A Mathematical Model of the Cardiovascular System under Exercise

Lu Wang,1 Steven W. Su,2 Gregory S. H. Chan1 and Branko G. Celler1*

Abstract—A mathematical model, based on our previous pulsatile nonlinear multi-element cardiovascular model, was tested and improved to study cardiovascular response under graded exercise levels. Ten healthy subjects were studied using cycle-ergometry exercise test with constant workloads ranging from 25 Watt to 125 Watt. Breath by breath gas exchange, heart rate, cardiac output, stroke volume and blood pressure were measured at each stage. Based on the experimental data, firstly we proved that our previous model is capable to regenerate the cardiovascular variables observed in the subjects under different exercise levels. Secondly, we improved the model by incorporating a robust and efficient function to estimate metabolic demand. Then the new model can estimate both cardiovascular variables and metabolic demand with its simulation results within the range of SD (Standard Deviation, N=10) of the experimental data.

I. INTRODUCTION

In our previous work, a highly simplified nonlinear multi-element cardiovascular model [1] was established based on Ursino’s model [2]. The simplicity of its structure makes it suitable as a starting point to build up more complex models to reflect cardiovascular characteristics, especially during the condition of moderate exercise. In this study, we examined the ability of our previous model to reproduce stroke volume (SV), cardiac output (CO) blood pressure (BP) and total peripheral resistance (TPR) recorded from normal subjects by tuning three of its parameters. We then improved the model by incorporating a new physiological interaction, making it capable of estimating another important physiological parameter - metabolic demand.

Firstly, we give a brief introduction of our previous model. As shown in Fig.1, it only consists of the following five compartments: left atrium (la), left ventricle (lv), systemic arteries (sa), systemic peripheral regions (sp) and systemic veins (sv). The left atrium and left ventricle form the heart. The systemic arteries, systemic peripheral regions and systemic veins make up the vascular compartments. The detail of the model can be found in [1].

II. EXPERIMENTAL DESIGN

A. Subject

The data recorded from 10 subjects (aged 26 ± 5yr, height 176 ± 5cm, body weight 73 ± 12kg). All the subjects knew the protocol and the potential risks, and had given their informed consent.

B. Experimental Procedures

All tests were conducted in the afternoon in an air-conditioned laboratory with temperature maintained between 23-24°C. The subjects were studied during rest and during exercise in an upright sitting position on an electronically braked cycle ergometer. Exercise was maintained at a constant workload for 6 minutes, followed by a period of rest. The initial exercise level was 25W and each successive stint of exercise was increased in 25W steps until a workload of 125W was reached. The rest periods were increased progressively from 10 to 30 minutes after each stint of exercise. Six minutes of exercise was long enough to approach a steady state since the values of oxygen uptake and the A-V oxygen difference had become stable by the 5th and 6th minutes even for near maximum exertion [3].

C. Measurement and Data Collection

Heart rate was continuously monitored beat by beat using a single lead ECG device, while ventilation and pulmonary exchange were measured on a breath by breath basis. The outputs of the ECG and gas measurement devices were interfaced to a laptop through an A/D converter (NI DAQ 6062E) with a sampling rate of 500 Hz. Beat by beat cardiac output was measured noninvasively using an ultrasound based cardiac output device (USCOM, Sydney, Australia) focused at the ascending aorta during the last minute of the 6 minutes exercise for each workload. This device has previously been reported to be both accurate and reproducible [4]. In order to get consistent accuracy of the measurement, all the measurements were conducted by the same person. A oscillometric blood pressure measurement device (CBM-
700, Colin, France) was used to measure systolic blood pressure (Psys), diastolic blood pressure (Pdia) and mean arterial blood pressure (Pmean) during the last minute of each stint of exercise.

III. EXPERIMENTAL RESULTS

We found that the percentage change of cardiovascular variables relative to their rest values, at different workloads are more uniform than their absolute values. This may be because using relative values diminish the variability between subjects. For example, Fig.2 (a) shows the response of the absolute value of oxygen uptake rate (litres/min) at different levels of workload for the ten subjects, while Fig.2 (b) is the percentage change in oxygen uptake rate relative to its rest value at different workloads. Obviously, the response in Fig. 2(b) is more consistent and gives clearer trend than that in Fig.2 (a). It is thus reasonable to believe that modelling of cardiovascular responses using relative changes gives more robust results than modelling with the absolute value. So the experimental data used in this study are their percentage change with respect to their corresponding rest value. We use SV%, HR%, CO%, Psys%, Pmean%, TPR% and $VO_2$% to represent their relative value (expressed as percentages), respectively. Table I summarizes the experimental results (percentage change).

Fig. 2. Oxygen uptake response to exercise for the 10 subjects (the bold line is the mean response)

IV. TESTING OF THE ORIGINAL MODEL

We re-implemented our previous model on a personal computer using Matlab 6.0. The input to this model is the heart rate corresponding to each workload. The outputs of the model are SV%, CO%, Psys%, Pmean% and TPR%. In order to simulate the cardiovascular system response during exercise, the experimental data in Table I were used to tune the parameters of the model. The following three parameters were selected to tune the model to make it reproduce our experimental results (Table I). The first selected parameter was Emax (the ratio of the left ventricular end-systolic pressure to the end-systolic volume). As described in Ursino’s model [2], it is the slope of the linear pressure/volume function at end systole and represents the left ventricular maximum elastance. The second was systemic peripheral resistance (Rsp). It is auto-regulated to guarantee a sufficient blood flow in the relevant muscles under exercise. The last one was the total unstressed blood volume (Vu) which is under vagal control. We tuned the parameters of the model to reproduce the experimental results (Table I) and summarized the parameter values in Table II. Other parameters assignments are listed in [1]. The tuning results are shown in Fig. 3. It can be seen that the simulation outputs are within the standard deviation band of the experimental results (Table I) and are close to their mean values. It indicates that this tuned model of human cardiovascular system can reproduce the experimental results accurately.

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>EXPERIMENTAL DATA UNDER GRADED EXERCISE LEVELS (N=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>workload</td>
<td>25W</td>
</tr>
<tr>
<td>SV%</td>
<td>8.0±</td>
</tr>
<tr>
<td>CO%</td>
<td>2.6</td>
</tr>
<tr>
<td>Psys%</td>
<td>42.7±</td>
</tr>
<tr>
<td>Pmean%</td>
<td>14.5</td>
</tr>
<tr>
<td>Psys%</td>
<td>6.2±</td>
</tr>
<tr>
<td>CO%</td>
<td>6.4</td>
</tr>
<tr>
<td>TPR%</td>
<td>2.0±</td>
</tr>
<tr>
<td>$VO_2$%</td>
<td>4.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE II</th>
<th>THE TUNED PARAMETER VALUES UNDER GRADED EXERCISE LEVELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workload (W)</td>
<td>0</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>62</td>
</tr>
<tr>
<td>Emax (mmHg/ml)</td>
<td>2.545</td>
</tr>
<tr>
<td>Rsp (mmHg/sec/ml)</td>
<td>0.88</td>
</tr>
<tr>
<td>Vu (ml)</td>
<td>3660</td>
</tr>
</tbody>
</table>

(a). Results for SV%   (b). Result for CO%   (c). Results for Psys%   (d). Results for Pmean%
V. THE IMPROVEMENT OF OUR PREVIOUS MODEL

A. Physiological Principle

The fundamental equation for Fick principle relative to oxygen is

\[
\dot{V}O_2 = (Ca_o - Cv_o)Q
\]

where \(\dot{V}O_2\) is the oxygen consumption rate, \(Ca_o\) is the arterial oxygen constant, \(Cv_o\) is the venous oxygen content, \(Ca_o - Cv_o\) is the arteriovenous oxygen difference and \(Q\) is the blood flow.

Based on the above equation, we investigated the models to estimate \(\dot{V}O_2\)% from CO% (CO = SV \times HR). We applied both linear method and nonlinear method to study the relationship. For the nonlinear model, an efficient nonlinear regression method, SVR was introduced to model the nonlinear characteristics of cardiac output and oxygen uptake rate. SVR is a new technique, which has been successfully applied to nonlinear function estimation. It applies the kernel methods implicitly to transform data into a feature space (this is known as kernel trick), and uses linear regression to get a nonlinear function approximation in the feature space. In this study, we selected radial basic function (RBF) kernels, that is

\[
K(x, x_i) = \exp(- \frac{|x - x_i|^2}{2\sigma^2})
\]

where \(\sigma\) are the kernel parameters, \(x_i\) is the ith input support value and \(x\) is the input value. Detailed discussion about SVR, such as the selection of regularization constant \(C\), radius \(\epsilon\) of the tube and kernel function, can be found in [5-8]. For the linear model, the traditional linear regression (Least Square Regression (LS)) is performed.

B. Model Identification

Based on the experimental data (Table I), first we estimated \(\dot{V}O_2\)% using CO%. However, both SVR and LS model can not give good estimation results with RMSE (Root Mean Square Error) of 44.0 for SVR and RMSE of 47.3 for LS model.

Since cardiac output can be expressed as \(CO=SV \times HR\), we estimated \(\dot{V}O_2\)% based on SV% and HR% using SVR method (see Table III for the parameters of SVR). Its RMSE is 35.4 which is compatible with the range of SD (23.9 – 36.3) of the measurement value (Table I). However, for traditional linear regression, the estimation results of \(\dot{V}O_2\)% based on SV% and HR% behaves worse with the RMSE of 52.8. Fig. 4 gives the SVR and LS estimation models for CO% based on SV% and HR%.

For the estimation of steady state of \(\dot{V}O_2\)% using SVR, the above two different sets of inputs were selected. The first set of input was CO% only (CO = SV \times HR). The second was SV% and HR%. From the regression results, we can see that the second selection obtained much better estimation results than the first selection did. The reason is that \(\dot{V}O_2\) may not be just a function of CO. It may have a more complex relationship with SV and HR. If we define the set of functions for the second selection as \(F_2 = \{f_2 | \dot{V}O_2 = f_2(SV, HR)\}\) and the set of functions for the first selection as \(F_1 = \{f_1 | \dot{V}O_2 = f_1(SV \times HR)\}\), then it is clear that \(F_1\) is only a subset of \(F_2\). Therefore, by using...
the nonlinear approach - SVR, the second selection searched a much bigger model set than the first selection did. Hence, the second selection obtained better $\dot{V}O_2$ estimation results. However, for traditional linear regression, the two inputs model (SV% and HR%) behaves worse than its single input model (CO%) with higher RMSE (52.8). The reason for the degrading is that stroke volume and Heart Rate are not linearly related with $\dot{V}O_2$. On the contrary, from physiological point of view, CO linearly contributes to $\dot{V}O_2$ in some specific working range.

<table>
<thead>
<tr>
<th>Kernel</th>
<th>Parameters</th>
<th>Regularization constant C</th>
<th>$\varepsilon$-insensitivity</th>
<th>Support vector number</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBF</td>
<td>$\sigma = 55$</td>
<td>2000</td>
<td>50</td>
<td>14 (23.3%)</td>
</tr>
</tbody>
</table>

By incorporating the proposed SVR model in Table III (also shown in Fig. 4(a)) to our previous model, we got the simulation results shown in Fig 5. It can be seen that the simulation results are quite close to the mean value of the experimental data and its variation is within the SD of the experimental results.

VI. CONCLUSIONS

The investigation of this study confirmed that our previous model has the ability to reproduce the experimental results just by tuning the three parameters (Emax, Rsp and Vu). Moreover, in order to improve its performance, we have incorporated a new function to the model to make it be capable of predicting the percentage change of both central cardiovascular variables and metabolic demand accurately.

ACKNOWLEDGEMENT

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REFERENCES


