Predicting Respiratory Depression in Neonates Using Deep Learning Neural Networks

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Abstract: Respiratory problems are one of the most common reasons for neonatal intensive care unit (NICU) admission of newborns. It has been estimated that as much as 29% of late preterm infants develop high respiratory morbidity. To this purpose invasive ventilation is often necessary for their treatment in NICU. These patients usually have underdeveloped respiratory system with deficiencies such as small airway caliber, few collateral airways, compliant chest wall, poor airway stability, and low functional residual capacity. Consequently ventilation control has been subject of considerable research interest. In this paper we propose an algorithm for detection of respiratory depression by predicting the onset of pO_2 depressions using physiological measurements. We train deep neural network using previously obtained data set from NICU, McMaster University Hospital with intra-arterial pressure measurements and evaluate its performance. Preliminary results indicate that adequate performance can be achieved if sufficient number of measurements is available.

1 INTRODUCTION

Newborn intensive care is one of the great medical success of the last 20 years. Current emphasis is upon allowing infants to survive with the expectation of normal life without handicap. Clinical data from follow up studies of infants who received neonatal intensive care show high rates of long-term respiratory and neurodevelopment morbidity. As a consequence, current research efforts are being focused on refinement of ventilated respiratory support given to infants during intensive care (Revow et al., 1989).

The main task of the ventilated support is to maintain the concentration level of oxygen (O_2) and carbon-dioxide (CO_2) in the blood within the physiological range until the maturation of lungs occur. Failure to meet this objective can lead to various pathophysiological conditions. Therefore one of the most critical components in the neonatal intensive care units (NICU) is an adequate ventilation control. In addition, due to a fragile state of neonatal lungs the ventilation control has to be designed very carefully as neither hyperventilation nor hypoventilation are acceptable.

In our previous work (Jeremic and Tan, 2007) we developed a deterministic inverse mathematical model of the CO_2 partial pressure variations in the arterial blood of a ventilated neonate. We evaluated the applicability of the proposed model using clinical data sets obtained from neonatal multi-parameter intra-arterial sensor which enables intra-arterial measurements of partial pressures. Using this model we developed statistical signal processing model (Jeremic and Tan, 2009) that predicts both inter-arterial pressure measurements and corresponding confidence intervals. In (Jeremic and Nikolic, 2019) we proposed an algorithm for prediction of clinical depression in neonates using parametric model based approach. The proposed algorithms performs detection of pO_2 depression events using intra-arterial pressure measurements and parametric model based on the log-Riemannian distance between sample covariance matrix measurements. However, intra-arterial pressure measurements are administered only in rare cases that warrant more intensive style of patient monitoring. To this purpose in this paper we design a deep neural network and use available data-set and intra-arterial pressure measurements as ground truth in order to train the network.

Deep neural networks are becoming increasingly popular in the biomedical signal processing due to the fact that they do not rely on the parametric model which may be beneficial due to patient-to-patient variability. In Section 2 we outline the structure of the

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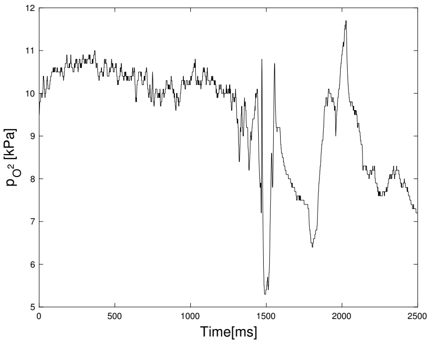

Figure 1: Sample of intra-arterial pressure measurements.

deep neural network and the corresponding signal processing algorithms. In Section 3 we illustrate the applicability of the proposed techniques by evaluating the performance of the proposed network using a validation set that was not used as a part of training. Our preliminary results indicate that the onset of oxygen depression can be predicted with potentially useful accuracy sufficient to alarm the clinical staff of the NICU. In Section 4 we provide concluding remarks and discuss further directions.

2 SIGNAL PROCESSING MODELS

To examine the applicability of the proposed algorithms we apply them to the data set obtained in the Neonatal Unit at McMaster University Hospital. The data set consists of intra-arterial partial pressure measurements obtained from 91 ventilated neonates. The sampling time was set to 10s and the expiratory rate was set to 1 breath per second. In Figure 1 we illustrate a sample of intra-arterial pressure measurements.

In order to predict the onset of respiratory depression (hypo-ventilating) condition in (Jeremic and Nikolic, 2019) we calculated the sample covariance matrix we propose to use Frechet mean (Jahromi, 2014) which is given as the point which minimizes the sum of the squared distances (Barbaresco, 2008): and the log-Riemannian distance measure given by (Moakher, 2005):

$$d_l(\mathbf{A},\mathbf{B}) = \left\|\log(\mathbf{A}^{-\frac{1}{2}}\mathbf{B}\mathbf{A}^{-\frac{1}{2}})\right\|_2 = \sqrt{\sum_{i=1}^{M} \log^2(\mathcal{L}_i)} \tag{1}$$

where the $\mathcal{L}_i$'s are the eigenvalues of the matrix $\mathbf{A}^{-1}\mathbf{B}$ (Absil et al., 2009) where A and B are arbitrary $M \times M$ matrices whose distance is being calculated. The details of this algorithm are provided in the aforementioned reference (Jeremic and Nikolic, 2019).

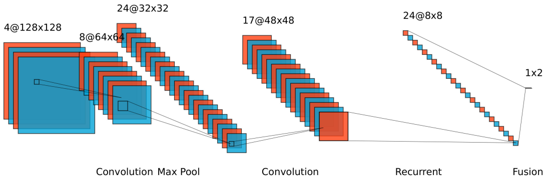

Figure 2: The schematic of the artificial neural network (ANN).

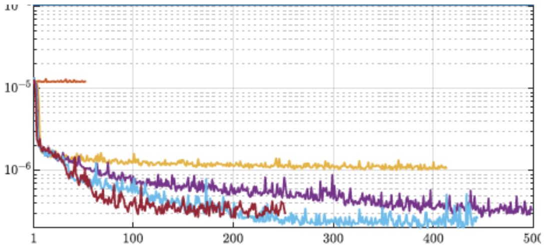

Figure 3: Validation results for ANN training for different scenarios.

In this paper we propose to use deep learning neural network (DNN) illustrated in Figure 2. We use the four dimensional physiological measurements consisting of partial pressure measurements of oxygen, breathing rate, electrocardiography measurements and intra-arterial pressure measurements (available only for some patients). The covariance matrix on the temporal window of N samples is calculated of the physiological signals is calculated (4 x 4) and provided as a time-series input to DNN. The training of the network is provided as an additional input of the critical event (respiratory depression) is labeled by a critical event triggered by an alarm which is used as a ground truth. In Figure 3 we illustrate the performance of the DNN to adequately predict the future values of the distance measure (i.e. distance between sample covariance matrix of the physiological signals). To illustrate the applicability of the proposed method and evaluate the need for intra-arterial pressure measurements we utilize two different designs which differ with respect to input dimensions with and without the presence of the intra-arterial pressure measurements. The orange line represents validation error in the absence of the intra-arterial pressure. The purple, red and blue lines represent validation errors for the DNN that are trained to predict critical event in time windows of 1, 5 and 10 minutes respectively. The above results indicate that in order to achieve lower validation error we would benefit greatly from intra-arterial pressure measurements.

3 RESULTS

We evaluate the performance of the proposed algorithms using the data set obtained at the Neonatal Intensive Care Unit, at McMaster University Hospital. At each cot in the Neonatal Intensive Care Unit at the McMaster Children's Hospital there is a cotside monitor displaying the physiological parameters measured. Moreover, these monitors are linked in a network with a central station into which data can be rapidly exported via Draeger Infinity Gateway software. Data is stored in the central station for 24 hours. The final dataset contained 91 patients with the number of recorded days for each patient varying between 1 and 90 with a mean of 32 days. In order to study the changes with respect to the length of stay we selected only patients who stayed up to 4 weeks and performed evaluation for different weeks using cumulative dataset.

In Figure 4 we illustrate the event corresponding to the respiratory depression as well as the change in the covariance matrix distance when calculated compared to the Frechet mean in the absence of respiratory depression. In our previous work (Jeremic and Nikolic, 2019) we evaluated performance of the model based approach whose application relies on the use of one particular distance. We believe that in complex physiological problems we may benefit by allowing the network to learn the processes in an unconstrained way as different distances may work better for different patients. Since the time is of essence in NICU, we may not have enough time to gather enough data for a particular patients and thus deep learning networks may be more useful regardless of patient to patient variability. To this purpose the original DNN was extended to include task of classification using the respiratory depression alarms as indicated by cot-bed monitors.

In order to evaluate the performance of the proposed DNN we train the network using the available data for (N-1) i.e. 91 patients and evaluate performance on the single patients that was not used for training. We then repeat these process for all the 92 patients thus effectively performing rotational evaluation of the proposed network. In Figures 5 and 6 we illustrate the respiratory depression detection for different subjects 5 min and 10 min before respiratory depression respectively. The four different colours represent different weeks of NICU hospitalization. Preliminary results indicate that for this particular set there is not a significant change in our ability to predict onset of respiratory depression. Please note that this may be the consequence of the physiological state of the patients which is general correlated with the length of stay. In Figure 7 we illustrate the overall accuracy for all the subjects where the overall accuracy is defined as inverse of both types of error (probabilities of false alarm and miss).

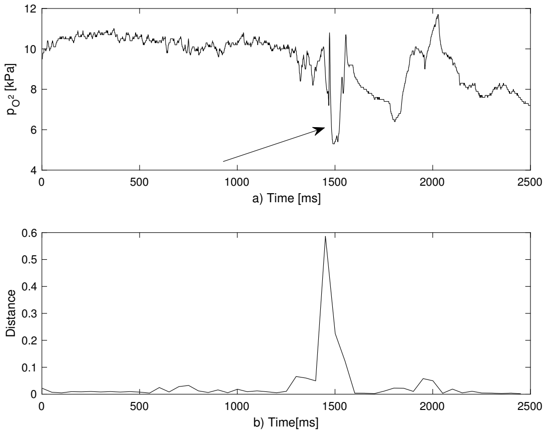

Figure 4: Sample of depression event as perceived by intra-arterial pressure measurement and breathing rate.

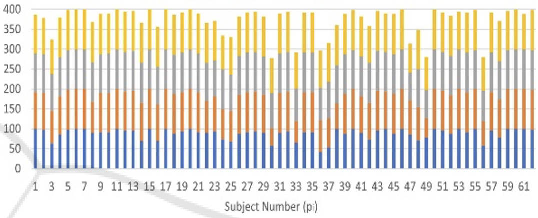

Figure 5: Detection probability as a function of false positives 5min window.

Finally in Table 1 we illustrate the precision, recall and F-score of the proposed system including all 91 patients. We can observe that the performance significantly deteriorates when compared to "more stable" patients due to the fact that in the case of long stay patients the number of respiratory depressions is much larger. In addition, the statistical variability of the measurements in these patients may be much higher.

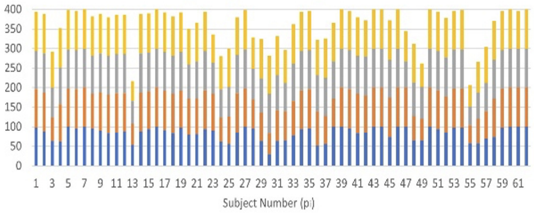

Figure 6: Detection probability as a function of false positives 10 min window.

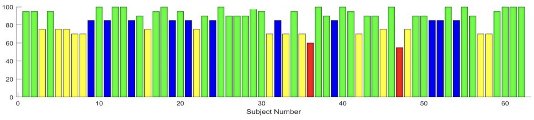

Figure 7: Overall probability of error per subject.

Table 1: Overall performance for all the patients.

Window	Precision	Recall	F-score
10 min	0.7099	0.6911	0.7003
8 min	0.7492	0.733	0. 741
5 min	0.7846	0.7709	0.7777
3 min	0.7546	0.7411	0.7478
2 min	0.7874	0.7774	0.7824
1 min	0.8294	0.8201	0.8247

4 CONCLUSIONS

One of the most important tasks that affect both long- and short-term outcomes of neonatal intensive care is maintaining proper ventilation support. To this purpose in this paper we develop signal processing algorithms for predicting the onset of hypoventilation in order to increase efficient control of ventilation system in timely manner. This is especially important for neonates due to a fragile state of their lungs and hence predicting the decrease oxygen levels can potentially enable us to control the ventilator with smaller dynamic range.

In this paper we propose to predict the onset using second order statistical properties by calculating sample covariance matrices using Frechet mean. Our experimental results indicate that the structure of covariance matrix is slowly changing once the hypoventilation begins. Due to the fact that the trend changes of intra-arterial pressure occur continuously they may not serve as a good indicator due to a large number of false positives. To this purpose we focus our attention on the second order properties i.e. covariance matrix and utilize Frechet mean as it is know to be able to capture different information about matrix structure depending on the distance measure used. Due to the fact that patient-to-patient variability and short length of stay per patient may prevent utilization of parametric models we evaluate applicability of deep learning networks. We illustrate the applicability of the proposed method for patients with the length of stay of up to four weeks. Our preliminary results indicate that DNN could be potentially used in a hybrid setting in which the rough estimate of model parameters could be obtained using DNN and the fine tuning for a particular patient could evolve throughout the patient's stay at NICU.

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