Decomposition of a multiscale entropy tensor for sleep stage identification in preterm infants

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Abstract. Established sleep cycling is one of the main hallmarks of early brain development in preterm infants. Therefore, automated classification of the sleep stages in preterm infants can be used to assess the neonate's cerebral maturation. Tensor algebra is a powerful tool to analyze multidimenionsal data and has proven successful in many applications. In this paper, a novel algorithm to identify neonatal sleep stages based on the decomposition of a multiscale entropy tensor will be presented. The method has been evaluated on a dataset of 67 test recordings, obtaining an average sensitivity, specifity, accuracy and area under the ROC curve of 0.75, 0.79, 0.78 and 0.84 respectively.

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1. Introduction

In human infants, the emergence of sleep cycles occurs at approximately 26 to 28 weeks postmenstrual age (PMA) [1]. During maturation of the sleep architecture, the distribution and duration of specific sleep states changes gradually. Very young preterm infants have an abundant amount of sleep, and active sleep is the dominating sleep stage. From then on, the proportion of time spent asleep decreases, while the relative amount of quiet sleep increases. Near term age, both active sleep and quiet sleep constitute approximately half of the total sleep time [2, 3]. Existing research recognises the importance of sleep in early brain development [1, 3, 4]. Sleep and established sleep cycling play a vital role in normal neurosensory development, learning processes, memory consolidation and in the protection of the infant's brain plasticity [1]. Moreover, studies such as that conducted by Shellhaas et al [5] have shown that the presence of sleep cycling and the quantity and quality of each sleep state are associated to neurodevelopmental outcome [6–8].

Most of the prematurely born infants stay in the neonatal intensive care unit (NICU) during the first critical weeks of rapid growth and development of the brain. In the NICU, neonates are exposed to a myriad of noxious environmental stimuli, such as high noise and light levels and painful procedures, which might disrupt their sleep state organization. In recent years, there has been an increasing interest in strategies to promote sleep in the NICU environment (e.g. kangaroo care, massage therapy, cycle lighting, etc.) [7,9].

Real time automated identification of the behavioural state can be used to optimize the planning of NICU caregiving in order to reduce disturbance of sleep-wake cyclicity [10]. Moreover, an automated sleep staging algorithm can be used to assess the sleep architecture and by that the functional brain maturation. In view of all that has been mentioned so far, one may suppose that there is a need to assess the sleep staging of neonates in order to provide developmentally appropriate care.

A number of algorithms for sleep stage classification in preterm neonates have been developed. The majority of these approaches are supervised and combine a set of EEG features (e.g. temporal features, spectral features, spatial features, complexity features) with a classification algorithm [11, 12]. Recently, deep learning has also found its way to sleep staging in preterm infants [13]. At last, Dereymaeker et al. [14] have proposed an cluster-based algorithm for quiet sleep detection.

This paper proposes a novel method to discriminate quiet sleep from non-quiet sleep in preterm infants. In this study, a tensor-based method exploiting the differences in EEG complexity between different vigilance states will be used. Due to the increasing amount data being collected nowadays and the specific properties of tensor decompositions, multiway analysis has received increasing attention during the last decades. Tensor algebra has been used in a broad range of applications, such as image and video processing, machine learning and biomedical applications [15, 16]. To the best of our knowledge, this is the first paper where tensor decompositions are used to discriminate sleep stages in preterm neonates.

The remaining part of the paper proceeds as follows. The first section of this paper will describe the dataset. It will then go on to the explanation of the different steps of the proposed method. Afterwards the results of the algorithm will be reported and discussed.

2. Database

The proposed method has been evaluated on a dataset consisting of EEG signals recorded at the neonatal intensive care unit of the University Hospitals of Leuven, Belgium. All neonates included in the study were born between 2012 and 2014 at a gestational age below 32 weeks (range: 24 weeks 4 days - 32 weeks). In total 97 multichannel EEGs were measured from 26 neonates at a postmenstrual age (PMA) between 27 and 42 weeks. So, each subject had at least 2 serial EEG recordings during their stay in the NICU. The study was approved by the Ethics committee of the University Hospitals of Leuven and parental consent was obtained for all Criteria for selecting the subjects were as follows: a normal recruited patients. neurodevelopmental outcome at 9 and 24 months corrected age (Bayley Scales of Infant Development-II, mental and motor score > 85), no severe brain lesions assessed by ultrasound and not taking any sedative or anti epileptic drugs during the EEG registration. EEG was recorded using nine electrodes: Fp1, Fp2, C3, C4, T3, T4, O1, O2 and Cz using the modified 10-20 system [17]. Electrode Cz served as a reference and was not taken into account during the analysis. The EEG data were acquired at a sampling frequency of 250Hz using BrainRT equipment (OSG byba, Rumst, Belgium). The analysis of the data is carried out in Matlab 2017b (The MatchWorks, Inc., Natick, Massachusetts, United States), and the tensor decompositions were performed using Tensorlab [18].

Quiet sleep periods were annotated by two independent expert clinicians upon agreement. All other sleep states are merged and will be referred to as non-quiet sleep. The goal of the proposed algorithm is to automatically label EEG segments as either quiet sleep (QS) or non-quiet sleep (NQS). The main feature of quiet sleep compared to non-quiet sleep is that the EEG signal is relatively more discontinuous. Moreover, non-quiet sleep is characterized by a higher variability of the cardiorespiratory pattern and more body movements [4].

The dataset is divided into a training set, used to optimize the parameters of the algorithm, and a test set, used to evaluate the performance. The training set consists of 30 recordings randomly sampled from the complete dataset, retaining the distribution of the postmenstrual age at the moment of recording of the original complete dataset. The test set is composed of the remaining 67 EEG recordings.

3. The proposed tensor-based sleep stage identification method

The pipeline of the proposed algorithm consists of 5 steps: 1) preprocessing of the EEG, 2) assessment of the EEG complexity via computation of the multiscale entropy, 3) tensorization of each EEG recording, 4) decomposition of the multiscale entropy tensor, 5) postprocessing and clustering of the factor matrix. Each step of the algorithm will be extensively described in the next paragraphs. Finally, the procedure to select the optimal parameters and the metrics to assess the performance will be explained.

3.1. EEG Preprocessing

In order to avoid distortion of the EEG time series by high or low frequency artefacts, a bandpass FIR-filter between 1 and 40Hz was applied on each EEG channel. Moreover, an additional notch filter at 50Hz is used to remove any remaining mains interference. The filters were applied in both forward and reverse directions in order to avoid phase distortion. The EEG signal is then downsampled with a factor 2. No advanced artefact removal or visual preselection of data has been performed.

3.2. Multiscale entropy computation

After filtering the data, the EEG signal is segmented into nonoverlapping windows of 100s [11]. To assess the complexity of each of these multichannel EEG segments, the multiscale entropy is computed. Multiscale entropy evaluates the complexity of a signal by measuring the regularity of the signal at multiple time scales [19, 20]. So, the first step in its computation is to obtain signals at different scales. This coarse-grained signal at scale τ is obtained by taking the average of all data points within consecutive nonoverlapping windows of length τ . So the coarse-grained time series of the signal $\{x_1, x_2, ..., x_N\}$ at scale factor τ can be written as: $y_j^{\tau} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i$ for $1 \leq j \leq \frac{N}{\tau}$. This actually corresponds to a moving average operation with a window of length τ followed by a downsampling with factor τ . Hence, at scale 1 the signal is simply the original time series, while with increasing scale the coarse-grained signal length reduces progressively. Following coarse-graining the EEG segment, the regularity of the signal at each scale τ is quantified using sample entropy. Sample entropy is a measure of the regularity or predictability of a time series. It is computed as the negative natural logarithm of the conditional probability that two sequences of m consecutive data points match within a tolerance r, will also be similar when an additional data point is added to the sequence. For a discrete time series of length N, this can be expressed as |21|:

$$SampEn(m, r, N) = -ln\frac{A}{B}$$
(1)

where A and B denote the number of matches of length m+1 and m within tolerance r, respectively. In this study, the template length m is set equal to 2, the tolerance r is defined as $0.2 \times$ the standard deviation of the original time series and the coarsegraining is performed for a scale from 1 to 20 [11, 22]. Once the sample entropy is



Figure 1: Illustration of the procedure to compute multiscale entropy. The first step consists of coarse graining the time series into different scales. In the second step, the sample entropy of each of these coarse grained time series are computed. At last, a multiscale entopy curve can be constructed by plotting the sample entropy in function of scale. The multiscale entropy curve is usually lower during quiet sleep compared to non-quiet sleep.

computed for each of the coarse-grained time series, a multiscale entropy (MSE) curve can be constructed. This curve shows the sample entropy in function of the scale factor τ . Hence, it reflects the regularity of the signal across multiple scales. The procedure to compute multiscale entropy of a time series is presented in Figure 1. The multiscale entropy curve of each 100s multichannel EEG segment is computed.

3.3. Tensorization

The entropy values of each EEG recording are then organized in a third order tensor with modes: channels, scales and time segments. So, the multiscale entropy curves of consecutive times segments are stacked in the third mode of the tensor $\mathcal{X} \in \mathbb{R}^{N \times S \times T}$. In this study, the number of EEG channels N is equal to 8, the number of scales for which the sample entropy is computed S is equal to 20 and the number of time segments T depends on the length of the EEG recording. Thus, the data of each EEG recording will be transformed into a third order tensor $\mathcal{X} \in \mathbb{R}^{8 \times 20 \times T}$, where each row fiber (mode-2 fiber) of the tensor represents a multiscale entropy curve from a specific EEG channel and time segment. In the remainder of this paper, this tensor will be referred to as the multiscale entropy tensor.

3.4. Tensor decomposition

Throughout this paper, a scalar, vector, matrix and tensor will be denoted by lowercase letters (a), boldface lowercase letters (a), boldface capitals (A) and letters in calligraphic script (\mathcal{T}), respectively. The canonical polyadic decomposition (CPD) or parallel factor analysis (PARAFAC) of a rank-R tensor \mathcal{T} factorizes the tensor in a sum of R rank-1

tensors [23]. This can be written as:

$$\mathcal{T} = \sum_{r=1}^{R} \mathbf{a}_r \circ \mathbf{b}_r \circ \mathbf{c}_r, \tag{2}$$

where \circ represents the outer product. The advantage of CPD compared to matrix factorizations is that is unique (up to scaling and permutation ambiguity) under mild conditions. Moreover, prior knowledge of the properties of the data can easily be taken into account by imposing constraints on the factor matrices (e.g. sparsity, smoothness, non-negativity, etc.) [15]. Because entropy values are positive, non-negativity is enforced during the decomposition of the multiscale entropy tensor.

However, selecting an appropriate rank for the problem at hand is not an easy task [24]. We opted for a rank R equal to 1. The procedure that was used to select the number of components will be explained later on.

The CPD of the multiscale entropy tensor with rank R equal to one will result in 3 factor vectors: the spatial signature $\mathbf{a}_1 \in \mathbb{R}^{N \times 1}$, the scale signature $\mathbf{b}_1 \in \mathbb{R}^{S \times 1}$ and the temporal signature $\mathbf{c}_1 \in \mathbb{R}^{T \times 1}$. An example of this decomposition is shown in Figure 2. The factor vector in the first mode \mathbf{a}_1 , will show the variation over the different EEG channels, the factor vector in the second mode \mathbf{b}_1 , contains information about the distribution over scales, while the factor vector in the third mode \mathbf{c}_1 , will capture the main variation of the EEG complexity over the different time segments.

Based on the assumption that the EEG complexity is different depending on the sleep stage [11], we expect that the temporal signature (\mathbf{c}_1) will reflect the sleep cycling. Since the goal of the algorithm is to perform automated sleep staging, only the factor vector in the third mode, the temporal signature, is of interest.

3.5. Postprocessing and clustering

Once the non-negative rank-1 polyadic decomposition of the multiscale entropy tensor is performed, the temporal signature is used to define the neonate's sleep stage. This temporal signature shows a cyclic pattern reflecting the sleep staging of the infant. However, there are high frequency oscillations superimposed on this pattern, which could lead to incorrect sleep stage identification. Therefore, a postprocessing step consisting of smoothing the temporal signature using a moving average filter is added. The length L of the moving average window is defined on the training set and is chosen equal to 5. This moving average filter is applied in both directions (to avoid phase distortion), so actually a weighted moving average filter is used with triangular shape and length $2 \times L$. This smoothing operation accounts for the fact that a sleep stage does not change instantly.

In order to divide the data into two distinct clusters, k-means clustering (k=2) is performed using the smoothed temporal loading. Since k-means clustering is heavily dependent on its initialization, k-means clustering is repeated 100 times with different initial cluster centroids and the clustering with the lowest sum of within-cluster pointto-centroid distances is selected. The cluster with the lowest EEG complexity will be assigned the label of quiet sleep, while the other cluster is labelled as non-quiet sleep. The effect of the smoothing and the result of the clustering is illustrated in the bottom plots of Figure 2.

3.6. Model parameters

In the proposed algorithm, there are two parameters that have to be tuned. First of all, the number of components R in the tensor decomposition has to be set. Secondly, the length of the smoothing filter L has to be defined.

To get an initial estimate of the number of components used to fit the multiscale entropy tensor, we investigated the multilinear singular value spectrum [15]. We observed one dominant singular value in each mode, which indicated that the tensor could be well approximated by few components. Therefore, we expected the rank to be low and tested in the range from 1 to 5.

In order to to optimize both parameters simultaneously, a grid search is performed using 6-fold crossvalidation on the training set. The rank and length of moving average filter are set equal to 1 and 5, respectively.

3.7. Classification performance

The performance of the algorithm is evaluated using the annotations by expert clinicians. The sensitivity, specificity and accuracy will be reported. Moreover, ROC curves are constructed based on the smoothed temporal signatures and the clinical labels. The performance metrics will be reported for the complete dataset and for the subset of recordings measured before 37 weeks PMA (i.e. preterm age) separately.

4. Results

Table 1 presents the mean and standard devation of the performance measures of the classification. As can be seen from the table, the performance is higher for the subset of EEG signals recorded before 37 weeks PMA. This is also confirmed by Figure 3 which shows the area under the ROC as function of the postmenstrual age. Each gray square repersents an EEG recording from the test set.

Moreover, to investigate how well the proposed decomposition fits the data, the relative error between the multiscale entropy tensor and the CPD approximation is computed. This average relative error between the multiscale entropy tensor and obtained factor matrices is equal to 13%.

5. Discussion

This study aimed to discriminate quiet sleep (QS) from nonquiet sleep (non-QS) using the nonlinear dynamics of the EEG signal in a data driven way. The algorithm reaches a relatively high performance with an average area under the ROC curve equal to 0.84



Figure 2: On top, the decomposition of the multiscale entropy tensor is illustrated. The factor vector in the third mode \mathbf{c}_1 , marked in dark blue, is the temporal signature. This temporal signature is plotted in blue in the plots at the bottom. As expected the temporal signature is reduced during the clinically labelled quiet sleep periods, which are highlighted in gray. The plot at the bottom left, shows the temporal signature without postprocessing. The plot at the bottom right shows the smoothed temporal signature after applying the weighted moving average filter. Moreover, the sleep stages estimated by the algorithm are marked by red dots.

Table 1: The classification performance of the proposed tensor-based method for all EEG signals recorded before 37 weeks PMA and for all EEG recordings. The mean(standard deviation) of the area under the ROC curve, the sensitivity, specificity and accuracy are presented.

	AUC	Sensitivity	Specificity	Accuracy
Preterm test recordings All test recordings	$\begin{array}{c} 0.86(0.14) \\ 0.84(0.18) \end{array}$	$\begin{array}{c} 0.78(0.22) \\ 0.75(0.26) \end{array}$	$\begin{array}{c} 0.79(0.15) \\ 0.79(0.14) \end{array}$	$\begin{array}{c} 0.79(0.12) \\ 0.78(0.13) \end{array}$



Figure 3: The area under the ROC curve as a function of the postmenstrual age at the moment of the recording. Each gray square represent the one of the test recordings.

for all test recordings. If only recordings measured before a postmenstrual age of 37 weeks are taken into account, the performance increases slightly. This indicates that the algorithm is mainly useful in the preterm population.

There are various possible explanations for the drop in performance near term age. First of all, this might be due to the emergence of 4 distinct sleep states around 36 weeks PMA [4]. Moreover, differences between the performance of the preterm and near term recordings might have been influenced by the amount of artefacts. It is expected that an older neonate will move more, which could lead to more severe distortions and lower quality of the EEG signal. At last, it is possible that EEG complexity is higher during QS compared to NQS near term age (instead of the reverse) due to maturational changes and specific graphoelements in the EEG.

The performance of the described algorithm is lower compared to state-of-the-art algorithms [25], [14], [13]. However, there are multiple advantages of the proposed method. Since the data driven algorithm is mostly based on clustering and there are only two parameters to optimize, the method can be easily applied on a new dataset. If sleep labels are available for only few EEG recordings of a new dataset, the parameters can be easily fine-tuned. As a result, this algorithm can also be used in new centers, where there is little expertise about EEG sleep labelling. Moreover, the tensor decomposition can be updated in an efficient way whenever a new batch of EEG data is available [26]. This allows real time tracking of neonatal sleep states.

In future investigations, it might be possible to use tensorization techniques which might improve the performance. This study was an exploratory analysis on the use of tensor decompositions for sleep stage identification in preterm infants. We only used differences in complexity between different sleep stages. However, in future work the temporal signature can be combined with other discriminating features (e.g. spectral edge frequency, power in specific EEG frequency bands, etc.) to boost the performance.

6. Conclusion

This study has confirmed that the complexity of brain dynamics exhibits fundamental differences between vigilance states in preterm newborns. Moreover, a novel approach to detect quiet sleep based on the data-driven tensor factorization of the multiscale entropy tensor is proposed.

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