

Multi-channel EEG based Neonatal Seizure Detection

Barry R. Greene, Richard B. Reilly, Geraldine Boylan, Philip de Chazal, Sean Connolly

Abstract— A multi-channel method for patient specific and patient independent, EEG based neonatal seizure detection is presented. Two classifier configurations are proposed and tested, along with a number of classifier models. Existing methods for neonatal seizure detection have been empirical threshold based or based on a single EEG channel. The optimum patient specific classifier for EEG based neonatal seizure detection was found to be an Early Integration configuration employing a linear discriminant classifier model. This yielded a mean classification accuracy of 74.66% for 11 neonatal records. The optimum patient independent classifier was an Early Integration configuration with a linear discriminant classifier model giving a mean accuracy of 72.81%.

I. INTRODUCTION

Seizures are often the primary indicator and first sign of neurological or central nervous system dysfunction in a newborn infant. Prolonged untreated seizures can result in long term neurological damage and impairment in the newborn. Newborns with seizures have poor health outcomes (morbidity in 50% of survivors) and a high probability of death (30%)[1]. There is disagreement about the incidence of neonatal seizures but it is generally accepted that they occur in 6% of low birth-weight infants [2] and in approximately 2% of all newborns admitted to the neonatal ICU [3, 4]. As such seizures are most common in the neonatal period. It is thought that early detection and treatment of seizure can significantly improve prognosis. As a result there is a need for a system that can detect the presence of seizure in the newborn, allowing timely medical intervention. The primary tool used by neurophysiologists in diagnosing seizure is the electroencephalogram (EEG) and as a result most seizure detection algorithms are based on the EEG.

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A number of algorithms have been proposed for detecting neonatal seizures from the EEG. The Gotman method [5] is based on epoched values of frequency, bandwidth and power in the frequency spectrum. It is based on a single channel of EEG and employs empirically derived thresholds for classification. Celka and Colditz [6] reported a patient specific method requiring pre-processing, based on measuring the complexity of the EEG in the time domain. The method of Liu *et al* [7] relies on quantifying the amount of periodicity in the autocorrelation function of 30s epochs of EEG. Like the Gotman method, the Liu method relies on empirically derived thresholds rather than those derived from real training data. The Gotman and Celka methods are defined for a single channel of EEG while the Liu algorithm declares seizure if one or more channels report a seizure. Altenburg *et al* [8] used a mathematical method called synchronization likelihood to quantify dynamical entrainment across EEG channels and used this to detect the presence of seizure in the neonatal EEG. A synchronization likelihood score above a given empirical threshold was used to perform a binary classification of that epoch.

To date, neonatal seizure detection algorithms have resisted successful transition to the NICU. An independent comparison of three such methods (Gotman, Liu & Celka) found that none were suitable for use in a clinical environment [9]. Algorithms based on empirical threshold values or a single channel of EEG, do not have the ability to cope with real multi-channel seizure EEG as would be encountered in the NICU. For this reason multi-channel neonatal seizure detection algorithms trained on real data may represent an important step towards neonatal seizure detection systems suitable for clinical deployment.

II. AIM

The aim of this study was to compare two novel multi-channel EEG classifier configurations and a number of statistical classifier models for accurate detection of seizures in the newborn.

III. DATA SET

A dataset of 11 recordings from 9 neonates containing 633 seizure events, with mean seizure duration of 4.22 minutes, were recorded and analyzed. The records had a mean duration of 12.5 hours. Each recording contained 7-12 channels of EEG. 10 recordings were made on the neonatal intensive care units of the Unified Maternity Hospitals in Cork, Ireland using the Taugagreining Nervus video EEG system and sampled at

256Hz. The remaining recording was made at Kings College Hospital London, U.K. and sampled at 200Hz. All the data for each recording was included in the analysis regardless of record length or quality. Electrographic seizures were identified and annotated by an expert in neonatal EEG (author: G. Boylan). Annotations give information on the time of onset and the duration of the electrographic seizure. Unlike some previously published research, our annotations did not contain information on seizure location.

IV. METHOD

A. Feature Extraction

The EEG for each channel was low pass filtered using a Chebyshev IIR filter with a corner frequency of 34Hz and then considered in terms of 2048 sample sliding windows. A 25% or 512 sample sliding step was used. Six features were extracted from each EEG epoch for each EEG channel.

The first three features were used by Gotman *et al* [5] (dominant frequency, bandwidth of the dominant spectral peak and spectral power ratio at the dominant frequency), to distinguish between seizure and non-seizure epochs in the newborn EEG. The frequency spectrum was calculated for each epoch using the FFT. The dominant frequency was defined to be the frequency in the spectrum with the largest average power in its bandwidth. The bandwidth of the dominant spectral peak was defined as the width in hertz between the two half power points of the dominant spectral peak. The power ratio was defined as the ratio of the power in the dominant spectral peak to the power at the same frequency in the ‘background’ EEG, where the background EEG is a point 60s behind the current window.

As neonatal seizure EEG shares many characteristics with adult epileptic seizure EEG, a number of features used in epileptic seizure prediction were tested and deemed suitable for this application. Spectral entropy is a feature often used in EEG signal analysis. Recent evidence suggests that seizure activity represents a reduction in the complexity of the underlying brain dynamics [6]. Spectral entropy is a measure of complexity and represents a potential feature for seizure detection. Several authors have used spectral entropy to quantify the behavior of the EEG during adult epileptic seizure [10, 11]. The EEG spectral entropy was calculated for each epoch using Shannon’s entropy formula (Eqn.1) where $P(x)$ is the power spectral density (PSD) for the epoch:

$$H(X) = -\sum P(x) \log_2 P(x) \quad (1)$$

D’Alessandro *et al* [10] employed spectral entropy as well as nonlinear energy and a number of other features to predict epileptic seizure activity in adult epileptic patients. Nonlinear energy is calculated for each sample per epoch using Eqn.2, the mean nonlinear energy is then taken as a feature for each epoch.

$$N(k) = x^2(k) - x(k-1)x(k+1) \quad (2)$$

Esteller *et al* [12] proposed curve length/fractal dimension as potential features for epileptic seizure detection in adults. Curve length is calculated on an epoched basis using Eqn.3.

$$L(k) = \sum_{i=1}^N abs[x(k-1) - x(k)] \quad (3)$$

The six features for each channel were then normalized and combined into feature vectors for each epoch.

B. Classifier Models

A number of statistical classifier models were used in this study, including linear discriminants (LD), quadratic discriminants (QD) and regularized discriminants (RD). Training of all classifier models estimates classifier parameters, class conditional mean vector and covariance matrices directly from the data. Parameters were calculated using maximum likelihood estimation. An LD classifier finds the linear combination of features that maximizes Fishers Discriminant ratio, assuming a common covariance matrix, separate mean vectors and normal distribution for each class [13]. The performance of the LD patient independent classifier was further improved by weighting the covariance matrix and mean vectors by the duration of the records in the training set as discussed in [14]. The LD classifier with weighting is referred to as LD* henceforth. A QD classifier uses a quadratic combination of features to maximize class discrimination. The model assumes separate mean vectors and covariance matrices for each class along with normal class distribution. Similarly any classifier model with mean and covariance weighting is referred to with an asterix (*).

In pattern recognition problems with small data sizes and large numbers of features, some of the parameters are not always identifiable from the data and so the problem is said to be *ill-posed*. This is often the case in biomedical signal pattern recognition. Regularization can present a solution to this problem, and can be viewed as an attempt to bias estimates away from their sample values towards more physically plausible values [15]. Two methods for stabilizing the covariance estimates for each class are combined and used in this study. Regularization towards common covariance matrix with parameter λ is given in Eqn.4, where Σ_k is an estimate of covariance matrix for class k:

$$\Sigma_k(\lambda) = (1 - \lambda)\Sigma_k + \lambda\Sigma \quad (4)$$

Regularization towards diagonal matrix with eigenvalues equal to the averaged eigenvalues of the sample based estimate of the covariance matrix is given in Eqn.5, where I is the nxn identity matrix.

$$\Sigma_k(r) = (1 - r)\Sigma_k + \frac{r}{n} tr(\Sigma_k)I \quad (5)$$

Combining these two equations gives a combined regularization formula (Eqn.6), where $0 \leq \lambda \leq 1$ and $0 \leq r \leq 1$:

$$\Sigma_k(\lambda, r) = (1-r)\Sigma_k(\lambda) + \frac{r}{n}tr(\Sigma_k(\lambda))I \quad (6)$$

The discriminant value used in regularized discriminant analysis is calculated using the new estimate for the class conditional covariance matrices and the quadratic discriminant formula [15]. Regularization parameters of $\lambda=1$ and $r=0$ correspond to a linear discriminant classifier while $\lambda=0$ and $r=0$ correspond to a quadratic discriminant classifier. The optimum set of regularization parameters was determined for each configuration for the patient specific and patient independent classifiers. The optimum classifiers were determined by finding the regularization parameters that yielded the most balanced values of accuracy and sensitivity. Fig.3 (referred to as a regularization plot) shows the classification accuracy as the parameters λ and r were varied over the range 0 to 1 in increments of 0.1. Weighting of the class specific mean vectors and covariance matrices was implemented for all pairs of regularization parameters and the results compared to the un-weighted results.

C. Classifier Configurations

Two classifier configurations for combining information across EEG channels are reported here. The first configuration, called the Early Integration (EI) configuration concatenated features vectors containing m features from n channels into a large feature vector which was then fed to a classifier. Six features were extracted from each EEG epoch for each channel. The features for each channel were sorted according to feature type and then sorted into numerical order. The grouped, sorted features were then concatenated into a ‘super’ feature vector (as shown in fig.1). The sorting function removes information about the spatial location of the seizure from the training set, preventing the classifier from expecting seizure activity in a particular channel. This has a numerical selection effect on the features for the patient independent classifier.

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Figure 1: Early Integration (EI) classifier configuration

The second configuration, the Late Integration (LI) classifier configuration, employed n separate classifiers for each m dimensional feature vector for each of the n channels. The output class labels from each of the classifiers were then combined to produce a decision. A number of classifier combination methods were investigated including majority voting, max score and mean score (mean probability) combination [15]. The mean score combination rule was found to give the best classification performance. The mean score combination rule takes the mean score or mean output probability from a collection of classifiers. The class decision is then that class with the highest mean probability. LI has the advantage that each channel is classified individually, this means that channels containing artifact or in which the lead

has dropped off can be ignored by the decision function. Fig 2 gives a graphical explanation of the LI configuration.

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Figure 2: Late Integration (LI) classifier configuration

In order to obtain better training of the classifier models, epochs thought to contain artifact were excluded from the training set. This exclusion was performed automatically, on a per channel basis in the training set in the LI configuration so that the classifier would be tested on real data containing movement artifacts, eye-blinks and electrode drop off. If the artifact measure for that epoch was over an empirically derived threshold the epoch was excluded from the training. As a result a more realistic measure of classifier performance could be obtained. In the EI configuration, an epoch was excluded from analysis if the mean of the artifact measure was over an empirically derived threshold for all records. Each epoch was automatically examined for the presence of artifact using the EEG stability measure introduced in [5].

D. Classifier Performance Estimation

Each configuration was considered as both patient specific and patient independent classifiers. The performance of each patient specific classifier was estimated using m fold cross validation on each record. Cross validation randomly splits each record into m sections or ‘folds’, $m-1$ of these folds are then used to train the classifier and the remaining fold is then used to test the performance of the classifier. By shuffling the data and repeating this procedure n times and averaging the resulting accuracies for the training and test sets, an unbiased, low variance estimate of the classifier performance can be obtained. In this study 10 folds and 10 shuffles were used. The performance of the generalized or patient independent classifier was estimated using cross validation across all records. This involved training the classifier model on $(z-1)$ of the z EEG records and using the z^{th} record to test the classifier performance and then rotating through the z possible combinations of training and test sets, taking the mean of the result for all iterations as the patient independent performance estimation.

E. Classifier Performance Measures

All classifier systems considered in this study were epoch based. For this reason all results quoted are on a 2048 sample epoch basis. The classification accuracy (Acc) is defined as the percentage of epochs correctly classified by the system. The sensitivity (Sens) is defined as the percentage of labeled seizure epochs correctly identified as seizure epochs by the system. The specificity (Spec) is defined as the percentage of labeled non-seizure epochs correctly classified as non-seizure by the system. The false detection rate (FDR) is then $100 - \text{Spec}$. A receiver operating characteristic (ROC) curve is a plot of class sensitivity against specificity as a threshold parameter is varied. The area under the ROC curve (calculated using

trapezoidal numerical integration) is an effective way of comparing the performance of different features or classifiers. A random discrimination will give an area of 0.5 under the curve while perfect discrimination between classes will give an area of 1 under the ROC curve. The ROC area is equivalent to the Mann Whitney version of the Wilcoxon rank-sum statistic [16].

V. RESULTS

A. Patient Specific

The results classifier performance metrics as detailed in the method section are given for each of the classifier models. The optimum patient specific classifier was the EI configuration with regularization parameters; $\lambda=1$, $r=0$. This is equivalent to an LD classifier. Table 1 gives the classification results for each configuration for the patient specific classifier. The results given for RD are for the best regularized classifier model for each configuration.

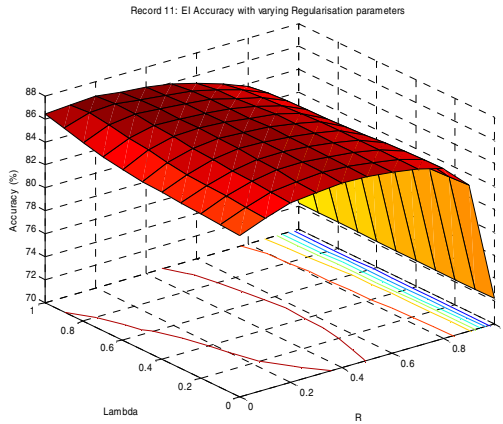


Figure 3: Classification accuracy for record 11 with varying regularization parameters. The optimum classifier had regularization parameters $\lambda=0.9$, $r=0.2$

ROC curves were generated for both patient specific and patient independent classifiers for both configurations and all classifier models. A value is given in table 1 for the area under the ROC curve in each instance. For the patient specific case the value given is averaged across all records. Fig.3 shows the patient specific regularization plot for record 11. The optimum patient specific classifier for each record may be determined from these plots. Similarly the optimum patient independent classifier for this application may be determined from a regularization plot.

Config/ Model	Reg		Acc (%)	Sens (%)	Spec (%)	ROC
	λ	R				
EI	LD	1 0	74.66	63.31	77.86	0.77
LI	LD	1 0	65.25	48.00	69.99	0.61

EI	QD	0	0	41.19	87.32	30.05	0.70
LI	QD	0	0	42.73	77.40	34.13	0.64
EI	RD	1	0	74.66	63.31	77.86	0.77
LI	RD	0.1	0.4	45.47	74.25	37.92	0.63

Table 1: Patient Specific Results

B. Patient Independent

The results given for each classifier were confirmed by ROC analysis. Fig.4 shows the ROC curves for the EI and LI patient independent classifiers.

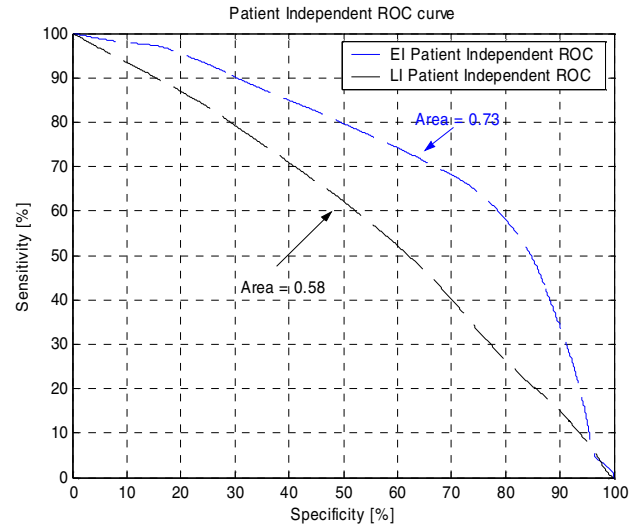


Figure 4: ROC curves for EI and LI patient independent classifiers using the LD* classifier model.

The optimum patient independent classifier was the EI LD* configuration with regularization parameters $\lambda=1$ and $r=0$. This is equivalent to an LD classifier model with covariance weighting. Table 2 gives the patient independent classification results for all classifier models and both configurations. The results given are for the best performing classifier for each classifier model and configuration. If the best result for that classifier model and configuration was achieved with mean and covariance weighting this is indicated by an asterisk.

Config/ Model	Reg	Reg		Acc (%)	Sens (%)	Spec (%)	ROC
		λ	R				
EI	LD*	1	0	65.02	72.73	62.28	0.73
LI	LD*	1	0	59.93	47.07	64.56	0.58
EI	QD	0	0	55.47	64.72	52.13	0.54
LI	QD	0	0	26.86	96.74	1.65	0.37
EI	RD*	1	0	65.02	72.73	62.28	0.73
LI	RD	1	0.6	59.21	37.22	67.14	0.51

Table 2: Patient Independent Results. * Indicates that classifier model employed weighting of mean vectors and covariance matrices by record duration.

VI. DISCUSSION

Two methods for combining features from n EEG channels are considered here, the EI configuration was found to be superior for all classifier models. The LI configuration makes the assumption that each EEG channel is statistically independent from the other channels whereas the EI configuration exploits their statistical inter-relationship and the synchronously recorded nature of the EEG; treating all channels as related. It is clear from this work that assumptions of independence made in the LI configuration are weak. The loss of information entailed by hardening the decisions for each channel in the LI configuration is another reason for the discrepancy in performance between the two configurations.

The performance of all configurations is limited by the unavailability of per channel annotations. While it is arguable that seizure manifestation will be present in all EEG channels, stereotyped seizure EEG manifestations may only be visible to the naked eye on a number of channels. As a result this multi-channel formulation makes the assumption of equal manifestation of seizure across channels. Obviously this is not the case and will place an upper limit on classifier performance. By simultaneously classifying all recorded EEG channels, the synchronously recorded nature of the EEG is exploited. This approach is validated by recent research that suggests that seizure EEG is characterized by a dynamical entrainment across EEG channels [17].

Classifier models based on regularized discriminant analysis represent a compromise between the linear and quadratic discriminant classifier models. The linear discriminant classifier with mean and covariance weighting by record duration was found to be the best classifier model for this application. For the patient independent classifier, weighting of the class specific mean and covariance matrices by the duration of the records in the training set, allowed each record to contribute equally to the classifiers' training.

Patient specific neonatal seizure detection may have utility in the modern NICU. When a clinician is alerted to the presence of electrographic seizures, they could then use relevant sections and channels of the seizure EEG to tailor the training of a base patient independent classifier towards the individual patients' electrographic seizure characteristics. The ideal neonatal seizure detection algorithm would be a generalized patient independent classifier, which could identify seizures from all neonates with perfect sensitivity and specificity. Our results are a step towards this ideal. There is a marked difference between the patient specific and patient independent results reported here. While one would expect superior performance from a patient specific classifier it can certainly be argued that improved feature normalization schemes may further improve the generalized classifier performance.

Faul *et al* [9] compared three major neonatal seizure detection algorithms [5-7] on the same data-set and found that none of the three were suitable for use in a NICU environment.

The data set used by Faul *et al* is same as is used in this study. A limitation on all three methods (along with the method of Altenburg *et al* [8]) is that they were empirically based, a seizure was declared when a parameter or combination of parameters met an empirically derived value. By taking a statistical approach to classification we have allowed decision thresholds to be directly determined from the data. Many of these methods are based on a single channel of EEG, applying the same algorithm independently to each channel, ignoring the evident statistical dependencies across channels.

A deficit in the literature to date is a lack of rigorous validation procedures for classifier performance estimation. Cross fold validation guarantees an unbiased measure of classifier performance. The performance estimates given for all configurations are made more pessimistic when the annotation paradigm used is considered. In much of the previously reported research on neonatal seizure detection, results are given based on short duration seizure and non-seizure records or epochs [7, 8, 18], as opposed to including continuous recordings of the duration and quality that would be found in real-world, neonatal ICU conditions. The results reported by Liu *et al* [7] were for selected for 'typicality'. Selection of EEG epochs has the effect of optimistically biasing results. Methods should be evaluated over a duration of several hours. Short duration recordings cannot be considered in the same light as results presented for methods such as Gotman [5], which use more realistic recording lengths and do not exclude any record regardless of length or quality. In this study we have used completely unselected recordings with an average length of 12.5 hours as a result we feel that our results will accurately reflect the performance of these algorithms under real world conditions.

The work presented here has applications in the wider field of long-term EEG monitoring. The multi-channel configurations reported here may be useful for a variety of medical and neuroscience applications as they could form the basis of a long term monitoring framework for multi-channel or multimodal biomedical signal monitoring. To the best of our knowledge this study is the first to propose multi-channel EEG classifier configurations and use statistical classifier models for neonatal seizure detection.

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