ROBUST PARAMETERS IDENTIFICATION OF THE OXYGEN KINETICS BY THE METHOD OF NONLINEAR LEAST SQUARES

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Abstract. The purpose of this paper is to identify the parameters that characterize the curve of oxygen absorption rate of a person during controlled physical activity. The exercise load is constant and its intensity is classified as heavy or severe. The values of the oxygen absorption rate were measured experimentally through the process of pulmonary ventilation.

The oxygen absorption rate is modeled by sequential exponential functions. Each exponential is identified as a distinct physiological stage and represents the body’s response to increased energy metabolism. The dynamic response of pulmonary gas exchange reflects the integrated response of the ventilator, cardiovascular, and neuromuscular systems to the exercise challenge.

The characterization of the curve for each patient requires the identification of the number of phases developed during the exercise and identification of the instants when the change of phase occurs. The parameter identification takes into account the uncertainties of the process. The identification is made by the nonlinear least squares method of Levenberg-Marquardt and stochastic descent. The curve of oxygen absorption rate can have three phases each one modeled by an exponential. The process is continuous and an robust optimization problem is solved to determine the instants of phase change.
1 INTRODUCTION

The physical exercise in human beings involves rather sudden transitions from one metabolic rate to another. The requirement of increasing energy metabolism during physical activity is directly related with the Oxygen Uptake Kinetics \( (V_o) \), which involves the study of the physiological mechanisms responsible for the dynamic \( V_o \) response to physical activity (see Jones and Poole, 2005).

The oxygen kinetics as a parameter of physiological function became a standard laboratory measurement. The measurement of \( V_o \) represents the values of the oxygen absorption rate of a person during controlled physical activity.

The study of \( V_o \) is important because oxidative metabolism is the principal means by which the human organism generates energy to do work in the most short-lived activities. Factors such as the highest attainable \( V_o \) and the rate at which \( V_o \) rises in the transition to an activity with a higher energetic requirement to reach the requisite steady-state level, will all influence an individual’s tolerance to physical activity.

The dynamic response of pulmonary gas exchange reflects the integrated response of the ventilator, cardiovascular, and neuromuscular systems to the exercise challenge. The measurement of \( V_o \) kinetics has become an important tool in the evaluation of the extent of dysfunction and in some instances the mechanism behind that dysfunction in many major chronic disease conditions. The capability for \( V_o \) kinetics determination to provide insights into physiologic function and pathophysiologic dysfunction accounts in large part for the recent explosion in publications in this area (see Jones and Poole, 2005).

2 OXYGEN KINETICS

The metabolic and gas exchange responses to controlled exercise is related to a number of identifiable exercise intensity domains (namely: moderate, heavy, severe and extreme), and to the fitness level of the individual. The systematic physical training results in physiological and biochemical body adaptations, leading to improved performance of specific tasks. The nature and magnitude of these changes are dependent on the type of activity performed, intensity, and genetic load.

The time course of the \( V_o \) response after the onset of exercise has been described in terms of a mono or multiple-component exponential function (see Jones and Poole, 2005). Each exponential represents body’s response to the exercise and is characterized by the development of a physiological phase.

**One Phase:**

The first seconds of exercise are characterized by a temporary delay in the response rate \( V_o \) caused by the dissociation between the rate of oxygen absorbed in the lung and consumed in the skeletal muscles. The Phase I characterizes the initial increase in \( V_o \) at exercise onset caused by elevated pulmonary blood flow, and is commonly called as a cardio-dynamic component. It is modeled by a mono-exponential equation (1):

\[
V_o(t) = V_{oBL} + A_c(1 - e^{(-t/\tau_c)})
\]

where:

\( V_{oBL} \) = rate of oxygen consumption at rest (base line) \( [ml/(Kg.min)] \)
\( A_c \) = Asymptotic Constant Phase I \( [ml/(Kg.min)] \);
\( \tau_c \) = Time Constant Phase I \( [1/s] \);
Two Phases:
Depending of the intensity of exercise, after the first few seconds of activity can be initialized the phase II. During Phase I, there are stocks of oxygen use by skeletal muscles, causing a reduction in oxygen content of mixed venous blood. The arrival of venous blood in the lungs generates as response the phase II (commonly called the primary component). When this second phase is developed, the $V_o$ is modeled by a two-exponential equation (2) and the instant when the second phase starts is called $TDP$ (time delay).

$$V_o(t) = \begin{cases} 
VO_{BL} + A_c(1 - e^{-t/\tau_c}), & \text{se} \quad t \leq TDP \\
A'_c + A_p(1 - e^{-(t-TDP)/\tau_p}), & \text{se} \quad t \geq TDP
\end{cases}$$

In this equation the term $A'_c$ guarantees the continuity of $V_o$ at the instant $TDP$. It is calculated by equation (3):

$$A'_c = VO_{BL} + A_c(1 - e^{-(TDP/\tau_c)})$$

the other terms of equation (2) are:

$A_p =$ Asymptotic Constant Phase II $[ml/(Kg.min)]$,
$\tau_p =$ Time Constant Phase II $[1/s]$.

Three Phases:
Depending of the intensity of exercise, it still can be initialized the phase III (called the phase or the slow component) at the instant $TDs$ (time delay). When this third phase is developed, the $V_o$ is modeled by a three-exponential equation (4):

$$V_o(t) = \begin{cases} 
VO_{BL} + A_c(1 - e^{-(t/\tau_c)}), & \text{se} \quad t \leq TDP \\
A'_c + A_p(1 - e^{-(t-TDP)/\tau_p}), & \text{se} \quad TDP \leq t \leq TDs \\
A'_p + A_s(1 - e^{-(t-TDs)/\tau_s}), & \text{se} \quad t \geq TDs
\end{cases}$$

In this equation, the term $A'_c$ is calculated by (3), and the term $A'_p$ guarantees the continuity of $V_o$ at the instant $TDs$. It is calculated by equation (5):

$$A'_p = A'_c + A_s(1 - e^{-(TDp-TDs)/\tau_s})$$

The other terms of equation (4) are:

$A_s =$ Asymptotic Constant Phase III $[ml/(Kg.min)]$,
$\tau_s =$ Time Constant Phase III $[1/s]$.

The number of physiological phases developed during an exercise is strongly correlated with the activity intensity, as shown in Figure 1. Moderate-intensity exercise results in a mono-exponential response to the steady state. Heavy-intensity exercise is characterized by a $V_o$ response that continues to increase throughout the test, and severe-intensity can be identified for work rates that are supra-maximal with respect to the expected $V_o$ requirement (see Jones and Poole, 2005). Thus, exercises with heavy or severe intensity commonly requires the development of two or three phases.
3 THE OPTIMIZATION PROBLEM

With the objective of studying the oxygen kinetics, one group of professors and students of UFRJ (Universidade Federal do Rio de Janeiro) made laboratory measurements of the $V_o$ rate in a group of twenty healthy women. For each patient, the values of $V_o$ were measured by the pulmonary ventilation during the performance of a controlled exercise with intensity classified as heavy or severe.

The characterization of the curve of $V_o$ for each patient requires the identification of number of phases developed during the exercise and identification of the instants when the change of phases occurs. The vector, $x$, of parameters that characterizes the curve of $V_o$ depends on the number of physiological phases developed, as showed in Table 1.

<table>
<thead>
<tr>
<th>Number of Phases</th>
<th>Vector, $x$, of parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>One Phase</td>
<td>$x = (VO_{BL}, A_c, \tau_c)^T$ (Phase I)</td>
</tr>
</tbody>
</table>
| Two Phases       | $x_1 = (VO_{BL}, A_c, \tau_c)^T$ (Phase I)  
|                  | $x_2 = (A_p, \tau_p)^T$ (Phase II) |
| Three Phases     | $x_1 = (VO_{BL}, A_c, \tau_c)^T$ (Phase I)  
|                  | $x_2 = (A_p, \tau_p)^T$ (Phase II)  
|                  | $x_3 = (A_s, \tau_s)^T$ (Phase III) |

Table 1: Relation between the vector, $x$, of parameters and the number of phases developed.

To determine the parameters values that best characterizes the curve of $V_o$ is necessary to
solve an optimization problem. The objective is to determine the vector $x^*$ which minimizes the sum of squares residuals between the curve and the measurements values of $V_o$ (see equation 6). The objective function is defined in equation 7.

$$x^* = \arg \min \left\{ \sum_{i=t_1}^{t_f} [V_{oi} - V_o(x, i)]^2 \right\} \quad (6)$$

$$F(x) = \sum_{i=t_1}^{t_f} [V_{oi} - V_o(x, i)]^2 \quad (7)$$

Since the $V_o$ is modeled by nonlinear functions (exponentials), the optimization problem solution requires methods for nonlinear least squares problems. One computer code was developed in MATLAB to solve this optimization problem. The identification of parameters is made by one combination of the nonlinear least squares method of Levenberg-Marquardt and the method of stochastic descent. The method of Stochastic Descent is applied to the determination of number of physiological phases developed during the exercise, and the Levenberg-Marquardt is applied to make the curve fitting of each one of this phases.

3.1 Stochastic Descent Method

The stochastic descent method is used to determine the value of $F$ for various different combinations of $TDs$ and $TDP$. Thus, the number of phases that best fits the measures of $V_o$, and the instants of phase change can be determined.

Initially, the values of $V_o$ are fitted in one, two and three phases with instants of phase change $TDP$ and $TDs$ arbitrarily chosen. Assuming that during the exercise $n \geq 10$ values of $V_o$ are measured, the domain of the variable $TDP$ is defined as the discrete interval $[t_3, \ldots, t_{n/2}]$. The domain of the variable $TDs$ is also defined as one discrete interval, but as $TDs \geq TDP$, the domain is defined as $[t_{TDP+2}, \ldots, t_{n-5}]$.

The curve fitting of each one of these phases is done through the method of Levenberg Marquardt optimization (searching the minimum of the function $F$). After this initial step, it is necessary to assess the value of $F$ for other possible combinations of $TDs$ and $TDP$, what is done through the method of stochastic descent.

In this method, $TDP$ and $TDs$ are drawn until one defined maximum number of times. One interpretation for this optimization method is that randomly drawing $TDs$ and $TDP$, the probability of drawing a point in a neighborhood of a point of global minimum is strictly positive, increases with the number of points drawn and tends to one when the number of draws tends to infinity (see Souza de Cursi).

3.2 Least Squares Method of Levenberg-Marquardt

To perform the fit of a particular phase through Levenberg-Marquardt, it is necessary previously to determine the instants that corresponds to beginning and end of the phase. Assuming that these instants are known (drawned through the Stochastic Descent Method), and that during this phase were experimentally measured $m$ values of $V_o$ and $m$ corresponding instants, the deviation between the curve and measured values of $V_o$ is defined by equation 8. drawn

$$F(x) = \sum_{i=1}^{m} [f_i(x)]^2 = \sum_{i=1}^{m} [V_{oi} - V_o(x, t)]^2 \quad (8)$$
Levenberg-Marquardt method uses an iterative process to obtain the vector $x^*$ of parameters to be identified. From an initial vector $x_0$, the method produces a series of vectors $x_1, x_2, \ldots$ that must converge to the solution $x^*$. The convergence is guaranteed if the deviation between the experimental points and fitted curve decrease with each iteration (see Madsen K., Adsen K., Nielsen H.B., and Tingleff, 2004). Thus for any $k$ iteration is desired that:

$$F(x_{k+1}) < F(x_k)$$

In each iteration, $x$ should be replaced by a new estimate $x + h$. The vector $h$ is calculated using the expression 10.

$$(J^T J + \mu I) h = -g$$

with:

$J = J(x)$ is the Jacobian matrix of $f(x)$: $(J(x))_{ij} = \frac{\partial f_i}{\partial x_j} (x)$

$\mu$ is the damping factor;

$I$ is the identity matrix;

$g = J^T f$ para $\mu \geq 0$.

The stopping criteria used for the algorithm in the MATLAB code were:

1. The number of iterations $k$ exceeds the defined maximum number of iterations. $k > k_{\text{max}}$
2. $\|\Delta x\|_\infty < \epsilon_1$
3. $\|F_k - F_{k+1}\|_\infty < \epsilon_2$

### 3.3 The MATLAB code

The computer code developed in MATLAB to solve the optimization problem consists of nine files, as showed in Figure 2. The values of experimentally measured $V_o$ and their corresponding instants $t$ are imported from one spreadsheet.

![Figure 2](image-url)
4 RESULTS

In this section of the paper is showed the results obtained for three of the patients of a group of twenty healthy women (Figures 3, 4 and 5). In all the patients, was verified that the best fitting of the $V_o$ curve was obtained with the three-exponential function, meaning that all the patients have developed Phase I, Phase II and Phase III. This result was expected because the controlled exercise had intensity classified as heavy or severe.

![Graph showing $V_o$ curve for a patient](image1)

**Figure 3:** First Patient - Vector, $x$, of parameters identified by the computer code developed.

![Graph showing $V_o$ curve for a patient](image2)

**Figure 4:** Second Patient - Vector, $x$, of parameters identified by the computer code developed.

5 CONCLUSIONS

The purpose of this paper was identifying the parameters that characterizes the curve of oxygen absorption rate of a person during controlled physical activity. Since the $V_o$ is modeled by nonlinear functions (exponentials), the identification of the parameters that characterizes
Vo optimization problem solution requires the using of methods for nonlinear least squares problems.

One computer code was developed in MATLAB to solve this optimization problem, and the identification of parameters was made by one combination of the nonlinear least squares method of Levenberg-Marquardt and the method of stochastic descent. The computer code was utilized to identify the parameters of Vo of one group of twenty healthy women.

The values of Vo were measured by the pulmonary ventilation. And to identify the instants when the change of phases occurs (TDp and TDS), is necessary to ensure that the time interval between two measurements of Vo is small enough. This requirement also is also important to ensure that the number of measured points of Vo in the beginning of the exercise is enough to make the parameters identification of the fist phase (VOBL, Ac and tc).

Since the measurement of Vo kinetics has become an important tool in the evaluation of pathologies, the computer code developed could be used in the future to identify the parameters of Vo of one group of persons with some known disease.

REFERENCES

