Monitoring Sleep with 40-Hz ASSR

Sahar Javaher Haghigih, Dimitrios Hatzinakos
The Edward S. Rogers Sr. Department of of Electrical and Computer Engineering
University of Toronto
{sahar,dimitris}@comm.utoronto.ca

***Abstract*—The 40-Hz auditory steady state response (ASSR) signals recorded from human subjects during sleep and wakefulness are investigated in this study for the purpose of monitoring sleep. The ASSR signals extracted from stimulated electro encephalogram (EEG), explored in search for differentiating and robust to noise features. Choosing appropriate features in time and frequency domain, the performance of linear and quadratic discriminant analysis in classifying signals in different scenarios are studied.**
While the developed method itself is novel in sleep monitoring, due to similarities between $N3$ stage of sleep and anesthesia, the method will pave the way for later analysis on monitoring consciousness with 40-Hz ASSR. The 40-Hz ASSR extraction and noise cancellation methods presented in this paper can also be used for extracting 40-Hz ASSR from its background EEG signal in general.

I. INTRODUCTION

The 40-Hz auditory steady state response (ASSR) signals recorded from 6 human subjects are closely studied and analyzed with the purpose of differentiation between awake $W0$ and $N3$ stage of sleep. Classifying algorithms are designed based on the differentiating features. $N3$ or slow wave sleep (SWS) is chosen due to its similarities to the surgical level of anesthesia [1]. In SWS sensitivity to pain is the lowest relative to other sleep stages and arousal needs stronger stimuli. SWS is the switching of thalamus from tonic mode in which somatosensory information is transmitted through thalamus, to its bursting mode, in which somatosensory information are inhibited to transmit [1].
Studying the 40-Hz ASSR signals in these two stages led to extracting peak to peak amplitude of ASSR at each sweep and the 33_{rd} component of digital wavelet transform (DWT) of the signal fast Fourier transform (FFT) as the classifying features. Defining the appropriate features linear discriminant analysis (LDA) and quadratic discriminant analysis (QDA) are used for classification. Based on the similarities between $N3$ and anesthesia, there is a good chance that these features be suitable features in monitoring consciousness and depth of anesthesia as well.
Kalman filter is used for computing the weighted average of the EEG sweeps and extracting the 40-Hz ASSR signal. In this paper 40-Hz ASSR signals are extracted by averaging over 900 sweeps on a 30 second window, which is a shorter duration of time and less number of sweeps comparing with the available literature: Plourde et al. extracted the ASSR signal in [2] by averaging over 1000 epochs of EEG signal which took 132.8 seconds of recording. In his other paper Plourde used 34.25 to 47.95 seconds of recording. Picton [3] used 100 seconds of recording for extracting ASSR during sleep and Bohorquez et al. averaged over 2219 sweeps.

A. Background

ASSR is a brain auditory evoked potential (AEP) which is elicited with a periodic stimuli with 40-Hz repetition rate. AEP is the electrical changes in the ear and the brain of a normally hearing person in response to acoustic stimuli. AEP signal shows how neural information propagates from the acoustic nerves in the ear to the cortex [4]. AEP signals are extracted from electro encephalograph (EEG) [5], [6]. Stach defines ASSR in the "comprehensive dictionary of audiology" as an auditory evoked potential elicited with modulated tones, a neural potential that follows, or is phase locked to the modulation envelope [7]. AEP and ASSR were mainly used as audiology tools for predicting the hearing threshold and hearing sensitivity.
In 1950 the first clear approach to distinguish the evoked response from background EEG was made by George Dawson [8]. First AEPs were generated by averaging the EEG response in 1958 by Geisler, Frishkopf and Rosenblith [9]. Latter in 1980's the 40-Hz ASSR was described by Galambos [10] as an ASSR which is stimulated with stimulus with 40 cycles per second repetition rate.
The amplitude of ASSR as well as AEP signal is much smaller than the amplitude of the EEG signal, hence extracting the AEP from the background EEG is a challenging process that involves noise cancelation techniques.
AEP is divided to three main parts, namely auditory brain stem response (ABR), mid-latency AEP (MLAEP) and late latency AEP (LLAEP) [4], [11]–[13].
ASSR is greatly affected by the stimuli modulation rate. It is phase locked to and follows the modulated envelope of the stimulus [7]. Different stimulus rates results in stimulation of different portions of the auditory nerves and hence different ASSRs. 40-Hz response ASSRs have the same neural generators as MLAEP hence similar to MLAEP 40-Hz ASSRs has small inter and intra-subjective variations [4], [14] and are strongly influenced by subject state of arousal [7]. The amplitude in 40-Hz response varies by the subject's level of arousal [7], [10], [15], [16], and consciousness [17], [18]. 40-Hz response can be used as a measure of depth of anesthesia [2], [3], [18]–[20].

II. Related works

There are some literature available on the effects of sleep on AEP and 40-Hz ASSR however the literature is not very clear about the effects of sleep on the auditory MLAEP and 40-Hz ASSR. Mendel and Goldstein [21] initially reported that the transient MLAEP was stable over a 24-hr waking period and in various stages of sleep. In 1971, they found that the latencies of the major peaks remained constant across the different stages of sleep and that the amplitudes were larger during REM and stage 2 comparing with stages 3 and 4 [22]. Mendel and Kupperman, reported no significant amplitude differences between REM and non-REM sleep, and Mendel found little difference in the latency or amplitude of the MLAEP between light (stage 2 and REM) and deep (stages 3 and 4) sleep [23]. After describing 40-Hz ASSR, Galambos et al. stated that the 40-Hz response was about half the amplitude in sleep comparing to the awake state [10]. Brown and Shallop [24] and Shallop and Osterhamme [25] reported that the response during sleep was approximately one third of that during wakefulness. Klein also found that the amplitude of the steady state response was smaller during sleep than during wakefulness.

In 1986 Jerger et al. [16] studied 10 subjects in three stages of awake state, stage 1 and stage 2 of sleep. The 40-Hz ASSR signal was generated by averaging over 128 sweeps. Amplitude and phase of the 40-Hz component of the FFT of the signal was studied and it was observed that while sleeping affects the amplitude, phase coherency remains unaffected by the level of subject arousal.

In 1995 Suzuki et al. [26] studied 40-Hz ASSR during sleep. 40-Hz ASSR were recorded from 12 subjects with normal hearing in the waking state and stage two of sleep. They also compared the recorded 40-Hz ASSR signals (rSSR) with synthesized ASSR (sSSR) generated from superposition of the MLAEP signals. Required SNR for the 40-Hz ASSR signals were achieved by averaging over 2048 sweeps. Amplitude is defined as the vertical distance from the positive peak to the straight line connected to the most negative peaks proceeding and succeeding the positive peak. They observed that the amplitude of the 40-Hz ASSR signal in awake state is twice as its amplitude during sleep, they also observed that the synthesized 40-Hz ASSR, that is generated by superimposing the MLAEP signals can not predict this reduction in amplitude correctly.

In this paper beside observing the signals and their changes during wakefulness and sleep we proposed a method for classifying 40-Hz ASSR signals of wakefulness and $N3$ stage of sleep and compared the performance of the proposed algorithm in different scenarios.

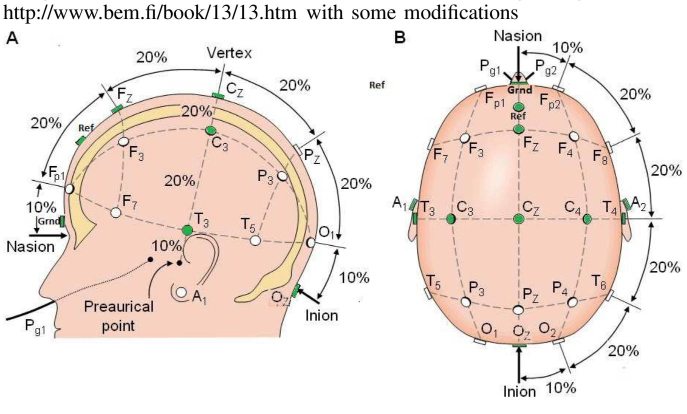
III. Method

A. Data acquisition

After ethics approval was obtained from the Office of research ethics of the University of Toronto, subjects, were recruited. Subjects had no history of hearing loss or neurological problems. Written informed consent was obtained from all the subjects and they were rewarded $\$100$ for their participation. The AM-ASSR stimulus had a modulation frequency of 40.68 Hz a carrier and a center frequency near 2 KHz. It was generated by the Vivosonic Integrity$^{\text{TM}}$ V500, presented using an ER-3A-ABR insert earphone (Etymotic Research) at a level of 60 dB HL, loud enough to generate an ASSR but not too loud to cause discomfort to the study participants.

EEG is recorded from 11 scalp sites of the international 10-20 system as shown in figure 1. The used electrode sites – F_z, C_z, $C_{3,4}$ $T_{3,4}$, $A_{1,2}$,O_z – are shown in green in figure 1. A reference electrode is used as the common electrode of all channels. A ground electrode is used to reduce the environmental noise, another electrode, LoC, is used for recording eye movements, to make sleep scoring based on raw EEG signals easier. An electrode cap by Bio-Medical Instruments Inc. is custom designed for the experiment with the 10 recording electrodes, and two leads for the ear clip electrodes. A pair of $3\frac{1}{2}$ inch DIN style EEG silver ear clips from the same company is used for A_1 and A_2. A 10 mm in diameter gold cup electrode is used for recording eye movements. The EEG amplifier used for EEG amplification is Nicolet$^{\text{TM}}$ EEGwireless 32 amplifier. Two extra electrodes are connected from the Integrity$^{\text{TM}}$ device stimuli generator to channel 25 of the EEG amplifier for recording the stimuli together with other EEG channels. Sampling frequency of the amplifier is $f_s = 12$ KHz and all electrode impedances are below $5\,K\Omega$.

Fig. 1. The international 10-20 system seen from (A) left (B) above, the green electrodes are the ones used in the recording. Diagram from http://www.bem.fi/book/13/13.htm with some modifications



B. Data processing

After recording, the raw mixed ASSR and EEG signals were reviewed and scored with the conventional sleep scoring methods to awake, $W0$ and three stages of sleep namely $N1$, $N2$ and $N3$ stages. Signals of the $W0$ and $N3$ stage were transferred to Matlab for processing. Frequencies below 20 and above 100 Hz were filtered out with third order butterworth low pass and high pass filters, the signals from seven recorded channels were synchronized and segmented into 295 sample

sweeps. The EEG amplifier has 12 KHz sampling frequency but the Integrity stimulus is sampled with 38400 Hz sampling rate. Hence the cycles for the 40 Hz response are not whole numbers; we got around this by only including cycles with 295 sample. It results in discarding some of the data but this was not be an issue in this experiment since the required time to acquire data was not essential.
In almost all cases in the literature ensemble averaging is used for extracting 40-Hz ASSR signal from the background noise [2], [3], [27]. Assuming the recorded signal as

$$x_i[n] = s_i[n] + r_i[n] \tag{1}$$

where $x_i[n]$ is the ASSR in response to the i_{th} sweep of the stimuli and $r_i[n]$ is the EEG and noise from other sources. Under the assumption that $s_i[n]$ is phase locked to the stimuli, noise $r_i[n]$ is zero mean, $E(r_i[n]) = 0$, has constant variance, $var(r_i) = \sigma^2$ and is uncorrelated from one sweep to another, $E(r_i[n]r_j[n-k]) = \rho_r[k]\delta(i-j)$ ensemble average is an unbiased estimator and increase the variance of the noise.
We used weighted ensemble averaging to extract the ASSR signals. The weights were calculated according to the Kalman filter coefficients. Each 40-Hz ASSR signal is extracted by averaging over a window of 900 sweeps. Each two adjacent windows have 83% overlap. After extracting 40-Hz ASSR signals, different features in time and frequency domain were compared in $N3$ and $W0$ stage in all seven channels. Peak to peak amplitude of 40-Hz ASSR decreases from $W0$ to $N3$. Figures 2 and 3 show four sweeps of ASSR during $N3$ and four during $W0$ for two subjects. The frequency content of ASSR is studied in the signal FFT. Getting digital wavelet transform (DWT) from the FFT and decomposing the signal with Biorthogonal wavelet in to 5 levels, it is observable that there is a meaningful difference between the amplitude of the 33_{rd} DWT coefficient between $W0$ and $N3$ stage. Figure 5 and figure 4 are zoomed plots of four sweeps in $W0$ and four in $N3$ stage in two subjects. It is observable that the solid lines which show the awake stage sweeps have larger amplitude comparing with the dashed lines which show the asleep stage sweeps.
Hence the peak to peak amplitude and 33_{rd} coefficient of DWT in all seven channels are chosen as features for classification of the signals.

The extracted 40-Hz ASSR signals of $W0$ and $N3$ stages are then classified based on the two chosen features in the seven recorded channels with LDA and QDA. The traditionally scored signals were used for labeling the training sets. Classification error rate is calculated for different training and testing sets. These results are presented in section IV

IV. Results

Three different scenarios were simulated with the classifiers. In the first scenario the classifiers are trained and tested with the ASSRs from same subjects. Training matrix is generated with one thousand $W0$ sweeps and one thousand $N3$ sweeps from one subject to train the classifier. The training matrix is constructed by randomly choosing from $W0$ and $N3$

Fig. 2. Sweeps of 40-Hz ASSR during WO, and $N3$ stage of sleep for Subject B in T4-Fz channel, WO:*solid lines*, $N3$: *dashed lines*

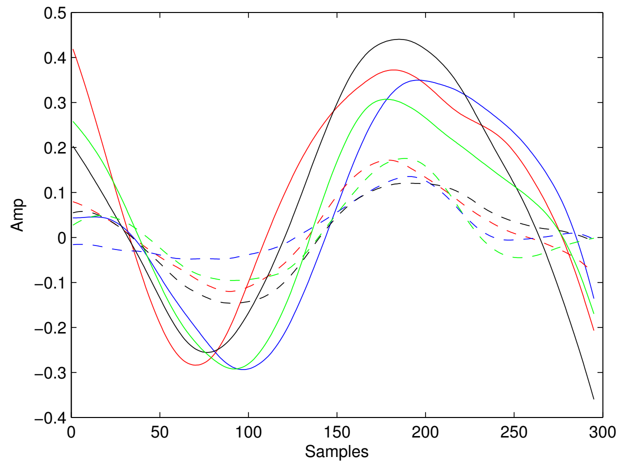
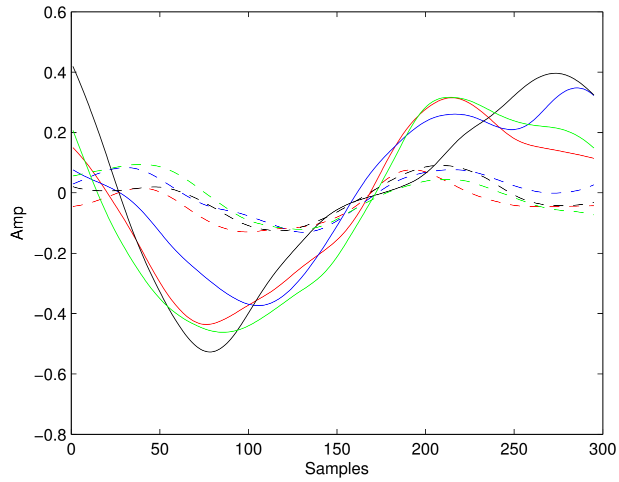


Fig. 3. Sweeps of 40-Hz ASSR during WO, and $N3$ stage of sleep for Subject D in T4-Fz channel, WO:*solid lines*, $N3$: *dashed lines*



sweeps of the same subject. The trained classifier is used for classifying sweeps of each stage choosing randomly among the non-training sweeps. Error rate in classification for each subject is calculated as the average error rate over 500 trails with different randomly chosen train and test matrices. Table I shows the average error rates for each subject. The average error rate for training and testing with the same subject will be 1.12% with LDA and 1.66% with QDA. It can be seen that LDA performs slightly better than QDA. Figures 6 and 7 show the classification results for hundred sweeps in $W0$ and hundred sweeps in $N3$ with LDA for subject B and subject D on channel T4-Fz. No classification error was occurred in classifying subject B ASSRs. The sweeps in 7 are chosen such that they include 5 classification errors in each stage. The second scenario simulated is when the 40-Hz ASSR from all subjects are used for training the classifier and one subject ASSR are tested to be classified. 2000 (1000 from $W0$ and

Fig. 4. The zoomed DWT of 40-Hz ASSR during WO, and $N3$ stage of sleep for Subject B in T4-Fz channel, WO:*solid lines*, $N3$: *dashed lines*

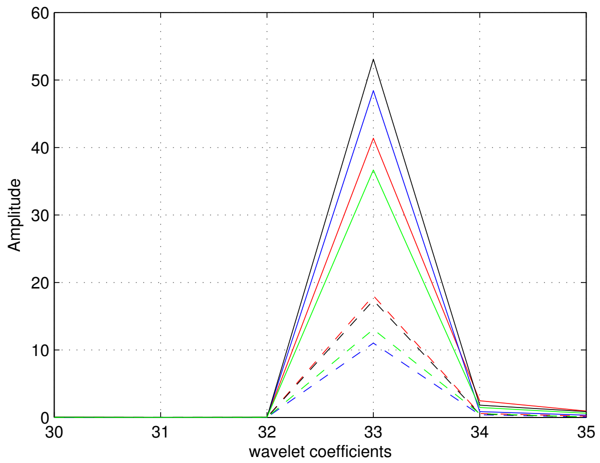


Fig. 5. The zoomed DWT of 40-Hz ASSR sweeps during WO, and $N3$ stage of sleep for Subject D in T4-Fz channel, WO:*solid lines*, $N3$: *dashed lines*

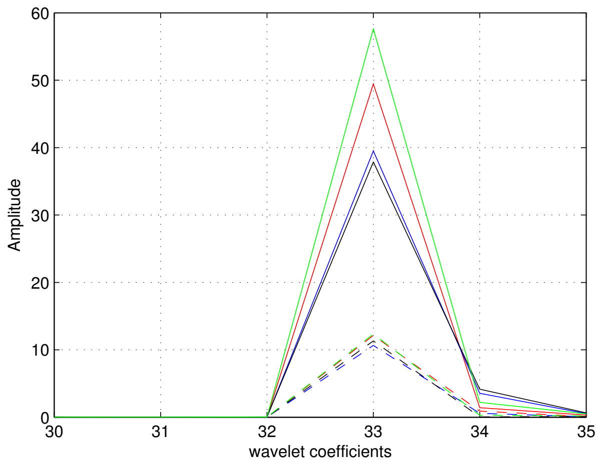


Fig. 6. LDA classification results on channel T4-Fz for subject B, blue diamonds: classified awake, red circles: classified asleep

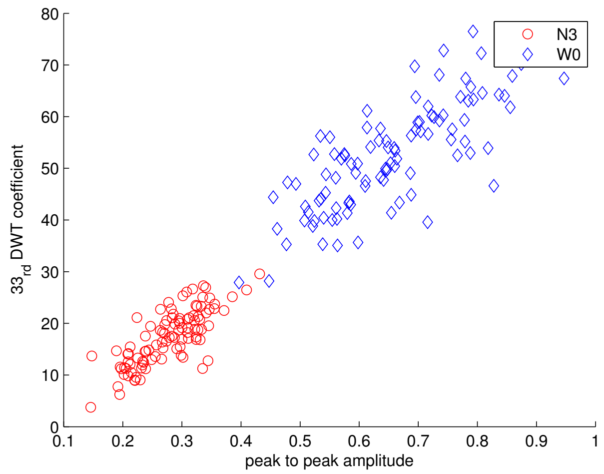
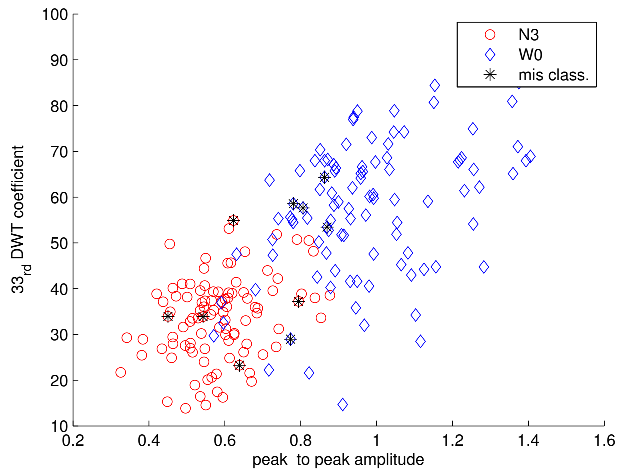


Fig. 7. LDA classification results on channel T4-Fz for subject D, blue diamonds: classified awake, red circles: classified asleep, black asterisk: classified wrong



1000 from $N3$) sweeps from each subject are chosen randomly and put in one matrix to generate one training matrix which includes all subject ASSR samples. Among the non-training sweeps of the subject to be classified 4000 (2000 from $W0$ and 2000 from $N3$) is chosen and classification performance is studied. Similar to the first scenario the error rate in classifying each subject is calculated by averaging over 500 trails. As it is expected this scenario will have higher error rate which can be explained by the variations in the values of the features in different subjects. Table II shows the average error rate over all six subjects. LDA has an acceptable error rate of 2.57% but the QDA error rate increases to 17.43%.

In the last scenarios the classifiers are trained with ASSRs from all subjects except for the subject whose ASSRs is to be classified. Training matrix has 2000 sweeps of 5 subject and test matrix has 4000 sweeps (2000 from $W0$ and 2000 from $N3$) of the sixth subject. Error rates are calculated over 500 trials for each subject. As presented in table II, the average error rate over all subject in this scenario is 5.91% with LDA and 20.69% with QDA.

	LDA	QDA
Subj A	0%	0%
Subj B	0%	0%
Subj C	0.003%	0.132%
Subj D	2.748%	4.950%
Subj E	0.067%	0%
Subj F	3.907%	4.895%
Average	1.12%	1.66%

TABLE I
ERROR RATE IN CLASSIFYING WITH LDA AND QDA METHODS

Case	Average error rate	
	LDA	QDA($)
same subject for train and test	1.12%	1.66%
all subjects for train	2.57%	17.43%
different subject for train	5.91%	20.69%

TABLE II

AVERAGE ERROR RATES FOR DIFFERENT SCENARIOS

V. CONCLUSION

40-Hz ASSR signals during sleep and wakefulness were investigated in this paper. Signals were extracted from raw stimulated EEG and compared with each other during wakefulness and $N3$ stage of sleep. Based on the observed changes in the signals, classifying features were extracted and the performance of LDA and QDA were checked in different scenarios. The comparison showed that both classifiers perform well with relatively low error rates in the cases that the classifier is trained and tested with same subject ASSRs. However error rate increases when multi subjects are used for training and testing with classifiers.

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