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Optimization techniques in respiratory control system models

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ABSTRACT

One of the most complex physiological systems whose modeling is still an open study is the respiratory control system where different models have been proposed based on the criterion of minimizing the work of breathing (WOB). The aim of this study is twofold: to compare two known models of the respiratory control system which set the breathing pattern based on quantifying the respiratory work; and to assess the influence of using direct-search or evolutionary optimization algorithms on adjustment of model parameters. This study was carried out using experimental data from a group of healthy volunteers under CO_2 incremental inhalation, which were used to adjust the model parameters and to evaluate how much the equations of WOB follow a real breathing pattern. This breathing pattern was characterized by the following variables: tidal volume, inspiratory and expiratory time duration and total minute ventilation. Different optimization algorithms were considered to determine the most appropriate model from physiological viewpoint. Algorithms were used for a double optimization: firstly, to minimize the WOB and secondly to adjust model parameters. The performance of optimization algorithms was also evaluated in terms of convergence rate, solution accuracy and precision. Results showed strong differences in the performance of optimization algorithms according to constraints and topological features of the function to be optimized. In breathing pattern optimization, the sequential quadratic programming technique (SQP) showed the best performance and convergence speed when respiratory work was low. In addition, SQP allowed to implement multiple non-linear constraints through mathematical expressions in the easiest way. Regarding parameter adjustment of the model to experimental data, the evolutionary strategy with covariance matrix and adaptation (CMA-ES) provided the best quality solutions with fast convergence and the best accuracy and precision in both models. CMAES reached the best adjustment because of its good performance on noise and multi-peaked fitness functions. Although one of the studied models has been much more commonly used to simulate respiratory response to CO_2 inhalation, results showed that an alternative model has a more appropriate cost function to minimize WOB from a physiological viewpoint according to experimental data.

1. Introduction

The primary function of respiratory system is to regulate the homeostasis of arterial blood gases and pH, through supplying oxygen to the blood and removing carbon dioxide (CO_2) produced by metabolic activities. From a modeling viewpoint, the respiratory system can be considered as a neurodynamic feedback system, nonlinear, multivariable with delays and continuously affected by physiological and pathological disturbances. Its behavior can be defined by a continuous interaction between the controller and peripheral processes are being controlled (respiratory mechanics and pulmonary gas exchange). The peripheral processes have been extensively studied in previous research [1–7]. Nevertheless, respiratory controller behavior and how the controller processes different afferent inputs are not completely inferred yet [8].

One of the most interesting issues concerning respiratory system modeling is the possibility of forecasting the respiratory

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system response of a critical patient connected to a mechanical ventilator. However, mathematical models are still far from allowing this, mainly because of the complexity of the respiratory control system that adjusts the breathing pattern according to mechanical and chemical components minimizing the work of breathing (WOB) and the system response can be affected either by the cost function or by the optimization technique.

The aim of this study is twofold: firstly, to compare two known mechanical cost functions to quantify the WOB [9] and, secondly, to assess the influence of several known optimization techniques, such as direct search and evolutionary algorithms [10–19], on the adjustment of the breathing pattern (by the controller) and the model parameters (in the identification process).

Two nested optimizations were carried out for this purpose: the first one in the controller that minimizes the WOB by using both mechanical cost estimations proposed in [9] and the second one in the search of the model parameters associated with the response that better matched with experimental data. These data were recorded from a group of subjects under different levels of ventilation ($\dot{V}_E$) produced by hypercapnic stimulation. Hypercapnia is characterized by changes in partial pressure of CO_2 in arterial blood (P_{aCO_2}) above the normal value (40 mmHg), so the neural control center respond adjusting $\dot{V}_E$ and, therefore, breathing pattern subject, in order to keep P_{aCO_2} near physiological values. In this study, hypercapnia was produced increasing partial inspiratory pressure of CO_2 (P_{ICO_2}).

Known evolutionary and deterministic optimization algorithms are applied in order to identify the best option for this kind of optimization problems and to guarantee that the model parameter adjustment allows to reproduce real situations with physiological meaning. The performance of these optimization algorithms are evaluated regarding the goodness of fit to experimental data, the convergence rate and the dispersion of the found solutions.

The paper is organized as follows. Section 2 presents previous studies about modeling of respiratory control system response and concerning optimization procedures used in biomedical applications. Section 3 presents a general description of the algorithms addressed in this study and their selected parameter values. Section 4 presents a mathematical description of the analyzed model and its variables of interest. Afterwards, Section 5 shows the optimization problem to be solved: experimental data for the model adjustment, the two nested optimizations solved in this approach (the breathing pattern fitting and the model fitting to experimental data), and finally, statistical tests and validation procedure to select the best algorithms and to compare the found solutions. Section 6 presents the results associated to the both fittings. Finally, Section 7 discusses and concludes the results found in the optimization problem and provides their interpretation in the respiratory model from a physiological point of view. A step by step description about how this approach was carried out is presented in Fig. 1.

2. Related work

2.1. Respiratory control system modeling

The respiratory controller may be seen as a central pattern generator in which rhythmic respiratory activity is produced in response to different afferent pathways [20]. Following this hypothesis, several approaches have been used to simulate this control law in respiratory control modeling. In this sense, some authors consider respiratory control system as a reflex-mechanism where breathing pattern is adjusted, from mathematical relationships obtained empirically, in order to meet a ventilatory demand [1,21,22]. This adjustment is carried out varying either respiratory frequency or volume or both.

The minimization of WOB has been extensively considered as a control criterion to adjust the breathing pattern [23–29]. Using this approach, several models have been proposed using minute ventilation as controlled variable. Early formulations were based on sinusoidal airflow patterns in which respiratory frequency was fitted in function of minimum work rate criteria [30,23] and minimum average driving pressure [31,32]. Optimal criteria were also developed to predict airflow patterns. One of these criteria used the integral of the square of volume acceleration as cost function for both breathing phases with constant inspiration and expiration intervals [33].

Models of overall control of the breathing pattern using a two-level optimization problem have been also presented in [34,35,9].Particularly, Poon et al. [9] proposed a mathematical model of respiratory control system based on minimization of WOB which includes mechanical and chemical costs of breathing and allows to optimize simultaneously ventilation and breathing pattern (detailed information is presented in Section 4). This model has been used in studies related to respiratory modeling not only by the same author [28,36,37] but also by others [38–40]. Recently, several studies have used its cost functions to determine the breathing pattern in subjects under assisted mechanical ventilation [39,41–43]. The WOB depended on model parameters whose values were not provided in any of the previous studies [9,28,36–43], which suggests that respiratory control modeling based on optimization criteria needs additional experimental and computational efforts. In addition, two different functions were also proposed in [9] to

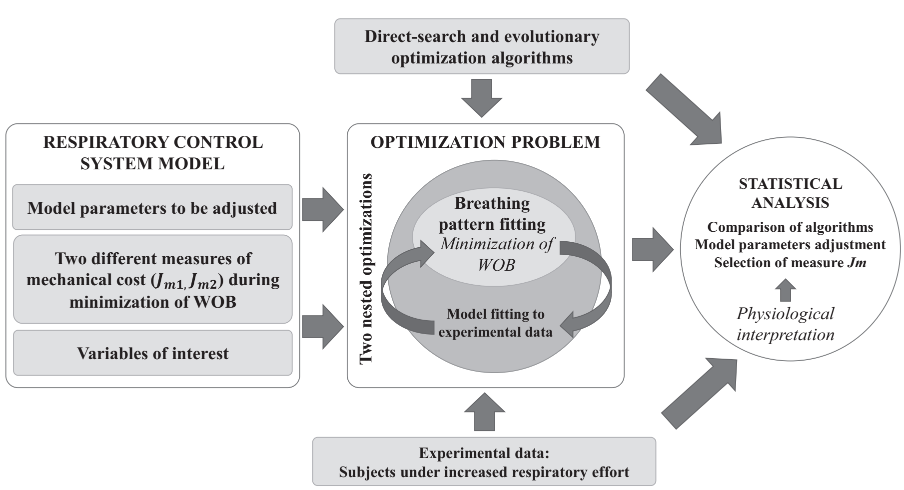

Fig. 1. Description step by step how the approach is realized.