Sensitivity analysis of a computer model of neonatal oxygen transport

Abstract: Computer models of neonatal oxygenation could serve as a tool for a comprehensive comparison of closed-loop automated oxygen control systems. The behaviour of such models depends, besides the input data of the inspired fraction of oxygen and the premature infant's breath pattern, on internal parameters of the model. The aim of this study was to perform a sensitivity analysis of a computer model of neonatal oxygen transport to clarify the influence of its internal physiological parameters on the output signal of peripheral oxygen saturation (SpO\textsubscript{2}). We performed a multi-parameter sensitivity analysis using Monte Carlo simulations for randomly generated values of eight internal parameters. The influence on the model output SpO\textsubscript{2} signal was evaluated using five characteristics of the output signal. The relations between the parameters and the output characteristics were displayed using scatter plots and analysed by linear correlation, standardized regression, and partial correlation. The main result of the study is that in our model the oxygen consumption in the tissue and the cardiac output have the greatest influence on the SpO\textsubscript{2} drop and minimal SpO\textsubscript{2} value during simulated desaturation. The rate of development of desaturation and its duration are most affected by the diffusion resistance of the alveolar-capillary membrane. The results of the sensitivity analysis will help to optimize the performance of the computer model of neonatal oxygen transport.

Keywords: Automated control, computer model, peripheral oxygen saturation, preterm infant, sensitivity analysis.

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2 Methods

We repeatedly run a 310s-long simulation that included a single desaturation episode due to apnoea. The desaturation episode was modelled based on the real clinical data of a premature male infant, 27 days old, weighing 1,019 grams that were used in our previous study [7] to preliminary validate the model.

The measured inspired fraction of oxygen (FiO\textsubscript{2}) and expiratory tidal volume (VTe) were the inputs of the model and the signal of SpO\textsubscript{2} was the output of the model (Figure 1). Five selected characteristics of the SpO\textsubscript{2} signal were chosen for the sensitivity analysis: the lowest reached value of SpO\textsubscript{2} (Minimum SpO\textsubscript{2}) during apnoea, the SpO\textsubscript{2} level before the onset of apnoea (Baseline SpO\textsubscript{2}), the relative drop of SpO\textsubscript{2} during apnoea (Delta SpO\textsubscript{2}), the rate of development of desaturation (Descent Time) evaluated as the time needed for SpO\textsubscript{2} to drop from 90% to 10% of Delta SpO\textsubscript{2}, and the duration of desaturation (Desaturation Time) evaluated as the time where SpO\textsubscript{2} was below 50% of Delta SpO\textsubscript{2}.

The sensitivity analysis evaluated the influence of eight internal physiological parameters of the model, summarized in Table 1, on the output SpO\textsubscript{2} signal shortly before and during the simulated desaturation. The analysis was based on Monte Carlo simulations: 100 samples of parameter vectors were generated as combinations of random values of the investigated internal parameters. All the parameters were described by the uniform distribution. The upper and lower boundaries of the generated parameter values were set according to typical values and variability of the relevant physiological parameters described in neonatal literature [8–10], with respect to the age and weight of a simulated neonate. The simulations were prepared, performed and analysed using Sensitivity Analysis Tool of Matlab–Simulink programming and simulating environment (MathWorks, Natick, USA).

![Table 1: Limits of the internal physiological parameters of the model used for sensitivity analysis.](image)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symbol</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>O\textsubscript{2} Capacity (mL O\textsubscript{2}/mL)</td>
<td>MAXX</td>
<td>0.097</td>
<td>0.149</td>
</tr>
<tr>
<td>2,3-DPG (mmol/L of RBCs)</td>
<td>cDPG</td>
<td>1.933</td>
<td>10.257</td>
</tr>
<tr>
<td>HbF (% of Total Hb)</td>
<td>xHbF</td>
<td>80.6</td>
<td>99.0</td>
</tr>
<tr>
<td>Cardiac Output (mL/s)</td>
<td>FB</td>
<td>2.5</td>
<td>6.3</td>
</tr>
<tr>
<td>O\textsubscript{2} Consumption (mL O\textsubscript{2}/s)</td>
<td>K</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Pulmonary Shunt (%)</td>
<td>S3</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>Diffusion Resistance (mmHg : s/mL O\textsubscript{2})</td>
<td>R\textsubscript{df}</td>
<td>58</td>
<td>873</td>
</tr>
<tr>
<td>SpO\textsubscript{2} Meas. Delay (s)</td>
<td>DelaySpO\textsubscript{2}</td>
<td>0</td>
<td>30</td>
</tr>
</tbody>
</table>

3 Results

The results of the multi-parameter sensitivity analysis using Monte Carlo simulations are presented in Figure 2 and Figure 3. Scatter plots in Figure 2 show relations between values of individual examined internal parameters of the model and values of selected characteristics of the model output SpO\textsubscript{2} signal. A pattern in scatter plots suggests a systematic dependence between an internal parameter and the model output. Histograms show the distributions of selected characteristics of the model output when tested with uniformly distributed internal parameters. Tornado plots in Figure 3
summarize and compare the systematic influence of each internal parameter on selected characteristics of the model output using linear correlation, standardized regression, and partial correlation.

The most influential internal parameter is the oxygen consumption in the tissue (K) which affects systematically both the absolute SpO₂ minimum and SpO₂ drop during apnoea. The high value of the oxygen consumption parameter in the model means stronger desaturation manifested both by a lower absolute minimum of the SpO₂ signal and a more significant SpO₂ drop. Both the output signal characteristics are also affected by cardiac output (FB), which also systematically affects the baseline of the SpO₂ signal. Among other internal examined parameters, pulmonary shunt (S3) affects indirectly the baseline of SpO₂ signal and the diffusion resistance (Rdiff) affects directly the rate of development and duration of desaturation (Descent Time and Desaturation Time, respectively). On the other hand, the simulations did not demonstrate a substantial influence of the examined parameters of ODC, the relative concentration of HbF, and 2,3-DPG, on any characteristics of the output SpO₂ signal.

4 Discussion and Conclusion

Our sensitivity analysis of the computer model of neonatal oxygen transport confirmed the dominant role of two parameters—the oxygen consumption in tissues and cardiac output—both on the absolute value of the model output SpO₂ signal and on the magnitude of desaturation. The findings are consistent with the study of Sands et al. [10]. The same authors found in [6] that increased lung diffusion resistance prolongs hypoxemia as it slows down reoxygenation. Our results correspond to that as the rate of development and duration of desaturation in our simulations were influenced the most by the diffusion resistance.

The sensitivity analysis evaluated the influence of selected internal physiological parameters on the output of the computer model of neonatal oxygenation and identified the parameters that are the most closely related to the model output. The results of the sensitivity analysis will help to decide on the clinical data that are the most important to collect.
with high accuracy for model validation and will help to focus the final optimization of the model performance.

**Author Statement**

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**References**


