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ROBUSTNESS ANALYSIS OF A MATHEMATICAL GAS EXCHANGE MODEL

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Abstract: *Mathematical gas exchange models can support decision making for clinicians in mechanical ventilation. For example individually optimized inspired oxygen fraction ($F_{i,O2}$) may be determined using patient specific prediction of blood gas oxygenation ($P_{a,O2}$). Before using a model for prediction purposes, the model parameters have to be adapted to the individual patient characteristics. Successful parameter identification depends on the required initial guess of the parameter values to be identified. The robustness of the identification process of a mathematical gas exchange model that considers shunt and ventilation/perfusion-mismatch (V̇/Q-mismatch) is analysed in this work using simulation data. Results show that parameter identification of the data sets tested is robust for f_s and f_A smaller than 0.8 and 0.9. This analysis provides an overview on the convergence of parameter identification of a two-compartment gas-exchange model.*

Keywords: *Gas exchange model, robustness analysis, parameter identification, mechanical ventilation*

Introduction

In mechanical ventilation, clinicians have to interpret different measured parameters to assess patient status and to set appropriate ventilator settings. Adequate oxygen (O_2) supply and removal of carbon dioxide (CO_2) has to be guaranteed while keeping the risk of ventilator induced lung injuries (VILI) minimal. Mathematical models can support the difficult decisions of the clinicians by simulating patient's gas exchange and estimating parameters that are not directly assessable. Gas exchange models describe distributions of O_2 and CO_2 inside the lung, the blood circuit and the body tissue.

Robustness of a model parameter identification process (PIP) usually depends on the initial parameter values, the model's complexity and data quality. The analysis of the PIP of a two-parameter gas exchange model with respect to robustness is described in this work using simulation data.

Methods

Gas exchange model:

The alveolar space is represented by two compartments to model different ventilation and perfusion rates simulating the so called V̇/Q-mismatch [1]. The model generally consists of three model parameters: shunt fraction (f_s), the fractions of ventilation (f_A) and perfusion distribution (f_Q). Karbing et al. reduced the number of free parameters to two by setting $f_Q = 0.9$ meaning that 90% of the non shunted blood ($1\text{-}f_s$) circulates to the first alveolar compartment as described in [2]. The structure of the analysed gas exchange model is shown in Fig.1.

Robustness analysis:

The presented gas exchange model was implemented in MATLAB (R2012a, The Mathworks, Natick, USA). To provide a controllable and reproducible environment, four data sets representing 4 different patients were generated using parameterized models with f_s and f_A defined at physiological plausible values (Tab. 1). Arterial partial pressure of oxygen ($P_{a,O2}$) and carbon dioxide ($P_{a,CO2}$) at four different levels of inspired oxygen fraction ($F_{i,O2}$ = 0.35, 0.5, 0.65, 0.8) were simulated for each patient. $P_{a,O2}$ and $P_{a,CO2}$ were used as measurement values for parameter identification for model parameters f_s and f_A.

Model fit was carried out by the Nelder-Mead Simplex-Search method [3] with boundary conditions, implemented in MATLAB as *fminsearchbnd* using a simple sum of squared error function for generated and modeled values of $P_{a,O2}$ and $P_{a,CO2}$. First, the error surfaces were plotted as a function of model parameters using a resolution of 99x99 to assess identifiability issues. Secondly, robustness was tested by evaluating the minimized sum of squared errors for all possible combinations of equally distributed initial values in the range of 0.1 to 0.9 for f_s and f_A using a step width of 0.1.

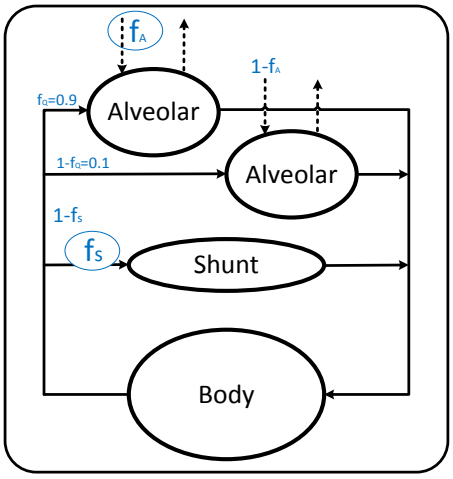

Figure 1: Structure of gas exchange model with two alveolar compartments enable to simulate V̇/Q-mismatch.

Table 1: Model parameters for simulation.

Parameter	Patient 1	Patient 2	Patient 3	Patient 4
f_s	0.4	0.2	0.3	0.1
f_A	0.9	0.3	0.2	0.5

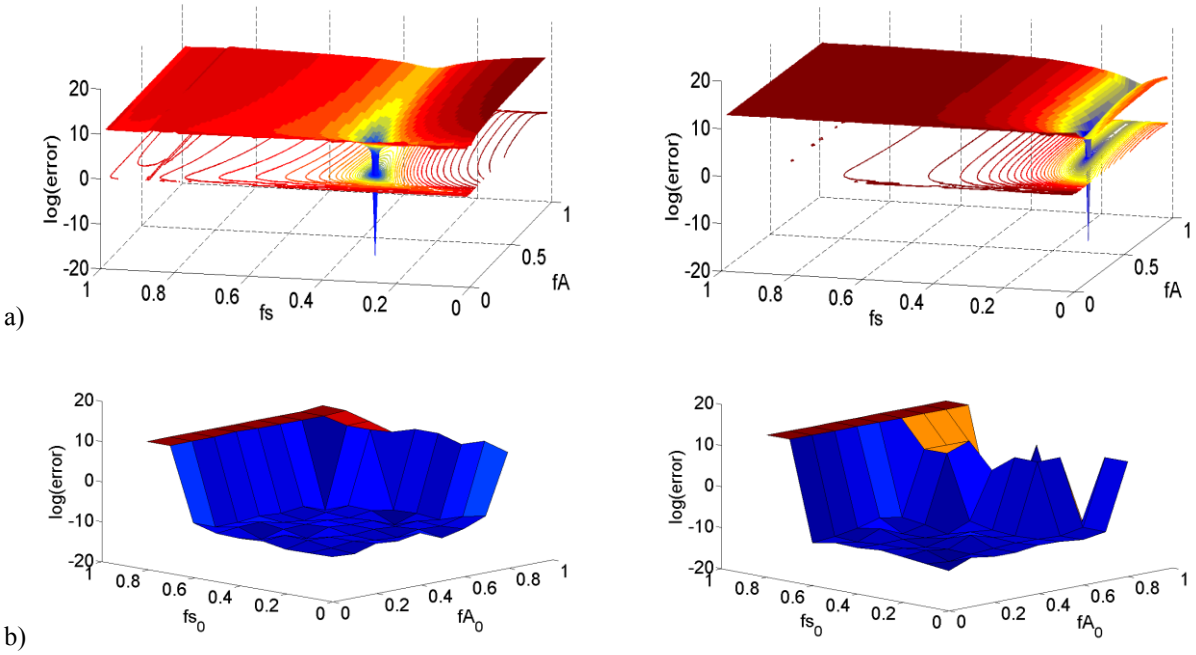

Figure 2: a) Error-surface plot of patient 3 (f_s = 0.3 and f_A = 0.2) (left), patient 4 (right) (f_s = 0.1 and f_A = 0.5). b) Resulting error-minima starting from various initial values.

Results

For all simulated patients a unique global minimum could be detected in the error plots as a function of model parameters (Fig. 2, a)). For high shunt fractions (f_s > 0.9) and ventilation distribution fractions (f_A close to 1), additional local minima could be observed in all patient at the edges of the error surface.

The results of robustness analysis are shown in Fig. 2, b) exemplarily for simulated patients 3 and 4. With initial values for f_{s0} < 0.7 and f_{A0} < 0.8, the optimization converged to the global minimum in the datasets tested. Initial values of f_{s0} > 0.7 mainly led to detection of the observed local minima at the edges of the error plots (f_A close to 1).

Discussion

Robustness analysis of a gas exchange model considering shunt and V /Q-mismatch was presented. The error-surface plots as a function of model parameters show one unique global error-minimum that may indicate structural identifiability for the model parameters in the range of 0 to 1. However, a general identifiability analysis is to be done. Additionally, the results of parameter identification revealed robust convergence to the global minimum with proper initialization for both parameters in the range of 0.1 to 0.7. Physiological range of shunt fraction f_s is constrained from 0 to 0.5, because $P_{a,O2}$ hardly changes with increasing $F_{i,O2}$ for a shunt of 50% [4]. Thus an initial guess for f_s should be smaller than 0.5.

This analysis was conducted on simulation data but nevertheless provides a number of insights on convergence of PIP using this particular model and suggests a range of suitable potential initial values applicable for real patient data.

Once convergence to the global minimum can be guaranteed this particular model can be used to predict $P_{a,O2}$ and $P_{a,CO2}$ levels to support the clinician in finding appropriate ventilator settings.

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