Veronika Huttova*, Jakub Rafl, Knut Möller, Thomas E. Bachman, Petr Kudrna, Martin Rozanek and Karel Roubik

Model of SpO2 signal of the neonate

Abstract: The advantages of automatic control of the fraction of inspired oxygen in neonates have been documented in recently published clinical trials. Many control algorithms are available, but their comparison is missing in the literature. A mathematical model of neonatal oxygen transport could be a useful tool to compare and enhance both automatic control algorithms and manual control of fraction of inspired oxygen. Besides other components, the model of neonatal oxygen transport must include a module linking arterial (SaO_2) and peripheral (SpO_2) oxygen saturation. The pulse oximeter module must reflect issues of SpO_2 measurement typical for clinical practice, such as overestimation of SpO_2 over SaO_2 documented by several studies, or inaccurate pulse oximeter readings due to high noise. The aim of this study was to describe both the bias between SaO_2 and SpO_2 and the noise, characteristic for continuous SpO_2 recording, for a computer model of oxygenation of a premature infant. The SpO_2–SaO_2 bias, derived from available clinical data, describes a typical deviation of the SpO_2 measurement as a function of the true SaO_2 value in three different SaO_2 intervals. The SpO_2 measurement noise was considered as a random process that affects biased SpO_2 values at each time point with statistical properties estimated from SpO_2 continuous recordings of 5 stable newborns. The results of the study will help to adjust a computer model of neonatal oxygenation to the real situations observed in the clinical practice.

Keywords: Measurement bias, neonatal model, noise model, oxygenation, pulse oximetry, SpO_2.

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1 Introduction

The advantages of automatic control of the fraction of inspired oxygen in neonates, especially in comparison with manual control, have been documented in recently published clinical trials [1, 2]. Many control algorithms are available, but the comparison of their efficiency is missing in the literature [2]. Due to safety and ethical risks of clinical tests on newborns, a mathematical model of neonatal oxygen transport could be a useful tool for testing of robustness and reliability of the automatic control algorithms, or for their preliminary comparison with manual control schemes of the fraction of inspired oxygen [3]. As both the automatic and manual control of oxygenation is primarily based on pulse oximetry measurement, a module linking arterial (SaO_2) and peripheral (SpO_2) oxygen saturation must be included in the model. Considering the inaccuracies in pulse oximetry measurements in children and neonates presented in the literature, the objective of this study is to establish the properties of the pulse oximeter module.

Many studies have shown that SpO_2 measurements systematically overestimate SaO_2 in children and neonates, especially at the lower values [4–6]. Ross et al. found the greatest SpO_2–SaO_2 bias in the SpO_2 range 81–85%, where the SpO_2 value was higher than SaO_2 value by an average of 6.6% [4]. In comparison, Bachman et al. published the SpO_2–SaO_2 bias amounting to 5% in the SpO_2 range 75–93%, based on an evaluation of 25,032 measurements from 1,007 critically ill neonates [6]. Both studies pointed out not only the SpO_2–SaO_2 bias, but also quite a large variability in the bias. Besides many other factors resulting in large variability in SpO_2 measurements, low perfusion or high noise arising from motion, bright lights, or electromagnetic interference can cause a low signal-to-noise ratio leading to inaccurate pulse oximeter readings [7, 8]. Even when SaO_2 remains practically unchanged, the SpO_2 values presented by the pulse oximeter changes in time and in case of abrupt motion of a neonate may even be falsely interpreted as rapid desaturations [8].

In this study we describe the bias between SaO_2 and SpO_2 typical for premature infants and the SpO_2 measurement noise, characteristic for continuous SpO_2 recording. The aim of the work was to prepare a credible model of the output of the pulse

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oximeter for a computer simulation of oxygenation of a premature infant.

2 Methods

The mathematical model of the output signal of the pulse oximeter consists of two principal components: The SpO_2–SaO_2 bias that describes a typical deviation of the SpO_2 measurement as a function of the true SaO_2 value, and the SpO_2 measurement noise that affects biased SpO_2 values at each time point. All data were processed in Matlab (MathWorks, USA).

2.1 SpO_2–SaO_2 bias

The bias function was determined based on data from a clinical study by Ross et al. [4], a prospective multicentre observational study on 225 mechanically ventilated hypoxemic children aged between the 37th week of gestation and the 18 years, with SpO_2 ranging 65–97%. The subset of data for preterm and term infants less than 60 days after delivery were acquired from and processed with the authors' consent. For calculation of the SpO_2–SaO_2 bias, we used the selection that included SaO_2 measured by CO-oximetry—ABL800 (Radiometer Medical Aps, Denmark), Rapidlab 1265 (Siemens Healthcare, Germany) or Gem 3000 (Instrumentation Laboratory, USA)—from an arterial blood catheter. An SpO_2 value was recorded at the time when the blood sample was obtained. SpO_2 was measured by Masimo (Masimo Corporation, USA) and Nellcor (Covidien-Nellcor, USA) pulse oximeters depending on the Paediatric Intensive Care Unit.

The bias function was evaluated from 1,423 SpO_2–SaO_2 data pairs in three neighbouring SaO_2 intervals. For the SaO_2 range 70–96%, a median of measured SpO_2 values was calculated for each value of SaO_2 and a third-order polynomial was fitted through the medians. For SaO_2 below 70%, the SpO_2 bias was kept constant and equal to the SpO_2 bias at $SaO_2 = 70\%$ as determined by the third-order polynomial function, due to the lack of clinical data and non-guaranteed accuracy of pulse oximeters in this interval. For SaO_2 above 96%, the bias was set as zero, that is $SpO_2 = SaO_2$, due to the lack of clinical data for SpO_2 higher than 97%.

2.2 SpO_2 measurement noise

The model of the SpO_2 measurement noise was based on continuous neonatal SpO_2 records measured at the General University Hospital in Prague. The data were collected based on a standard informed consent to hospitalization and to collection of anonymous observational data for research and educational purposes signed by a legal representative of a neonate. SpO_2 was measured by Masimo Rad-97 pulse oximeter (Masimo Corporation, USA). Data of 5 stable spontaneously breathing newborns without known pathologies acquired within the first day after delivery with a minimum recording time of 10 hours were processed. The sampling time of the SpO_2 records was 2 s with the averaging time set to 2 s.

In the available records, the most stable 50% of data points were isolated using a moving window algorithm: At each position of the window, the median of the measured SpO_2 values in the window was computed as well as the sum of absolute differences between the measured SpO_2 values and the median. The data points with the lowest 50% of sums of the absolute differences in the corresponding moving window were chosen for the noise evaluation. For each of the points, the difference between the median and the measured SpO_2 value at the point was considered as the noise level. An example of an SpO_2 signal record and the points selected for further calculations is shown in Figure 1. Statistical properties of the random noise were extracted from a histogram of the estimated noise that aggregates all chosen points from all patients. In addition, the statistical properties of the random noise in the two side intervals, $SaO_2 \leq 96\%$ and $SaO_2 \geq 97\%$, were evaluated separately.

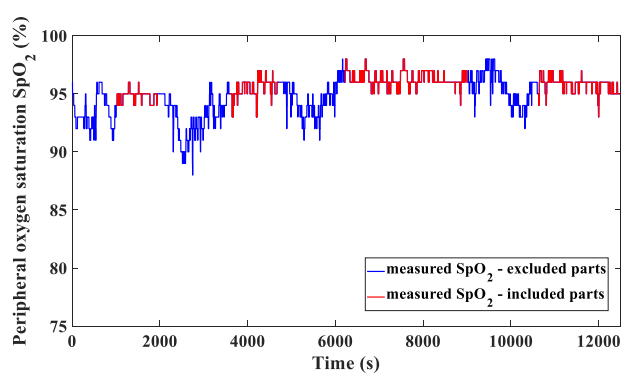

Figure 1: An SpO_2 record with a selection of the most stable 50% data points.

In order to determine the optimal length of the moving window, the algorithm described above was repeated for moving window lengths in the range of 2–60 minutes, with a 2-minute step. Normalized histograms of noise belonging to each length of the moving window were compared and the optimal window length, 20 minutes, was chosen, where the relative change was minimal in the zero noise level of SpO_2 between two consecutive histograms (Figure 2).

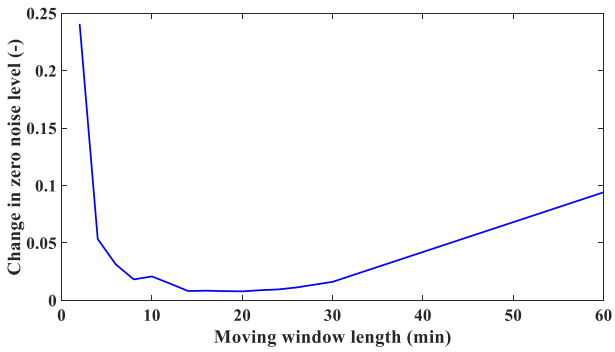

Figure 2: Relative change in the zero noise level between two consecutive histograms as a function of the moving window length.

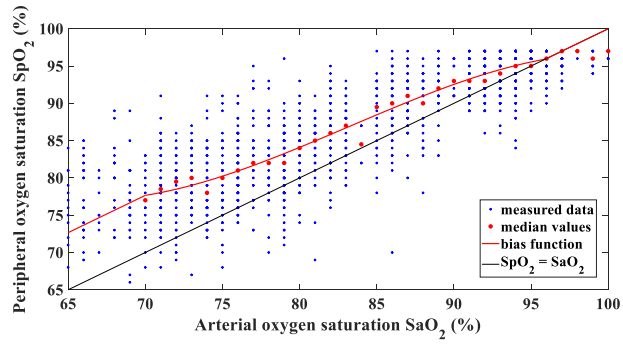

Figure 3: The SpO_2–SaO_2 bias function calculated from the data of Ross et al. [4].

3 Results

The SpO_2–SaO_2 bias function that is an estimate of a typical deviation of the SpO_2 measurement from the corresponding SaO_2 value is presented in Figure 3. The bias function consists of three distinctive parts:

For the SaO_2 range 0–70%:

$$\boldsymbol{SpO_2}(\%) = \boldsymbol{SaO_2} + \boldsymbol{SpO_2^{SaO_2=70\%}} = \boldsymbol{SaO_2} + \mathbf{7.66} \quad (1)$$

For the SaO_2 range 70–96%:

$$\boldsymbol{SpO_2}(\%) = -\mathbf{0.001} \cdot (\boldsymbol{SaO_2})^3 + \mathbf{0.262} \cdot (\boldsymbol{SaO_2})^2 - \mathbf{20.896} \cdot \boldsymbol{SaO_2} + \mathbf{617.496} \quad (2)$$

For the SaO_2 range 96–100%:

$$\boldsymbol{SpO_2}(\%) = \boldsymbol{SaO_2} \quad (3)$$

Table 1: Cumulative distribution function (CDF) of the SpO_2 measurement noise.

Deviation of SpO_2 (%)	CDF (–) for all SaO_2 values	CDF (–) for $SaO_2 \leq 96\%$	CDF (–) for $SaO_2 \geq 97\%$
-4	0.0019	0.0015	0.0022
-3	0.0076	0.0071	0.0079
-2	0.0338	0.0428	0.0293
-1	0.2257	0.2355	0.2212
0	0.8144	0.7773	0.8334
1	0.9864	0.9771	0.9912
2	0.9991	0.9978	0.9998
3	0.9999	0.9996	1
4	1	1	–

Figure 4 shows the normalized histograms of the SpO_2 measurement noise for all SaO_2 values and also for $SaO_2 \leq 96\%$ and for $SaO_2 \geq 97\%$. The cumulative distribution function of the noise model is presented in Table 1.

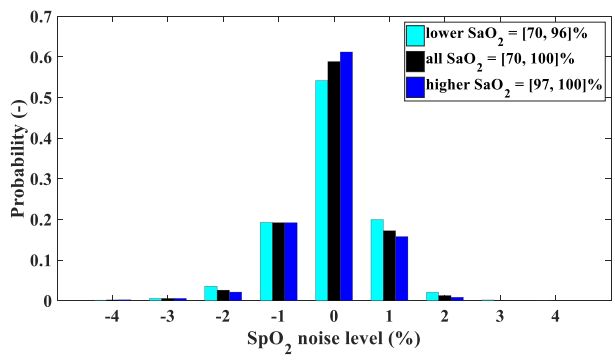

Figure 4: Normalized histogram of the SpO_2 measurement noise.

4 Discussion

In this study, we quantified the bias between SaO_2 and SpO_2, typical for premature infants and neonates. In addition, the SpO_2 measurement noise characteristics of continuous SpO_2 recording were extracted from clinical data files.

Bias was determined based on the clinical data from the multicentre study provided by Ross et al. [4] in three different SaO_2 intervals separated by SaO_2 = 70% and 96% (Figure 3). In the main SaO_2 interval 70–96%, the SpO_2–SaO_2 bias was expressed as a third-order polynomial function. In this interval our results are in accordance with the results of Rosychuk et al. [5]. Bachman et al. [6] showed the SpO_2–SaO_2 bias with the similar trend as Ross [4], but with 1 to 2% higher bias values, probably due to different methods of measuring SaO_2 (CO-oximetry vs. blood gas analyser). In the side intervals SaO_2<70% or SaO_2>96%, the SpO_2–SaO_2 bias was kept constant due to the lack of clinical data in these intervals, because the study included only patients with SpO_2 65–97%.

Moreover, for the model of neonatal oxygenation these side intervals are not critical as they are far beyond the SpO_2 target range used to minimize severe hypo- or hyperoxaemia in premature infants.

During the bedside monitoring, the SpO_2 value changes in time, even if SaO_2 is stable, due to low perfusion, motion artefacts, or another noise, such as bright light or electromagnetic interference [7–9]. We provided the characteristics of the noise by a histogram (Figure 4) and a cumulative distribution function (Table 1) from SpO_2 recordings, at least 10-hour long, of 5 stable newborns. The most stable 50% samples of signals were utilized, based on the findings of Fletcher et al. [10] that motion artefact can affect in overall up to 50% of SpO_2 recorded time. Distinct drops in the SpO_2 signal were excluded, as those could be caused either by strong motion artefact or by desaturation, which could have not been distinguished without motion capture. The motion artefacts leading to significant drops in the SpO_2 signal will be modelled separately in a future study with simultaneous recording of the SpO_2 signal and the motion capture.

This pulse oximeter model has some limitations. We estimated one general SpO_2–SaO_2 bias function based on the multicentre study on a relatively large number of SaO_2–SpO_2 pairs from various infants from different PICUs, but the biases among children may systematically vary depending on their diagnosis [4, 11], amount of fetal haemoglobin [4, 5, 11] or skin pigmentation [7, 8]. On the other hand, the SpO_2 measurement noise was only estimated from the stable newborn recordings without known pathologies. The main target group of the model—premature infants or newborns requiring ventilation support—may have less stable SpO_2 recordings that need to be investigated in a future study.

5 Conclusion

This study proposed methods for quantifying the bias between arterial and peripheral oxygen saturation that is typical for premature infants and the noise in peripheral oxygen saturation signal presented in SpO_2 recordings during bedside monitoring of a premature infant. These results may help to improve the model simulations of neonatal oxygenation compared to the real situations observed in clinical practice, and thereby enhance development of automized controllers for neonatal ventilation.

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