Predicting Respiratory Depression in Neonates using Intra-arterial Pressure Measurements

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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 intra-arterial pressure measurements and second order statistical properties of these signals. We calculate the average covariance matrix of intra-arterial pressure measurements in the absence of respiratory depression. We then use this matrix as a reference measure and monitor the changes in the actual covariance matrix measurements. We predict the onset of respiratory depression once the distance is larger than empirically determined threshold. We demonstrate the applicability of our results using a real data set.

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 neurodevelopmental 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 this paper we present a new statistical signal processing model for predicting the onset of respiratory depression. We focus on advance detection of falling edge events of oxygen partial pressure and consequently rising edge events of carbon-dioxide partial pressure measurements. To this purpose we propose to detect the change by calculating distance between the sample covariance matrix and reference matrix obtained in the training stage. In Section 2 we describe the training procedure in which the reference estimate of the covariance matrix is calculated and operating mode in which the actual sample co-

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variance matrix is calculated using the sliding window approach. The sample covariance matrices are calculated by using Frechet mean by utilizing our previously developed algorithms (Jahromi et al., 2015). In Section 3 we present experimental results obtained by applying our algorithms to real data set. Finally in Section 4 we present conclusions and discuss possibilities for future research.

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 St. James's University Hospital. The data set consists of intra-arterial partial pressure measurements obtained from twenty ventilated neonates. The sampling time was set to 10s and the expiratory rate was set to 1 breathe per second. In Figure 1 we illustrate a sample of intra-arterial pressure measurements.

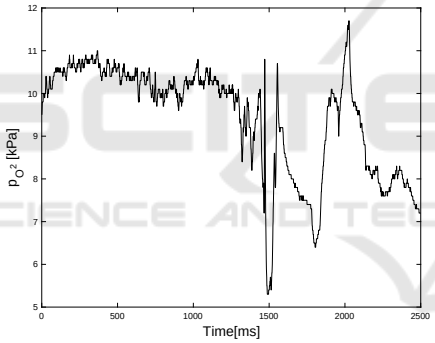

Figure 1: Sample of intra-arterial pressure measurements.

In order to predict the onset of respiratory depression (hypo-ventilating) condition we propose to calculate the sample covariance matrix and compare it to a reference value obtained from the training period. In order to achieve this goal we first select a training data set by selecting time intervals without respiratory depression event. Note that these intervals have to be selected for every patient by a trained neonatologist. Then we calculate the sample covariance matrix by using the sliding window over the measured intra-arterial pressure measurements. To determine the size of the window we first calculate the autocorrelation function, see Figure 3.

Note that there are various techniques for detecting signal jumps / edges in arbitrary signals. However since our goal is to predict the onset of these events, i.e. detect conditions that lead to hypoventilation we propose to use second-order statistical properties instead of simple trend changes. Namely, our preliminary results indicate that trend changes are frequent in intra-arterial pressure measurements due to the nature gas exchange and hence lead to significant number of false positives.

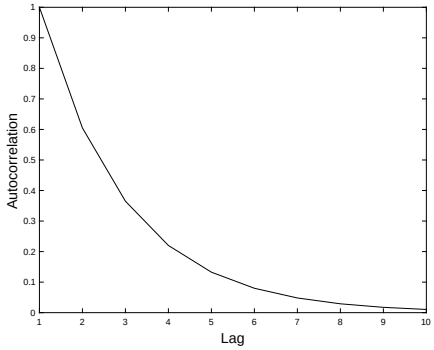

Figure 2: Autocorrelation function.

In order to calculate 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):

$$\hat{\mathcal{S}} = \text{argmin}_{\mathcal{S}\in\mathcal{M}} \sum_{i=1}^{n} d^2(\mathbf{S}_i, \mathcal{S}) \tag{1}$$

where $\{\mathbf{S}_i\}_{i=1}^{n}$ represents the symmetric positive definite matrices and $d(.,.)$ denotes the metric being used respectively. Therefore the above expression can be interpreted as a way of calculating an averaged sample covariance matrix using a sliding window where S_i represents an $i-th$ window sample covariance estimate.

In this paper we propose to use log-Riemannian distance measure given by (Moakher, 2005):

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

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. In our particular application matrix A refers to sample covariance matrix of the measured signal and B is the reference covariance matrix obtained in the training phase i.e. on an interval where no depression events were recorded.

In order to determine the threshold for distance comparison between the reference and testing covariance matrices we propose to use multiple signal segments and calculate multiple reference covariance matrices. Using these matrices we then calculate the histogram of mutual distances and pick the threshold based on the desired percentage of false positives. Note that as a preliminary approach we choose to use

the same distance measure both for training and evaluating performance although other distance measures (e.g. square root, Frobenius norm) could be used as well.

Let y_i be the i-th sample of inter-arterial pressure measurements. Then the outline of the algorithm is as follows

- within the training data set create windows $\vec{data}_k = [y_{(k-1)*l1+1}, \cdots, y_{k*l1-1}]$ where $l1$ is the length of the window
- within the above window select subwindows of length $l2$ and label them $\vec{data}_k^j$ where $j = 1, l1 - l2 + 1$
- remove the sample mean from the window vectors
- calculate rank 1 sample covariances $\vec{data}_k^{j,T} \vec{data}_k^j$ and average them using Frechet mean instead of commonly used addition

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 cot-side 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 16 patients with the number of recorded days for each patient varying between 1 and 90 with a mean of 32 days.

In Figure 4 (a) we illustrate the event corresponding to the respiratory depression and in Figure 4 (b) we illustrate the corresponding change in the covariance distance calculated using the aforementioned logarithmic Riemannian distance. In Figure 5 we illustrate the same results but in the absence of respiratory depression. Note that the dynamic range of the distance is much smaller compared to Figure 4.

As we stated before the performance of the algorithm will be dependent on adequate threshold selection. As a preliminary approach we arbitrarily set the false positives rate to 10% and calculated the corresponding threshold empirically using the part of data set (for each patient) without hypoventilation events. Using sliding window we calculate multiple sample covariance matrix estimates. Then we use the testing part of the data set and detect onsets of hypoventilation events by comparing distance between training

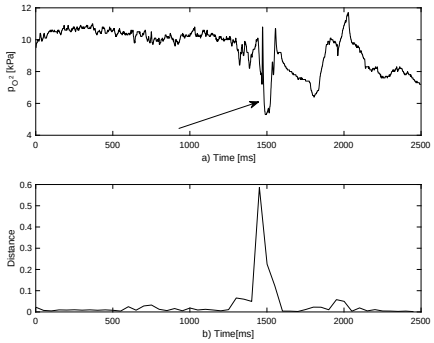

Figure 3: a) Sample of inter-arterial partial pressure b) Covariance distance calculated using logarithmic measure.

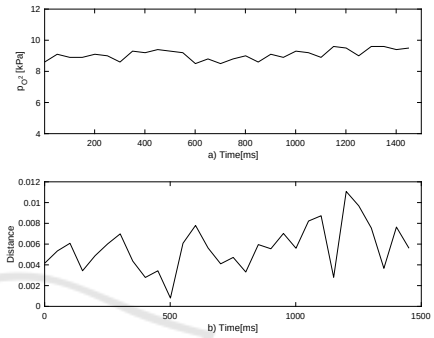

Figure 4: a) Sample of inter-arterial partial pressure b) Covariance distance calculated using logarithmic measure.

set covariance estimates to reference covariance matrices. In both cases we calculate sample covariances using sliding window of 100 samples and within that window we use 5 samples to construct 5-dimensional vector of lagged measurements which are then averaged using Frechet mean in order to calculate sample covariances.

In order to evaluate the performance of the proposed algorithm we count the number of detected onsets and compare it to the actual count performed by trained physicians. In Figure 6 we illustrate the performance of our algorithm as a function of the false alarm positives.

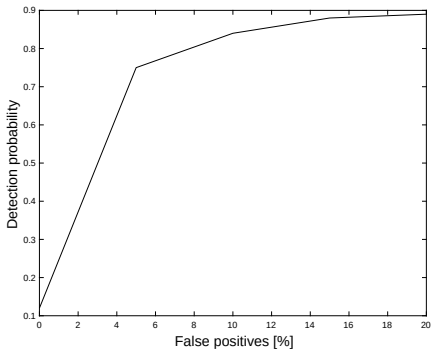

Figure 5: Detection probability as a function of false positives.

In Figure 6 we illustrate the performance measures for all the patients. Note that due to the large patient-to-patient variability the performance may vary significantly. This may partially be due to the fact that the respiratory patterns are very dependent on the gestation length and hence an effort should be made in selecting adequate training sets.

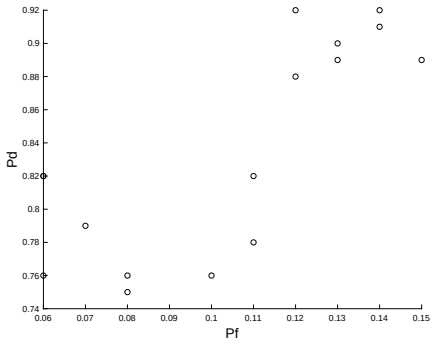

Figure 6: Scatter plot of performance parameters for all the patients.

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. We evaluate the performance of our algorithm using a real data set previously labeled by trained physicians. In future work we propose to develop multichannel information fusion system that will use different distance measures as onset detectors. In addition, we will compare performance of our algorithm versus thresholding. Note however that currently used thresholding algorithms detect depression once it starts to occur while our algorithm attempts to predict the onset of the depression.

REFERENCES

Absil, P.-A., Mahony, R., and Sepulchre, R. (2009). *Optimization algorithms on matrix manifolds*. Princeton University Press.

Barbaresco, F. (2008). Innovative tools for radar signal processing based on cartan's geometry of spd matrices & information geometry. In *Radar Conference, 2008. RADAR'08. IEEE*, pages 1–6. IEEE.

Jahromi, M. (2014). Frechet means with respect to riemannian distances: Evaluations and applications. *Ma.Sc. Thesis*.

Jahromi, M., Jeremic, A., and Wong, K. (2015). Estimating positive definite matrices using frechet mean. *Biosignals*, 3:295–299.

Jeremic, A. and Tan, K. (2007). Estimating respiratory parameters using intra-arterial partial pressure measurements. *Asilomar*, 2:851–854.

Jeremic, A. and Tan, K. (2009). Estimating respiratory parameters using intra-arterial partial pressure measurements and stochastic differential equations. *2009 Canadian Conference on Electrical and Computer Engineering*, 2:559–564.

Moakher, M. (2005). A differential geometric approach to the geometric mean of symmetric positive-definite matrices. *SIAM Journal on Matrix Analysis and Applications*, 26(3):735–747.

Revow, M., England, S., Beirne, H., and Bryan, A. (1989). A model of the maturation of respiratory control in the newborn infant. *IEEE Trans. on Biomedical Engineering*, 36(4):415–423.