figure 11 : First fifty trials of simulated data

4.2 EXTRACTION OF SINGLE TRIAL EVOKED POTENTIAL

In this section we present a new method for extraction of single trial EPs and we will call it *variation-based extraction method*. But before explaining the method we will discuss the properties of the EEG data.

PROPERTIES OF EEG DATA

Correlation

EEG matrix is constructed by dividing a long EEG signal into equal segments. Each segment of EEG signal represents the row of EEG matrix.

$$C_v = E(vv^T) \tag{4.9}$$

The Autocovariance matrix C_v which computes the correlation between these EEG segments is almost a diagonal matrix and the power spectrum is approximately flat for all the frequencies as shown in Fig.12 and Fig.13 .This shows that there is no correlation between the segments of the EEG.

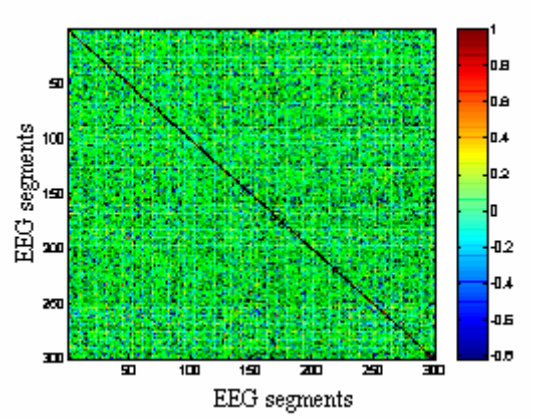

Figure 12 : Part of Autocovariance matrix of EEG matrix showing the no correlation between the EEG segments

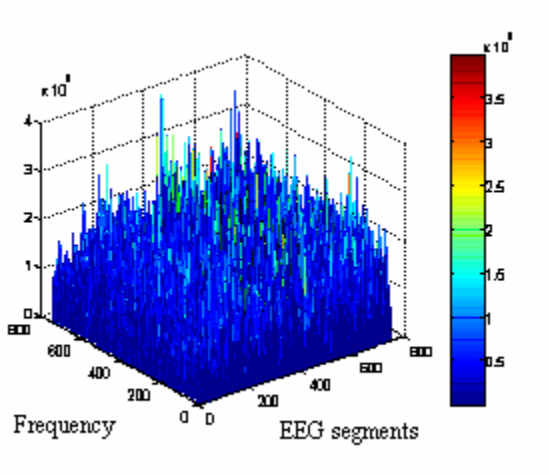

Figure 13 : Power spectrum of the EEG matrix

Distribution

The normalized histogram of a column of the EEG matrix is shown in Fig 14. It shows that the distribution of this histogram is close to a Gaussian distribution.

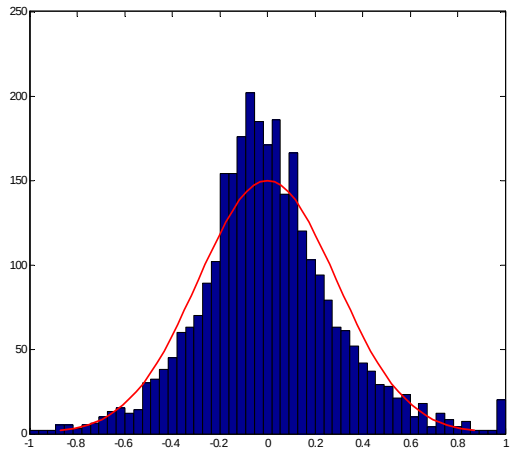

Figure 14 : Histogram showing the distribution of a column of EEG matrix

As the EEG segments $v_1, v_2, \ldots, v_N$ are uncorrelated and their distribution is close to a Gaussian distribution the joint probability density for EEG segments is

$$f\left(v_1, v_2, \ldots v_N \mid \mu, \sigma^2\right) = \prod_{i=1}^{N} \frac{1}{\sqrt{2\Pi\sigma}} e^{-\left[\frac{x_i - \mu}{\mu}\right]^2 / 2} \qquad (4.10)$$

The log of the above function is

$$\ln\left(f\left(v_1, v_2, ...v_N \mid \mu, \sigma^2\right)\right) = \ln\left(\prod_{i=1}^{N} \frac{1}{\sqrt{2\Pi}\sigma} e^{-\left[\frac{v_i-\mu}{\mu}\right]^2} \Big/ 2\right) \tag{4.11}$$

This function is also defined as the likelihood function, which can be written as

$$L\left(\mu, \sigma^2\right) = \left(N \ln \frac{1}{\sqrt{2\Pi}\sigma} - \sum_{i=1}^{N}\left(\frac{v_i - \mu}{\sigma}\right)^2 \Big/ 2\right) \tag{4.12}$$

The maximum likelihood estimator for the mean and the variance can be found by taking the derivative with respect to μ and σ. The maximum likelihood estimator for the mean is

$$\hat{\mu} = \frac{\sum_{i=1}^{N} v_i}{N} \tag{4.13}$$

Therefore, the maximum likelihood estimator for Gaussian distribution is the average of the variables. As the distribution of the EEG segments is not a perfect Gaussian distribution averaging would be the suboptimal estimator.

VARIATION-BASED EXTRACTION METHOD

All the assumptions mentioned in section 4.1.2 for variation-based simulation method also hold here.

- The variations occurring in single trial EPs have low frequencies which means that the waveform of EPs changes slowly with the stimulus..
- The background EEG is uncorrelated with the evoked potential as well with the stimulus.
- The background EEG is a stationary signal and has a zero mean.
- The background EEG segments are random and uncorrelated with each other.
- The background EEG is additive to the evoked potential i.e. it follows the additive noise model z = *s* + *v* where *z* is the measurements, *s* is the evoked potential and *v* is the EEG.

First we describe each step of the new extraction method by applying it on the simulated data followed by results for real auditory data.

The proposed method is as follows

1. Measure a set of raw data from a channel that has EPs embedded in it $z = (z_1, \ldots, z_N)$.
2. Compute the average y of raw data z As the EEG present in z is random, zero mean and stationary all the background EEG will be cancelled and we will be left with one EP waveform.

$$y = \frac{1}{N}\sum_{i=1}^{N} z_i \tag{4.14}$$

3. Subtract this averaged EP waveform y from each trial of the raw data z.

$$g_i = z_i - y \tag{4.15}$$

After subtracting we will be left with matrix g that has background EEG and the variations that are occurring in the single trial EPs. First fifty rows of matrix g are shown in Fig 15

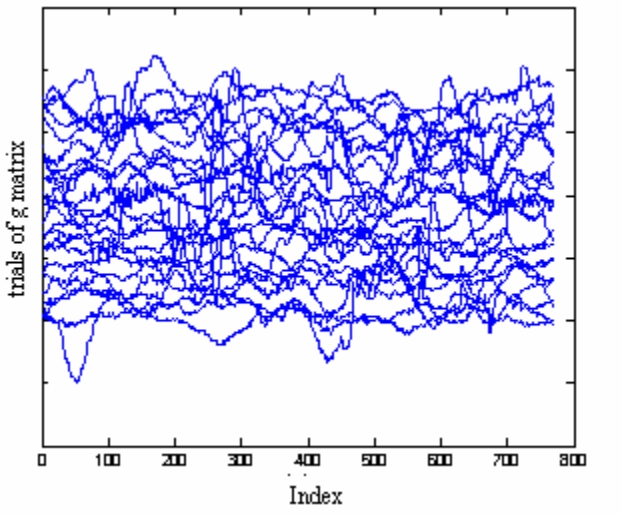

Figure 15 : Resultant data *g* contains the background EEG and variations present in single trial EPs

4. The g matrix contains the EEG and the variations that are occurring in single trial EPs. To extract the variations from g we need to filter out the EEG. The EEG segments are not

correlated to each other and the variations present in each trial are correlated .If we take average of some trials of *g* matrix we will be able to cancel out most part of the EEG. For this purpose we used a moving average window. The moving average window takes *p* number of trials and computes their average and then slide down by one trial and again does the same operation. The moving average window can be summarized by this equation.

(4.16)

5. For the size of the window *p* we have to do a *whiteness test*. When the size of the moving average window is optimum, the *h* matrix will contain all the variations and minimum EEG. So if we subtract this *h* matrix from the matrix *g* we got in equation 4.15 we will get *a* matrix that will have only EEG, as the variations will be subtracted out.

$$a = g - h \tag{4.17}$$

We will perform the whiteness test on matrix *a*.

6. **Whiteness Test** Compute different *h* matrices using different sizes *p* of moving average window and then for different *h matrices, c*ompute the corresponding *a* matrices by using equation 4.17.Calculate *C* autocovariance matrix for each *a* matrix.

$$C = E[(a-E(a))(a-E(a))^T] \tag{4.18}$$

For each element of C matrix (except the diagonals) calculate the absolute correlation coefficients $r_{a_i a_j}$.

$$r_{a_i a_j} = \left| \frac{C_{ij}}{(\sigma_{a_i} \sigma_{a_j})} \right| \qquad i \neq j \tag{4.19}$$

Compute the mean *w* of absolute correlation coefficients $r_{a_i a_j}$

$$w = mean\left(r_{a_i a_j}\right)$$

(4.20)

This *w* is the measure of whiteness. Closer it is to zero, whiter the matrix *a* is. If *w* is close to one then the data in matrix *a* is correlated. Compute the value of *w* for each *a* matrix. Plot the different values of *w* for different values of *p*. The value of *p* corresponding to the minimum mean absolute correlation coefficient *w* would be the optimum window size. The result of the whiteness test for a SNR of -5.13dBis shown in Fig 4.16.

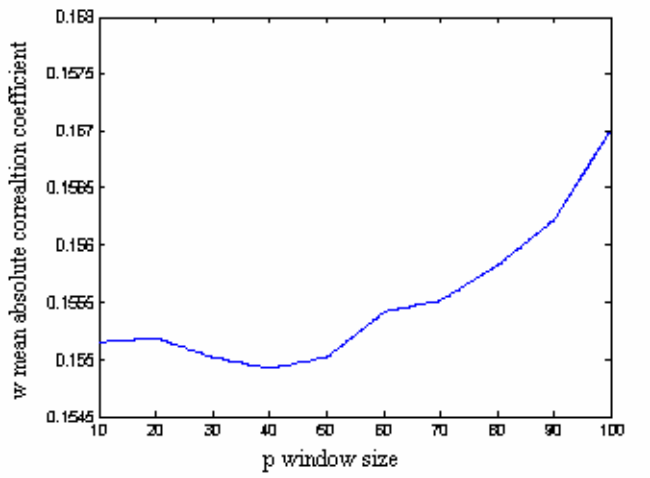

Figure 16 : Result of whiteness test. The value of mean absolute correlation coefficients for different window sizes for SNR of -5.13dB.

From the Fig 16, we can see that the value of mean absolute correlation coefficient is minimum for *p* (size of the window) equal to 40.Therfore; p equal to 40 will be the best size for moving average window to extract the variations *h*. As we are dealing with the simulated data we know how much variations we have added in originally. We can check the accuracy of the whiteness test by finding the mean absolute error *e* for different sizes of the window.

$$e_i = mean(|h_i - f_i|) \tag{4.21}$$

Where *h* is the extracted variation and *f* is the original variation. The error occurred in extraction of the variation for different sizes of the window are shown in Fig 17.

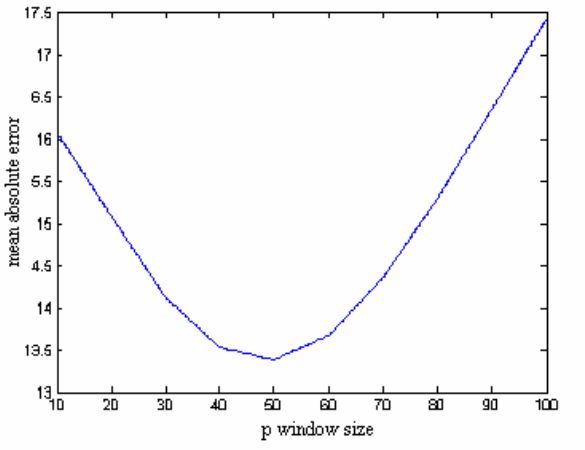

Figure 17 : Mean absolute error occurred in extracting the variations for different window sizes *p*

The minimum error occurred for size of the window equal to 50.But the mean absolute error for size 40 is almost equal to size 50.As for real data we do not know the variations, we will rely only upon the result of whiteness test to find out the optimal size of the window.

7. Use the computed size of the window for the moving average window to filter out the EEG present in g matrix. In our case we used a size of 40. Extracted variations are shown in Fig 18.

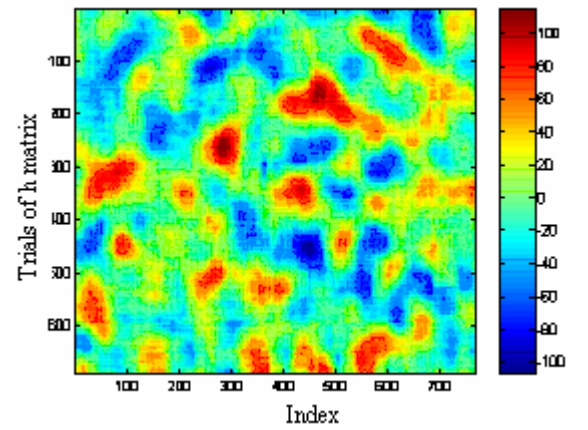

Figure 18 : Extracted variations using a window size of 40 when the SNR was -5.13dB

8. There is still some high frequency EEG left in the extracted variations, which has a similar distribution in both vertical and horizontal direction. We can apply a 2-dimensional Gaussian

filter to remove the remaining high frequency EEG. In our case we decide experimentally to use a 2-dimensional Gaussian filter of size 40x40.The results are shown in Fig 19.

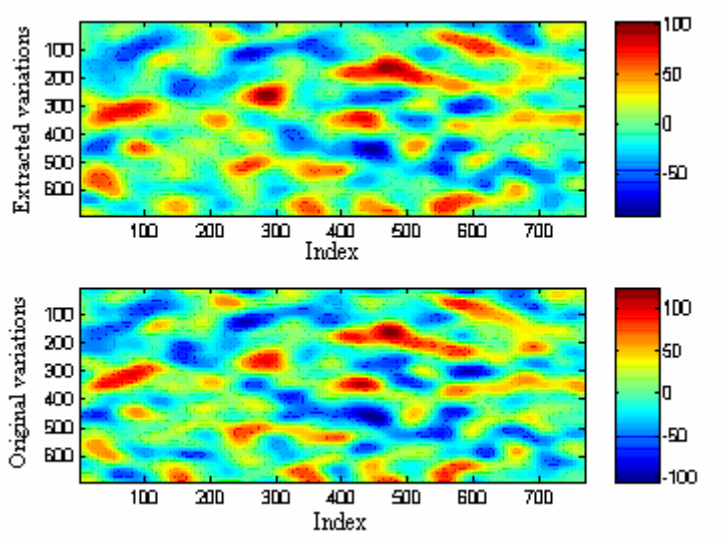

Figure 19 : Top: Extracted variation after 2-dimensional Gaussian filtering when the SNR was -5.13dB. Bottom: Original variations we have added to simulated the EPs

9. The extracted variations look very similar to the original variations. Add the averaged evoked potential *y* calculated in equation 4.14 to get the single trial EPs.The results are shown in Fig 20 and Fig 21.

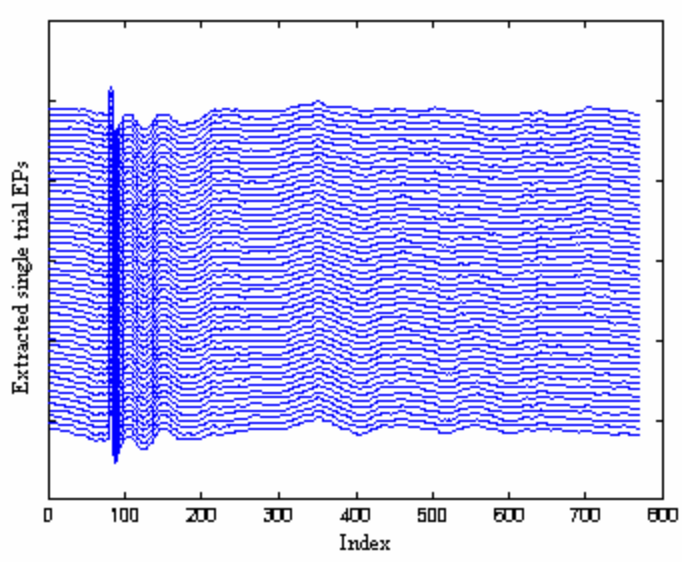

Figure 20 : First 50 Extracted single trial EPs when SNR was -5.13dB

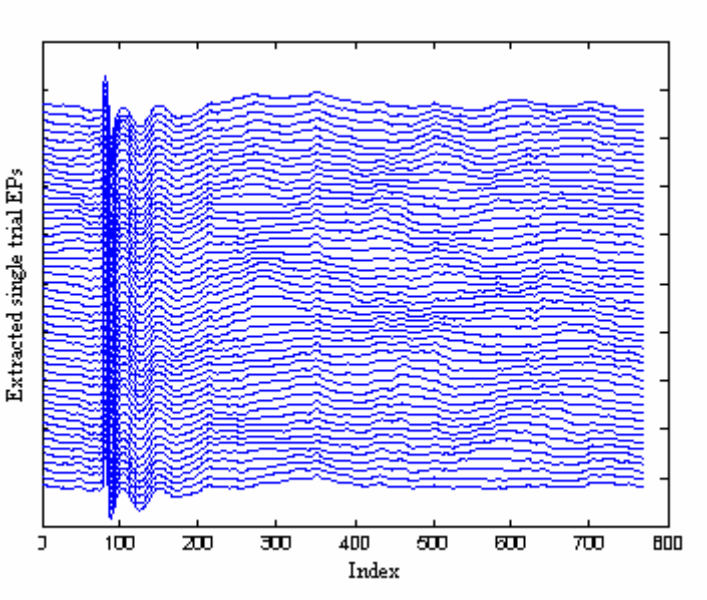

Figure 21 : Every tenth extracted EPs when SNR was -5.13dB

The results for different signal-to-noise ration are shown below.

1. SNR = 7.63dB

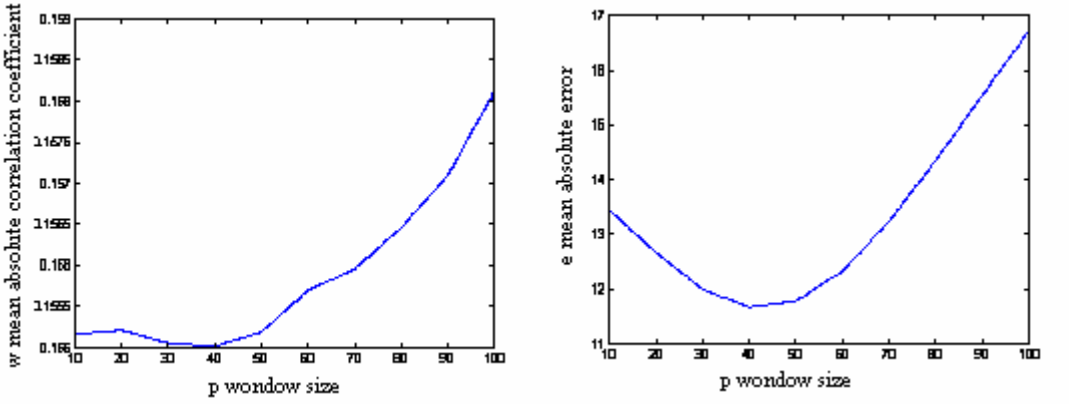

Figure 22 : Left: Result of whiteness test. Right: Mean absolute error when the SNR was -7.16dB

As the mean absolute correlation coefficient is minimum for size equal to 40.We used a size of 40 for moving average window.

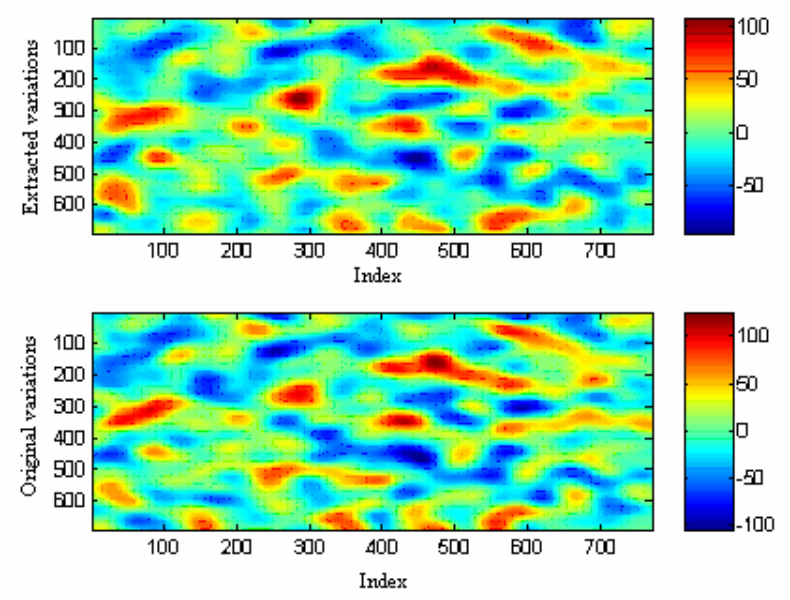

Figure 23: Top: Extracted variation after 2-dimensional Gaussian filtering when the SNR was -7.63dB. Bottom: Original variations we have added to simulated the EPs

2. SNR = -11.16dB

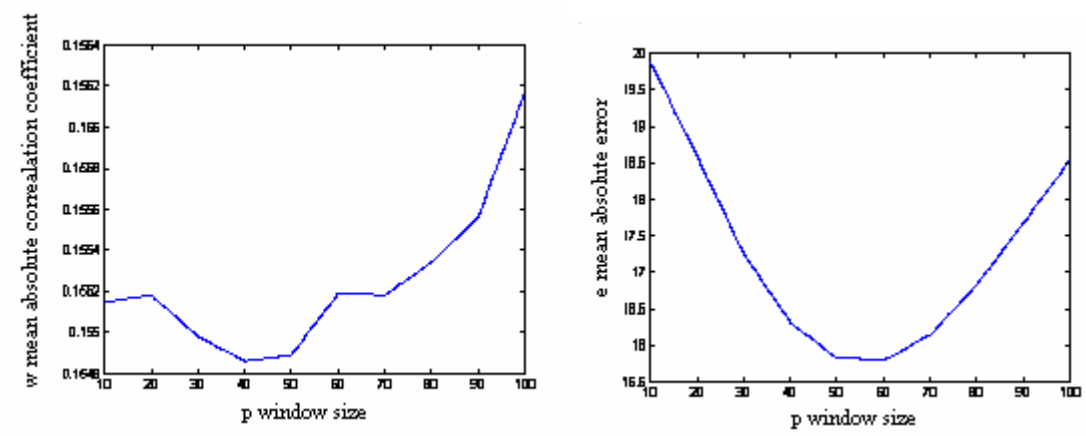

Figure 24: Left : Result of whiteness test. Right: Mean absolute error when the SNR was -11.1 6dB

As the mean absolute correlation coefficient is minimum for size equal to 40.We used a size of 40 for moving average window though the mean absolute error is minimum for size equal 60.The mean absolute error has increased due to the presence of high frequency EEG in extracted variation as the SNR is low .

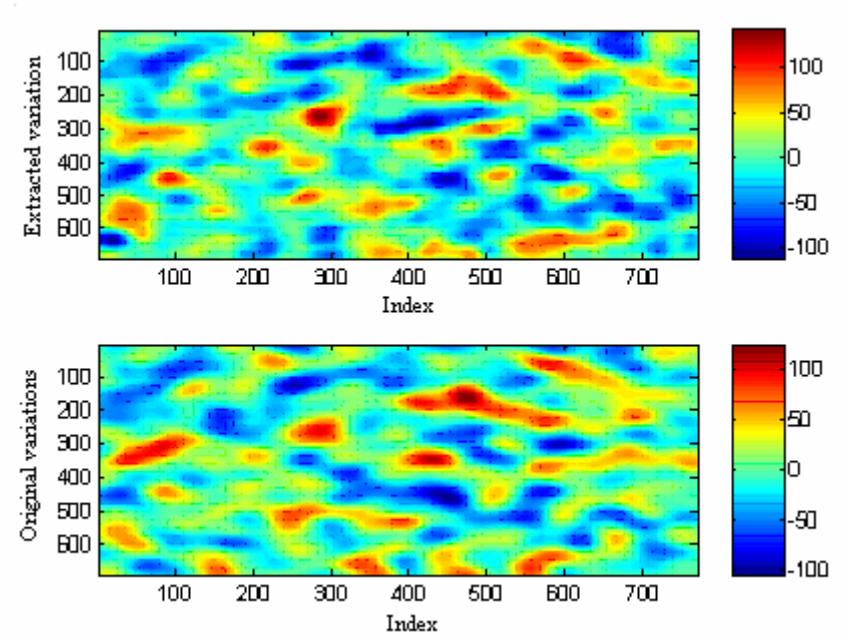

Figure 25: Top: Extracted variation after 2-dimensional Gaussian filtering when the SNR was -11.16 dB. Bottom: Original variations we have added to simulated the EPs

3. SNR = -14.67 dB

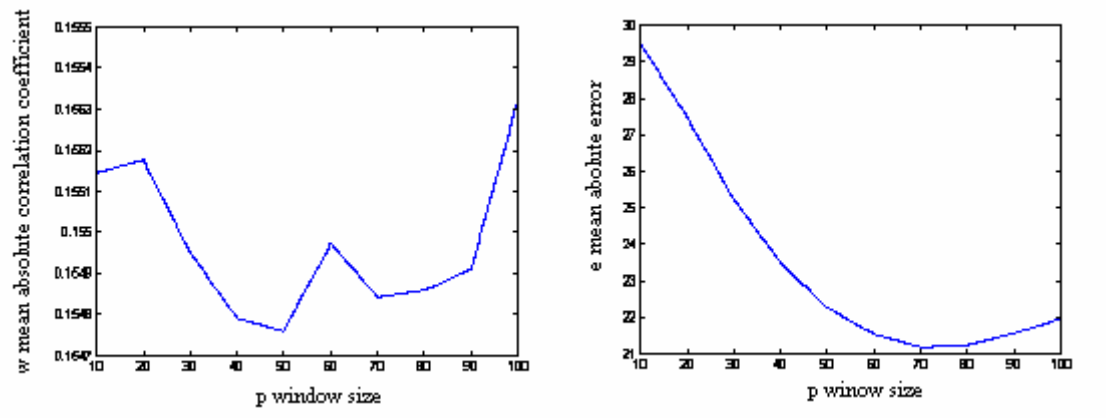

Figure 26 : Left: Result of whiteness test. Right: Mean absolute error when the SNR was -14.67dB

As the mean absolute correlation coefficient is minimum for size equal to 50.We used a size of 50 for moving average window though the mean absolute error is minimum for size equal 70. The mean absolute error has increased due to the presence of high frequency EEG in extracted variation as the SNR is very low.

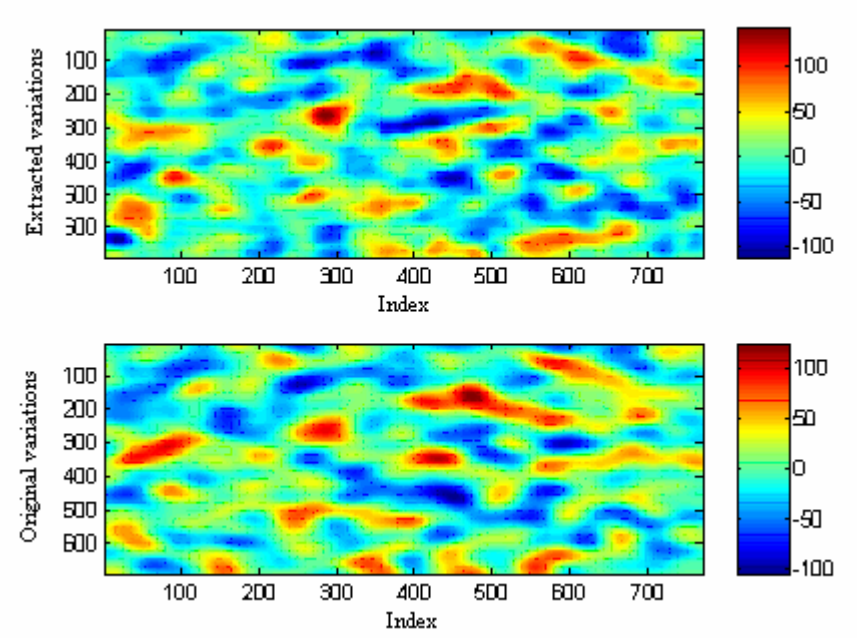

Figure 27: Top: Extracted variation after 2-dimensional Gaussian filtering when the SNR was -14.67 dB. Bottom: Original variations we have added to simulated the EPs

4. SNR =17.17 dB

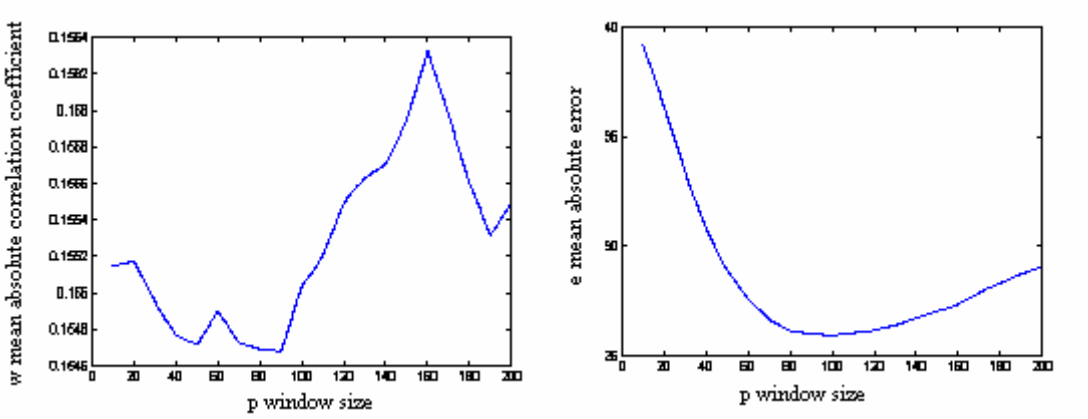

Figure 28 : Left: Result of whiteness test. Right: Mean absolute error when the SNR was -17.17dB

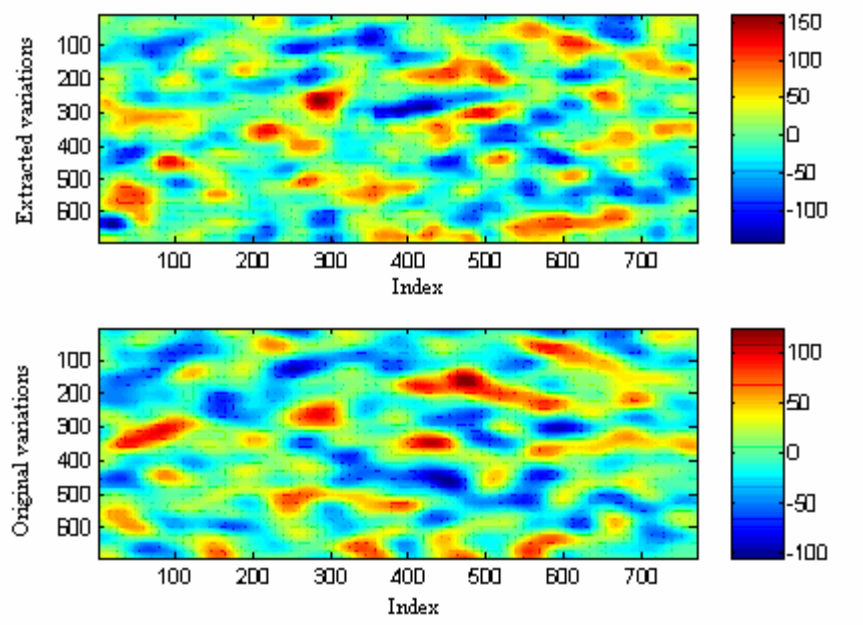

Figure 29 : Top: Extracted variation after 2-dimensional Gaussian filtering when the SNR was -17.17 dB. Bottom: Original variations we have added to simulated the EPs

For SNR of -17.17 dB the mean absolute error increased a lot and the extracted variations has high amount of high frequency EEG.

RESULT FOR REAL DATA

We applied our variation-based extraction method on auditory P300 data from channel Cz. Fig.30 shows the result of whiteness test .It shows that for window size 250 the absolute correlation coefficient *w* is minimum. But if we use such a large window for moving average we will lose 250 single trials. Due to this we have used a window of size 50 which has a low value of mean absolute correlation coefficient. The extracted variations and the extracted single trial EPs are shown in Fig 31, Fig 32 and Fig 33.

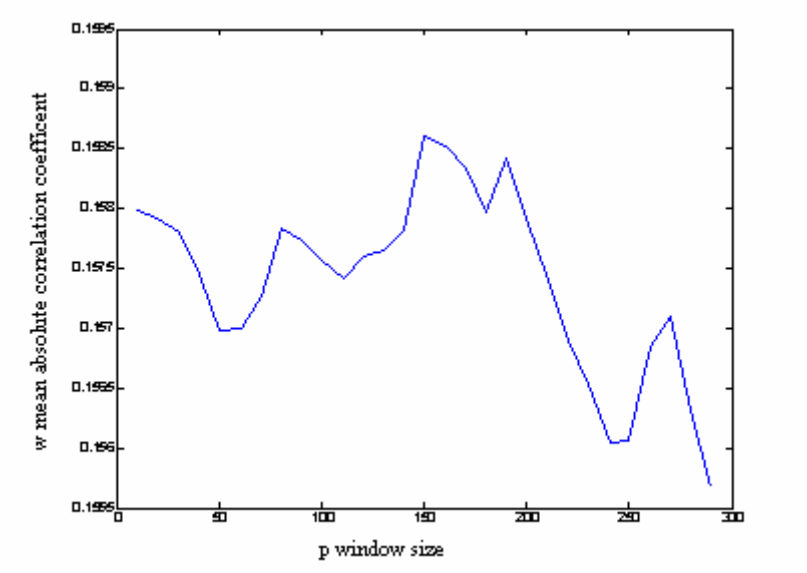

Figure 30 : Result of whiteness test for real auditory P300 data.

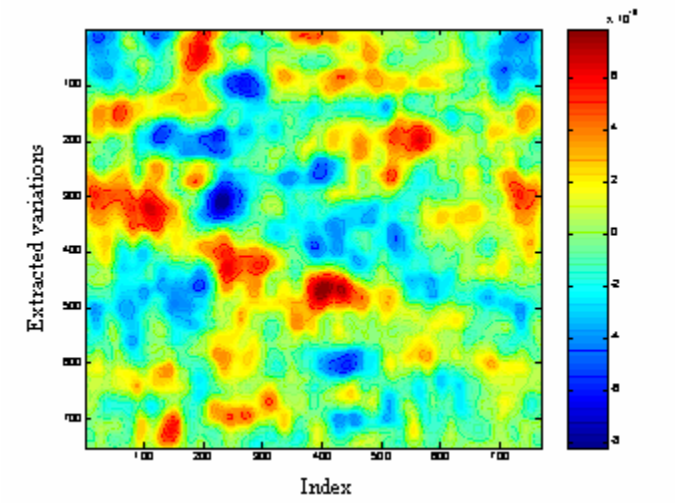

Figure 31 : Extracted variations for real auditory P300 data.

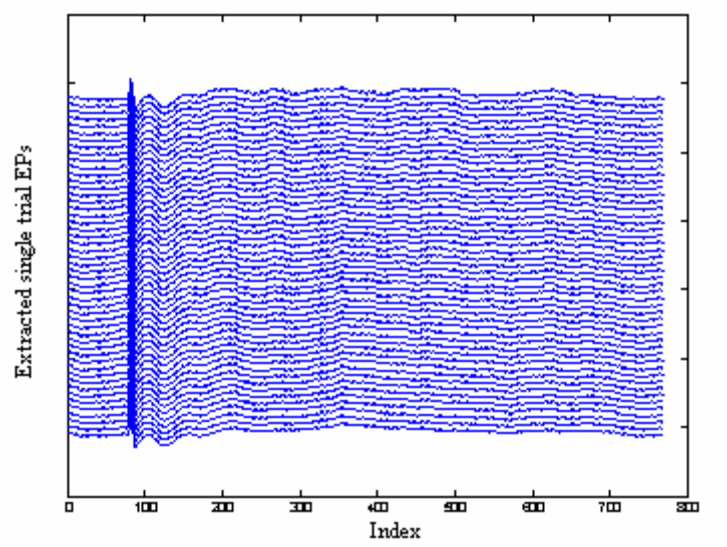

Figure 32: First 50 extracted single trials of evoked potential for real auditory P300 data

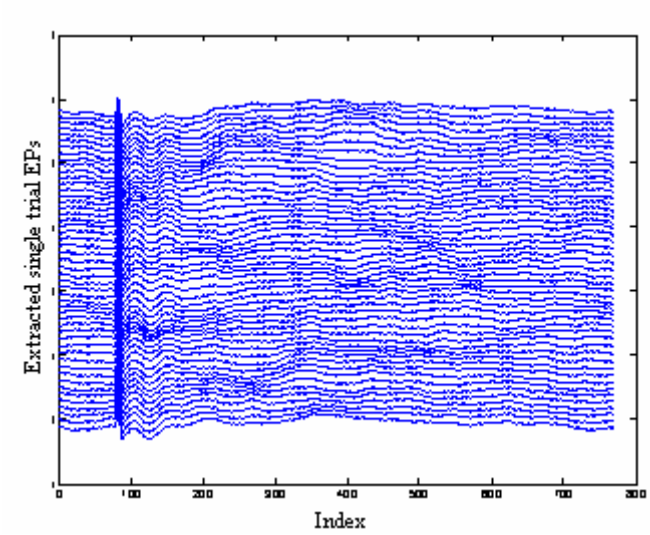

Figure 33 : Every tenth extracted single trial evoked potential for real auditory data

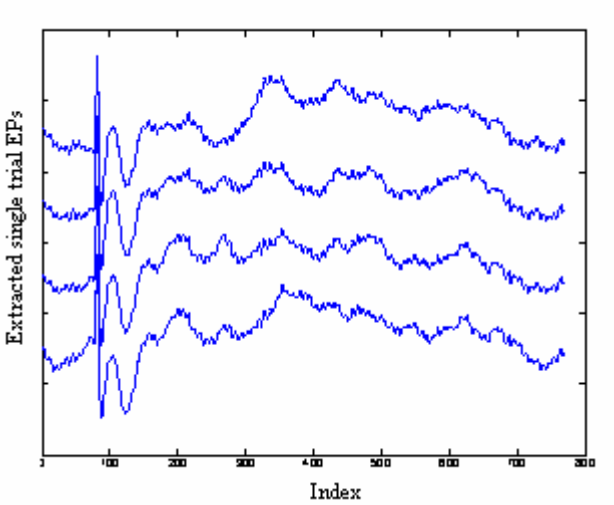

Figure 34: Every twentieth extracted single trial evoked potential for real auditory P300 data

5.0 DISSCUSSION AND CONCLUSION

In this thesis we have presented a very novel method for simulation and extraction of single trial EPs. The simulation is a very important part in evaluating the efficiency of any estimation method. Earlier methods used sine, cosine or Gaussian functions to simulate the evoked potential but did not simulate the varying evoked potentials based on real measurements. In our simulation method, we have assumed that the single trial EP varies slowly across the trials. We have added the averaged EP waveform of real measurements to the *variation matrix (*which has the variations that are occurring in the single trial EPs) to simulate the single trial EPs. In our approach we simulated only the amplitude variations. It will be more realistic if latency variations are also simulated.

Our extraction method gave good results for simulated as well as real data. For simulated data, our method extracted the variations close to the original variations that had been added. In extraction we are using a moving average window, which is optimal under certain statistical conditions, to filter out the background EEG .To compute the optimal size of the window we used a *whiteness test.* This test measures linear correlation in multiple trials of data, although it is possible that the data is correlated non-linearly. Our extraction method works well when the variations across the trials are slow, which we believe is reasonable in most cases of evoked potentials.

5.1 FUTURE DIRECTIONS

Our extraction method worked well in extracting the variations with low frequencies. Future work should focus on formulation of a method by which we can estimate the maximum variations our extraction method can extract. The whiteness test should be extended to measure

the whiteness when the trials are non-linearly correlated. For the simulation of single trial EPs latency variation should also be considered.

APPENDIX A

Matlab Code

SIMULATION OF SINGLE TRIAL EVOKED POTENTIALS

Compute the average of real data

```
%This Program calculates the average of the single trials to get a waveform Evoked Potential
%Sampling frequency is 512
clear all;
close all;
%loading the Auditory data of channel Cz
load wpi_02011_Cz.txt
%loading the fudicial marks
load wpi_02011
trials=zeros(80,800);
for i=1:800
   test=wpi_02011_Cz(wpi_02011_fid(i)-70:wpi_02011_fid(i)+729);
   for j=1:800
   trials(i,j)=test(j);
end
end
sum_trials=sum(trials);
% Finding the average to get ERP
erp=sum_trials/80;
figure(1)
plot((-70:729),erp*1e6);
line([1,1],[-150,100],'color','red','LineWidth',1);
title('Averaged Evoked Potential');
ylabel('Amplitude in micro volt');
xlabel('index');
figure(2)
erp=erp(1:770)*1e6;
plot((-70:699),erp);
line([1,1],[-150,100],'color','red','LineWidth',3);
title('Averaged Evoked Potential');
ylabel('Amplitude in micro volt');
xlabel('index');
hold on;
%1-Dimesional denoising of averaged ERP signal using wavelet
y=wden(erp,'minimaxi','s','mln',3,'bior3.3');
plot((-70:699),3*y);
xlabel('index');
hold off;
zoom xon;
```

Simulation of variations and single trial EPs

```
%warping averaged evoked potential of channel Cz to get 770 single trail evoked potential
%y is the averaged evoked potential
% mask is the 770x770 white Gaussian noise with zero mean and unit
% variance.
%Autocorrelatiom and power spectrum of mask1(variations) are computed to see the correaltion
%mask1 is the variation mask
%erp-trials are the simulated evoked potential.


clear all;
close all;
%loading the averaged evoked potential
load y;
%Creating a  random guassian mask
mask=randn(770,770);
k=mask;
X=mask;
m = mean(X)';
Xc = X'-repmat(m,1,size(X,1));
k=Xc';
mask=k;

%creating Guassian filter with size [120,120] and standard deviation 10

h=fspecial('gaussian',[120 120],20);
h=h/(max(max(h)));
f=-59:60;
c=-59:60;

%Lowpassing the mask
mask1=imfilter(mask,h);
%warping signal y(evoked potential) to get singale trials
for i=1:770
   erp_trials(i,:)=y+mask1(i,:);
end
R=cov(mask');
for i=1:770
   for j=1:770
      a=sqrt(R(i,i));
      b=sqrt(R(j.j));
      R1(i,j)=R(i,j)/(a*b);
   end
end
P=fft(R);
mesh(f,c,h);
% title('Plot of the 2D Guassian filter');
ylabel('y axis');
xlabel('x axis');
zlabel('amplitude');
figure(2);
subplot(2,1,1);
plot(erp_trials(1,:));
hold on;
```

```
plot(erp_trials(770,:),'-.m');
title('first and last trial and averaged evoked potential');
plot(y,'-r');
g=legend('first trial','last trial','averaged signal');
hold off;

subplot(212);
plot(erp_trials(10,:));
hold on;
plot(y,'r');
plot(erp_trials(50,:),'m');
title('10th and 50th trial');
g=legend('10th trial','averaged signal','50th trial');

hold off
figure(3);
imagesc(mask1);
title('Low passed mask');
figure(4);
imagesc(k);
title('Original mask');
figure(5);
for i=700:750


   tmp=erp_trials(i,:)+(i-1)*80;
   plot(tmp);
   hold on;
   title('First 50 single trials');

end
xlabel('index');
hold off;
figure(6);

for i=1:50
   j=i*10;

   tmp=erp_trials(j,:)+(i-1)*80;
   plot(tmp);
   hold on;
   title('every tenth simulated single trials');
end
xlabel('index');
hold off;
m=mean(erp_trials);
figure(7);
plot(m);
hold on
plot(y,'r');
title('Averaged ERP of simulated ERPS and averaged ERP from real data');
xlabel('index');
k=legend('Averaged ERP from simulated ERPs','Averaged ERP from real data');

figure(8);
imagesc(R1);
```

```
title('Autocorrelation matrix of variations');
figure(9);
mesh(abs(P));
title('Power spectrum of variations');
```

Processing of EEG signal

```
 %This programs creats the matrix of 741*770 of EEG data which  has a zero
%mean in horizontal as well as vertical direction
%Autocovariance of EEG matrix is also calculated to see the correlation of EEH segments
%Power spectrum is computed
%Pansy Bansal
%03/01/2004
close all;
clear all;

load eeg_mat.mat
 for j=1:39
       for k=1:19

            eeg_newmat(k+(j-1)*19,:)=eeg_mat(j,(1:770)+(k-1)*770);
          end
      end


%demeaning the EEG data in both x and y direction and H is the demeaned
%matrix in both the direction
X=eeg_newmat';
    m = mean(X)';
    Xd = X'-repmat(m,1,size(X,1));
    C=Xd;
    m1=mean(C)';

    D=  C'-repmat(m1,1,size(C,1));
    H=D';

     % Center and transpose

     R = cov(H');

     for s=1:741
        for t=1:741
           a=sqrt(R(s,s);
           b=sqrt(R(t,t);
           R1(i,j)=R(i,j)/(a*b);
        end
     end

     P=fft(R);

     figure(1);
     for i=1:25

   j=i*10;
   tmp=H(i,:)+(i-1)*150;
   plot(tmp);
   hold on;
   title('First 10 segments of EEG signal');

end
hold off;
```

```
figure(2);
imagesc(R1);
title('Covariance matrix of EEG');
figure(3);
mesh(abs(P));
title('Power spectrum of EEG');
xlabel('segments');
ylabel('frequency');
```

Simulation of raw data

```
%This program simulates the raw data
%H is the EEG matrix
#erp_trials is the simulated EPs
close all
clear all;
load erp_trials.mat;
load H.mat;

for i=1:741
for j=1:770
response(i,j)=H(i,j)+erp_trials(i,j);
end
end
figure(1);
for i=1:25


   tmp=response(i,:)+(i-1)*150;
   plot(tmp);
   hold on;
   title('First 25 trials of EEG+ERP signal');
end
```

EXTRACTION OF SINGLE TRIAL EVOKED POTENTIALS

Pre-processing of raw data

```
%response is the data having single trial EPs and EEG
%This programs subtract the mean of the measurements from the measurements to get EEG and variation
close all;
clear all;
load response;

mm=mean(response);
for k=1:741
   res(k,:)=response(k,:)-mm;
end
figure(3);
  for i=1:25
   tmp=res(i,:)+(i-1)*150;
   plot(tmp);
   hold on;
   title('First 25 signals containing EEG and variation');

end
```

Whiteness test

%This program performs the whiteness test on g matrix(res) and also computes the mean absolute error.

```
close all;
clear all;
load res;
load mask1;
load H;
 mask3=mask1(1:741,:);

% load erp_trials;
filtersize=[ 10  20  30   40 50   60   70  80   90   100   110  120 130  140  150  160  170  180  190 200 220 240 260
280 300];
   for f=1:25
     f=5;
 [r c]=size(mask3);
    A=[];
    A=mask3((filtersize(f)/2)+1:r-filtersize(f)/2,:);
   [r1 c1]=size(res);
   B=[];
   B=res((filtersize(f)/2)+1:r1-filtersize(f)/2,:);
   win_av=[];
   z=0;
   %Moving window average
for i=(filtersize(f)/2)+1:741-filtersize(f)/2
   z=z+1;
   l=0;
   for j=i-(filtersize(f)/2):i+((filtersize(f)/2)-1)
      l=l+1;
      G(l,:) = mask3(j,:);
   end
   win_av(z,:)=mean(G);
end


% %filtering using 2D gaussian filter
h=fspecial('gaussian',[40 40],8);
mask2=imfilter(win_av,h);
for i=1:741-filtersize(f)
   gg(i,:)=mm+mask2(i,:);
end
error=mask2-A;
 norm_error(f)=mean(mean(abs(error)));
eeg_sig=B-mask2;
 R=[];
 R1=[];
 R = cov(eeg_sig');

sum=0;
k=0;

for i=1:741-filtersize(f)
```

```
    for j=i+1:741-filtersize(f)
        k=k+1;
        a=sqrt(R(i,i));
        b=sqrt(R(j,j));
        corre(k)=R(i,j)/(a*b);
        sum=sum+abs(corre(k));
    end

end

mean_corre=sum/k;
corre_val(f)=mean_corre;
end

figure(1);
plot(filtersize,corre_val);
figure(2);
plot(filtersize,norm_error);
```

Moving window average and 2-dimensional filtering

```
%this program uses the filtersize computed by the whiteness test to perform moving window average.
%mask2 is the extracted variations
%gg is the extracted single trial evoked potential.
close all;
clear all;
load mask1;
load res;
load H;
 mask3=mask1(1:741,:);

% load erp_trials;
filtersize=[ 10  20  30   40 50   60   70  80   90   100   110  120 130  140  150  160  170  180  190 200 220 240 260
280 300];
      f=5;
 [r c]=size(mask3);
     A=[];
     A=mask3((filtersize(f)/2)+1:r-filtersize(f)/2,:);
    [r1 c1]=size(res);
    B=[];
    B=res((filtersize(f)/2)+1:r1-filtersize(f)/2,:);
    win_av=[];
    z=0;
    %Moving window average
for i=(filtersize(f)/2)+1:741-filtersize(f)/2
    z=z+1;
    l=0;
    for j=i-(filtersize(f)/2):i+((filtersize(f)/2)-1)
        l=l+1;
        G(l,:) = mask3(j,:);
    end
    win_av(z,:)=mean(G);
end


% %filtering using 2D gaussian filter
h=fspecial('gaussian',[40 40],8);
mask2=imfilter(win_av,h);
for i=1:741-filtersize(f)
    gg(i,:)=mm+mask2(i,:);
end

figure(1)
for i=1:50

    j=i*10;
    tmp1=gg(j,:)+(i-1)*80;


   plot(tmp1);
   hold on;
%
%     title('every 10th single trials');
end
```

```
figure(2);
subplot(211)
mesh(mask2);
colorbar;
subplot(212);
mesh(mask3(26:715,:));
colorbar;
%
% figure(1);
% plot(filtersize,corre_val);
% figure(2);
% plot(filtersize,norm_error);
```

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