Modelling of Human Cardiovascular Response to Moderate Exercise

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Abstract. This paper investigates the steady state relationships between key central cardiovascular variables (i.e. stroke volume, heart rate, total peripheral resistance and cardiac output) and oxygen uptake rate ($\dot{V}O_2$) during moderate incremental exercise. Ten untrained normal males exercised in an upright position on an electronically braked cycle ergometer with constant workloads ranging from 25 Watt to 125 Watt. Throughout the experiment $\dot{V}O_2$ was determined breath by breath and heart rate (HR) was monitored beat by beat. During the last minute of each exercise session, cardiac output was measured beat by beat using a novel non-invasive ultrasound based device and blood pressure was measured using a tonometric measurement device. Based on the analysis of experimental data, nonlinear steady state relationships between key central cardiovascular variables and $\dot{V}O_2$ were qualitatively observed except for HR which increased linearly as a function of increasing $\dot{V}O_2$. Quantitative descriptions of these complex nonlinear behaviours were provided by nonparametric models which were obtained by using Support Vector Regression.

Keywords: Cardiovascular models, Non-invasive measurement, Oxygen uptake rate, Support Vector Regression, Upright cycle ergometer exercise.

1. INTRODUCTION

The cardiovascular response to exercise has been widely documented by several investigators (Dexter, Whittenberger, Haynes, Goodale, Gorlin & Sawyer 1951) (Barger, Richards, Metcalfe & Gunther 1956) (Freedman, Snider, Brostoff, Kimelblot & Katz 1955) (Reeves, Grover, Filley & Blount 1961*a*) (Reeves, Grover, Filley & Blount 1961*b*) (Rowland, Popowski & Ferrone 1997) (Kobayashi, Andoh, Fujinami, Nakayama, Takada, Takeuchi & Okamoto 1978) (Reeves, Grover & Filley 1961) (Bevegard, Freyschuss & Strandell 1966) (Astrand, Cuddy, Saltin & Stenberg 1964) (Denniston, Maher, Reeves, Cruz, Cymerman & Grover 1976) (Stenberg, Astrand, Ekblom, Royce & B 1967) (Turley & Wilmore 1997) (Fairbarn, Blackie, McElvaney, Wiggs, Pare & Pardy 1994) (Allor, Pivarnik, Sam & Perkins 2000) (Richard, Lonsdorfer-wolf, Dufour, Doutreleau, Oswald-Mammosser, Billat & Lonsdorfer 2004). Some of the reports demonstrated a linear function between the cardiac output (CO) and oxygen uptake rate during steady state of graded exercise, with a slope of approximately 5-6 in normal and athletic subjects (Rowell 1986). However, Reeves (Reeves et al. 1961*a*) (Reeves et al. 1961*b*) investigated the circulatory changes in normal people during rest and during mild supine exercise and suggested that the linear relationship between cardiac output and oxygen uptake existed during supine rest, but for variations in metabolic demands ranging from rest to heavy exercise, there was not a simple linear relationship. For the heart rate response to oxygen uptake rate, a linear relationship was found by the researchers (Fairbarn et al. 1994) (Turley & Wilmore 1997). However, for the other cardiovascular variables such as stroke volume (SV) and total peripheral resistance (TPR), the earlier reports (Reeves et al. 1961*b*) (Richard et al. 2004) (Rowland, Popowski & Ferrone 1997) (Reeves, Grover & Filley 1961) (Dexter et al. 1951) (Astrand et al. 1964) described the nonlinear behaviour of the change of oxygen uptake rate during graded levels of exercise, but no suitable models were presented.

It is of considerable physiological interest to investigate suitable models to reflect the real function between cardiovascular variables and metabolic demand. However, because of the complexity of physiological responses it may not be appropriate to describe the response of human cardiovascular system to exercise by a fixed model structure. In this study, an efficient nonparametric nonlinear regression method, Support Vector Machine based regression (Vapnik 1995) (Support Vector Regression (SVR)) was introduced to model the non-linear characteristics of cardiovascular variables to exercise. SVR is a new technique, which has been successfully applied to nonlinear function estimation. The formulation of SVM embodies the structure of the risk minimization (SRM) principle, which has been shown to be superior to other traditional empirical risk minimization principles (Vapnik 1995). We have applied SVR to model the nonlinear relationships of the cardiovascular response to exercise and obtained several valuable results. In order to show the effectiveness of SVR, traditional linear regression is also performed. These two approaches are evaluated by the difference (Mean Square Error) between the predicted and actual cardiovascular response value change to metabolic demand. The

results demonstrate the efficiency and advantages of SVR.

The rest of the paper is organized as follows: In Section 2, we introduce the details of experiment design and data processing. Section 3 gives the experimental results and analysis. Then SVR is applied to model the nonlinear relationships of the central cardiovascular variables to exercise in Section 4. Finally, some conclusions are drawn in Section 5.

2. METHODS

2.1. Subjects

We studied 12 normal male subjects. They are all active, but do not participate in formal training or organized sports. However, since two of them could not complete 6 minutes of higher level exercise, only the data recorded from 10 subjects (aged 26 $\pm$ 5yr, height 176 $\pm$ 5cm, body weight 73 $\pm$ 12kg) are used for this study. All the subjects knew the protocol and the potential risks, and had given their informed consent. The protocol was approved by the Ethics Committee of the University of New South Wales.

2.2. Procedures

All tests were conducted in the Biomedical System Laboratory of The University of New South Wales in Australia. A typical experimental scenario is shown in Figure 1. The laboratory is air-conditioned with temperature maintained between 23-24 ^oC. Each subject was studied during rest and during a series of exercise in an upright position

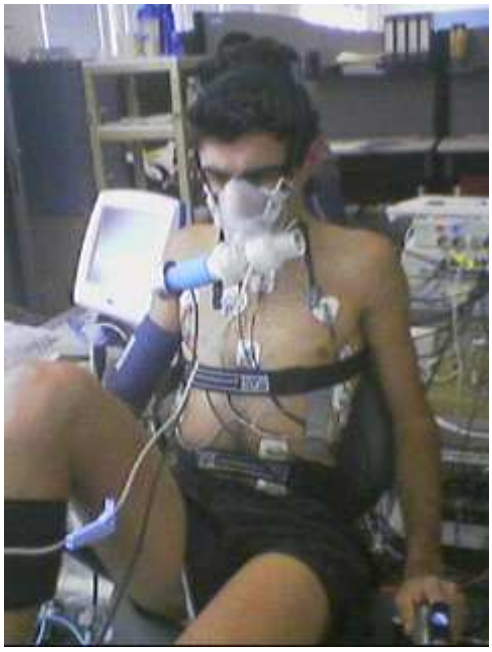

Figure 1. A typical experimental scenario.

on an electronically braked cycle ergometer (Tunturi Exercise Cycle E6). The seat and handlebar heights were set for each subject and held constant for all their tests. 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 5 to 15 minutes after each stint of exercise. Six minutes of exercise was long enough to approach a steady state since the values of oxygen uptake rate and the A-V oxygen difference had become stable by the 5th and 6th minutes even for near maximum exertion (Reeves, Grover & Filley 1961).

2.3. Measurement and data processing

During the whole exercise and recovery stage, heart rate was monitored beat by beat using a single lead ECG device, while ventilation and pulmonary exchange were measured on a breath by breath basis. Minute ventilation was measured during inspiration using a Turbine Flow Transducer model K520-C521 (Applied Electrochemistry, USA). Pulmonary gas exchange was measured using S-3A and CD-3A gas analyzers (Applied Electrochemistry, USA). Before each individual exercise test, the turbine flow meter was calibrated using a 3.0 liters calibration syringe. Before and after each test, the gas analyzers were calibrated using reference gases with known O_2 and CO_2 concentrations (15.00 $\pm$ 0.02 % O_2, 4.0 $\pm$ 0.8 % CO_2). The outputs of ECG device, the flow transducer and the gas analyzers were interfaced to a laptop through an A/D converter (National Instruments DAQ 6062E in 12-bit resolution) with a sampling rate of 500 Hz. Programs were developed in Labview 7.0 for breath by breath determination of pulmonary gas exchange variables but with particular reference to $\dot{V}O_2$ ($\dot{V}O_2$ STPD). The ECG signals were pre-processed using band-pass filtering, the differentiation technique, squaring and moving average. The HR was then detected by finding the top point of the R wave. This method of HR detection is more reliable without missing or mis-calculating any single beat. The oxygen uptake rate and heart rate were later reduced to one minute average based on the data collected in the last minute of the six minute exercise carried out for each workload.

Beat by beat cardiac output was measured non-invasively using an ultrasound based device (USCOM, Sydney, Australia) in the last minute of each workload. This device has previously been reported to be both accurate and reproducible (Knobloch, Lichtenberg, Winterhalter, Rossner, Pichlmaier & Philips 2005). All the cardiac output measurement was conducted by means of a Doppler transducer (2.2 MHz) at the tip of a flexible probe. The USCOM unit uses Continuous Wave Doppler ultrasound technology to provide key haemodynamic information.

Typically, the flow velocity signal is sampled at the aortic valve by putting a ultrasound probe on the suprasternal notch. However, it is often difficult to obtain a clear stable signal at this position during exercise because of the artefact introduced by a subject's respiratory movement. So, in this study, the probe was positioned above

the right supraclavicular fossa area, lateral to the sternocleidomastoid muscle, pointing toward the aortic valve. Therefore, the flow velocity signal we measured is somewhere along the ascending aorta rather than at the aortic valve level. The flow volume is smaller than the actual value, but we believed that the proportional change in the estimation of SV from this flow signal would correspond to the proportional change of the actual stroke volume. During all the measurements, an attempt was made to consistently obtain a flow velocity signal from the same region of the aorta by measuring the flow velocity waveform at the same position, that is, above the right supraclavicular fossa area and with a similar beam angle for every exercise workload. Also, the flow waveform was checked in each measurement to make sure it had a similar profile to that in previous measurement. Furthermore, all the measurements were conducted by the same person. A novel method was used in this study to improve the accuracy of the cardiac output measurement. During the measurement, the Doppler spectral profile was streamed to a computer via an Ethernet port. Streaming is performed using Windows Sockets which was programmed by Microsoft Visual C++ (version 6.0). The Windows Socket implementation uses TCP, therefore all packets are guaranteed to reach the client. Figure 2(a) shows the Doppler spectral image. The outline contour of the velocity curve (see Figure 2(b)) over time was traced with integration of the velocity time integral (VTI). The end of each VTI was taken as the observed closure of the aortic valve. Values of VTI were averaged from 5-10 curves with highest values which demonstrated crisp spectral envelopes. As stated above, these measurements were taken during the final minute of each workload.

The cross section area of the ascending aorta was calculated based on the following formulas (Nidirf, Picard, Triulzi, Thomas, Newell, King & Weyman 1992):

$$\begin{cases} D &= 0.01 \times Ht(cm) + 0.25, \\ S &= (\frac{D}{2})^2 \times \pi, \end{cases} \tag{1}$$

where D is aortic annulus diameter, Ht is the height of the subject and S is the cross

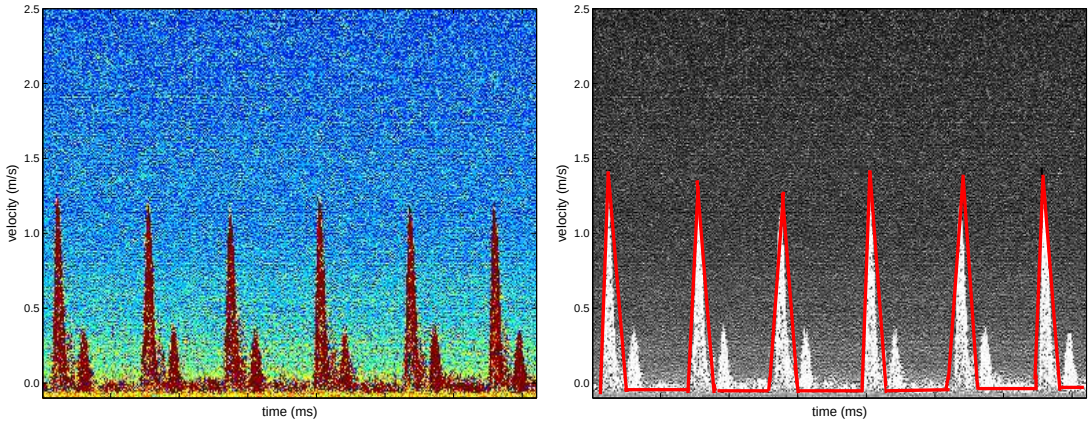

Figure 2. Images for blood velocity measurement: a) Doppler spectral image (left). b) The outline contour of the velocity curve (right).

section area. Cardiac output was calculated as the product of Doppler estimated stroke volume ($VTI \times S$) and the heart rate.

Tonometric blood pressure measurement device (CBM-700, Colin, France) was used to measure blood pressure non-invasively during the 5_{th} and 6_{th} minute of each certain level of exercise.

3. RESULTS

The highest workload in our test was 125W. In order to define the exercise intensity, first the maximal rate of oxygen uptake ($\dot{V}O_{2max}$) was determined for each subject based on the procedure proposed by Astrand and Rhyming (Astrand & Ryhming 1954), where heart rate and relative oxygen uptake were taken for the determination of $\dot{V}O_{2max}$. The values used for heart rate and oxygen uptake rate refer to the last minutes of exercise on the workload of 125W or 100W. Then $\dot{V}O_2$ at workload of 125W (the highest workload in this test) in percentage of $\dot{V}O_{2max}$ for individuals was calculated. The data are shown in Table 1.

Subject	Measured $\dot{V}O_2$ at 125W (liter/min)	Calculated $\dot{V}O_{2max}$ (liter/min)	$\dot{V}O_2$ at 125W in percentage of $\dot{V}O_{2max}$
No.1	2.0	2.85	70%
No.2	1.9	3.05	62%
No.3	1.84	3.4	54%
No.4	1.95	3.3	59%
No.5	1.41	1.9	74%
No.6	1.87	2.55	73%
No.7	2.85	4.8	59%
No.8	1.6	2.2	72%
No.9	2.52	4.0	63%
No.10	1.81	2.7	67%

Table 1. Oxygen uptake at workload of 125W in percentage of maximal oxygen uptake for individuals

Aerobic exercise intensity can be characterized as low, moderate or high (American College of Sports Medicine 1993). Moderate intensity of exercise is that eliciting 50% to 74% of $\dot{V}O_{2max}$. Exercise eliciting a lower response is considered as low intensity, and eliciting a greater response is considered as high intensity. In Table 1, we know that $\dot{V}O_2$ (at workload of 125W) for all the subjects ranges from 54% to 74% with respect to their $\dot{V}O_{2max}$. This indicates that for those subjects, our exercise test can be classified as of moderate intensity.

For the work performance, because of variations in fitness among different individuals when they do exercise on cycle ergometer, oxygen consumption rate has been taken as the measure of work intensity.

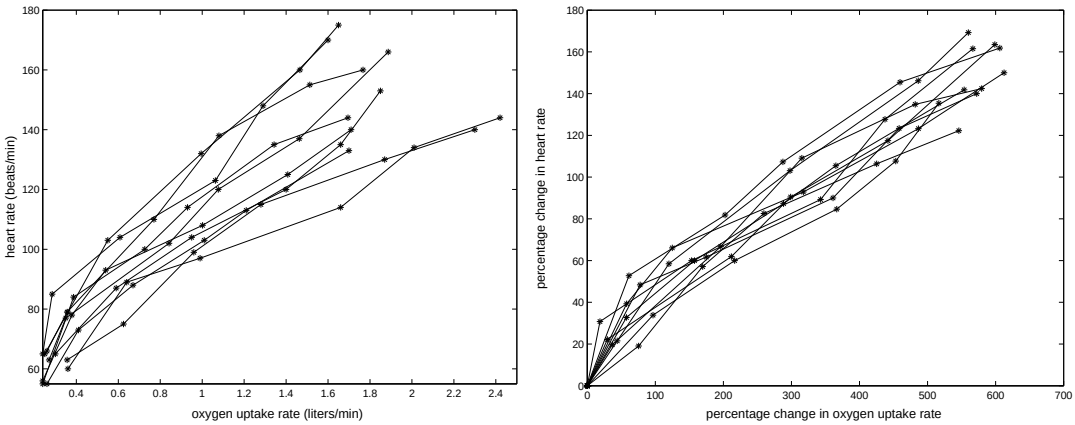

Figure 3. Heart rate response to oxygen uptake rate for the ten subjects: a) absolute value (left). b) relative value (right).

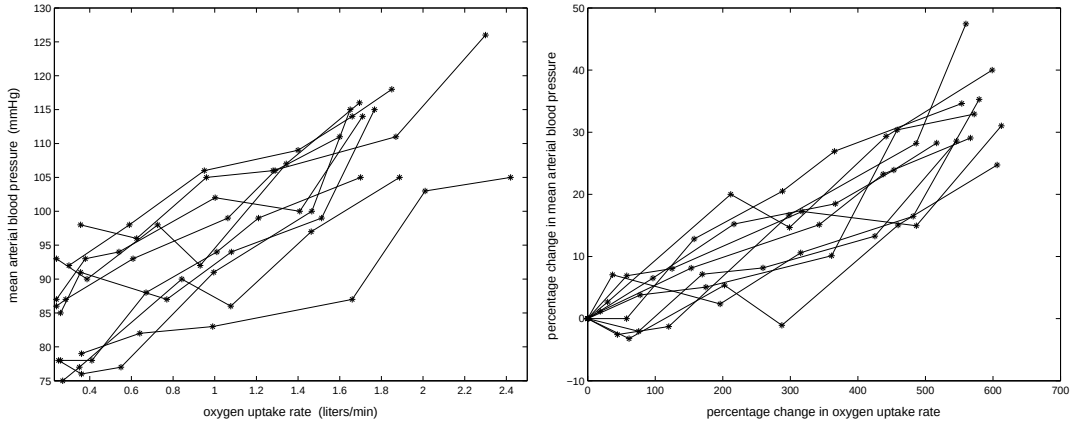

Figure 4. Mean arterial blood pressure response to oxygen uptake rate for the ten subjects: a) absolute value (left). b) relative value (right).

As we mentioned above, the blood flow velocity signal we measured was from the position above the right supraclavicular fossa area. The calculated SV based on this value is smaller than the actual value. So, the value can not be used in absolute terms. For evaluation of stroke volume and cardiac output change, it is used as a *relative*, rather than an absolute value. We also found that the *relative* responses of cardiovascular system to exercise are more uniform than the absolute responses across subjects. We present the comparison for just two cardiovascular parameter responses to oxygen uptake rate in Figure 3 and Figure 4. Figure 3(a) shows the absolute value of heart rate response to the absolute value of oxygen uptake rate for all the ten subjects, while Figure 3(b) is the percentage change in heart rate relative to its value at rest with the percentage change in oxygen uptake rate to its value at rest for the ten subjects. Obviously, the response in Figure 3(b) is more consistent and gives clearer trend than that in Figure 3(a). The same observation can be seen in Figure 4 as well. The mean arterial blood pressure (MBP) response to oxygen uptake rate (both in absolute value)

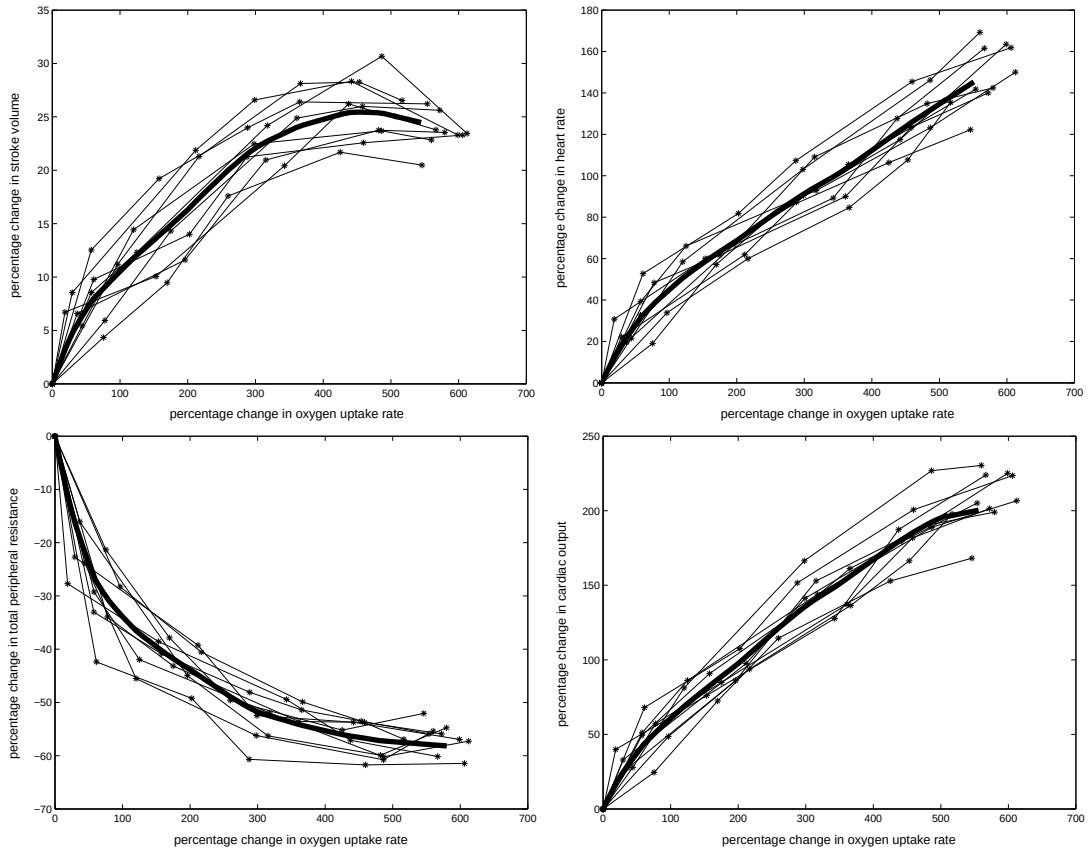

Figure 5. Cardiovascular variable changes in percentage with respect to their rest value with the percentage change in $\dot{V}O_2$ for the ten subjects: a) Percentage change in SV to percentage change in $\dot{V}O_2$ (top left). b) Percentage change in HR to percentage change in $\dot{V}O_2$ (top right). c) Percentage change in TPR to percentage (bottom left). d) Percentage change in CO to percentage (bottom right).

in Figure 4(a) demonstrates a more scattered distribution than that in Figure 4(b) where the relative value was used. Both Figure 3 and Figure 4 imply that the relative response of cardiovascular system to exercise has more consistent trend than the absolute responses do. It is thus reasonable to believe that modelling of cardiovascular responses using *relative* changes gives more robust results than modelling with the absolute value.

Based on the above findings, we model stroke volume, heart rate, total peripheral resistance and cardiac output to exercise by modelling their percentage changes with respect to their corresponding rest value with the percentage change in $\dot{V}O_2$ with respect to its rest value. We use SV%, HR%, TPR% and $\dot{V}O_2$ % to represent their relative value (expressed as percentage), respectively.

Figure 5 shows the relative change of SV, HR, TPR and CO to the relative change of $\dot{V}O_2$. All the subjects demonstrated fairly uniform response to the various levels of exercise. Figure 6 presents a comparison of our data with that of Bevegard (Bevegard, Freyschuss & Strandell 1966) where cardiac output was determined by the direct Fick procedure with analysis of oxygen saturation and hemoglobin concentration of the blood

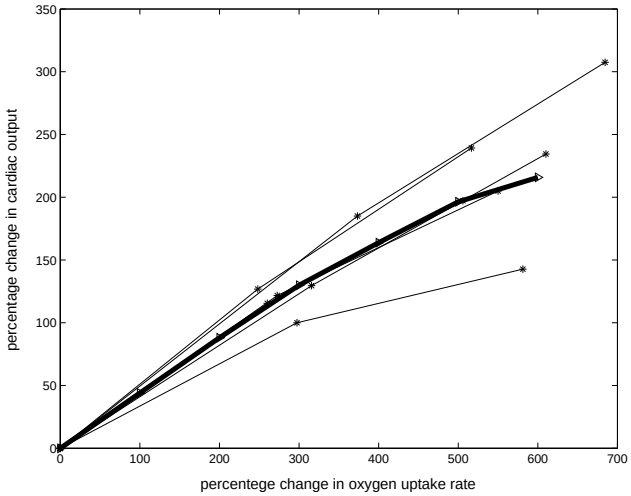

Figure 6. Percentage change in cardiac output to percentage change in oxygen uptake rate from published report by Bevegard (Bevegard, Freyschuss & Strandell 1966). The thin lines are for the individual people and the bold line is the mean of the individuals.

spectrophotometrically according to Drabkin. Our data is quite consistent with the data reported by Bevegard (6). The range of $\dot{V}O_2$ changes from 0 to 600, while the corresponding range of CO changes from 0 to 200

Figure 5(a) shows the relationship of SV% change comparing with $\dot{V}O_2$%. The SV increases by about 20% while the $\dot{V}O_2$ increased by 300%. Then the SV% began to level off, whereas the $\dot{V}O_2$ % continues to increase. In this study, we observed that SV can increase between 21% and 31% before reaching to a plateau.

SV represents the amount of blood ejection from the heart during each beat. It equals end-diastolic volume (EDV) minus end-systolic volume (ESV). Exercise-induced increases in SV are believed to be the results of the increased EDV and the decreased ESV. A greater venous return of blood to the heart during exercise results in a greater EDV. Meanwhile, according to Frank-Starling law, a stronger stretch is placed on the muscle fibers of the heart resulting in a more forceful contraction of those fibers, and consequently, a decreased ESV. However, with the increase of workload, the heart rate increases, thus reducing the diastolic filling time which then limits any further increase of EDV.

Although some investigators have suggested that stroke volume may continue to increase at higher levels of exercise (Chapman, Fisher & Sproule 1960), our observations are similar to those who found that stroke volume, after increasing promptly with low levels of exertion, reaches a plateau and does not increase progressively as exertion becomes more intense (Astrand et al. 1964) (Knobloch et al. 2005) (Plotnick, Becker, Fisher, Gerstenblith, Renlund, Fleg, Weisfeldt & Lakatta 1986) (Rodeheffer, Gerstenblith, Becker, Fleg, Weisfeldt & Lakatta 1984) (Thadani & Parker 1978).

During exercise, a combination of parasympathetic withdrawal and sympathetic activation leads to an increase in heart rate to satisfy energy demands of the working

muscles. Both somatic exercise reflexes and central command mechanisms mediate those autonomic changes. Figure 5(b) demonstrates that HR% rises linearly with the rise of $\dot{V}O_2$ %. The average increase for the heart rate is as high as 130% when $\dot{V}O_2$ increases by 500%.

The sum of all the factors that oppose blood flow in the systemic circulation is expressed by the term total peripheral resistance which is calculated as MBP/CO. TPR% has been examined in relation to $\dot{V}O_2$% in Figure 5(c). Inspection of these data indicates that a marked percentage decrease in TPR occurs during lower intensity exercise until the point where oxygen uptake rate rises approximately 3 times its resting value, and then little decrease or even no decrease is observed when $\dot{V}O_2$ increases further. During exercise, the increase of metabolic demand of working skeletal muscles results in a very large increase in blood flow to the muscles. This leads to a reduction in the resistance of vessels supplying muscles and skin. On the other hand, as resistance in those vessels that supply the non-exercising tissue is increased, blood flow to those areas of the body is reduced. TPR decreases during exercise because vasoconstriction in non-exercising tissue is not enough to compensate for the vasodilation in active muscles. But when the resistance vessels dilate to near maximum, little further change is possible, although the metabolic demand may continue to increase in the working muscle.

Cardiac output, which is the product of heart rate and stroke volume can increase between 170% to 230% with respect to its resting value when $\dot{V}O_2$ increases to 500 % (Figure 5(d)). But the rate of increase is diminished thereafter. Obviously there is not a simple linear relationship between CO% and $\dot{V}O_2$% for higher degrees of exertion. The exercise-induced increase of CO is due to alterations of both HR and SV. From Figure 5(a) and Figure 5(b), we can conclude that the increase in CO at lower workload is due to both increasing in HR and SV. But at higher exercise intensity, increasing HR is largely responsible for the observed increases in CO. However, although the rise in HR% (see Figure 5(b)) compensates for the plateau in SV %, it is not enough to permit CO % to increase as sharply as it does in the lower workload. That is the reason why CO % shows a slower rate of increase at higher workload.

Only Figure 3(b) demonstrates a linear characteristic between HR % and $\dot{V}O_2$ %. However, the other 3 figures (Figure 5(a), Figure 5(c) and Figure 5(d)) do not depict clear evidence of response linearity. In contrast, both Figure 5(a) and Figure 5(c) go to a plateau from the middle range of the response.

4. MODELING

Nonlinear steady state relationships between key central cardiovascular variables and $\dot{V}O_2$ were qualitatively observed except for HR which increased linearly as a function of increasing $\dot{V}O_2$. To quantitatively describe these complex nonlinear behaviours, a powerful nonlinear regression approach - Support Vector Regression was utilized to model the respective relationships. In order to show the effectiveness of SVR, traditional linear regression was also performed. These two approaches are compared using the

difference (Mean Square Error) between predicted and actual percentage change in cardiovascular response to percentage change in $\dot{V}O_2$.

4.1. Support Vector Machine based regression

Support Vector Machine (SVM) is firmly grounded in the framework of statistical learning theory, which is a small sample statistical theory introduced by Vapnik (Vapnik 1995). It has been widely applied in classification, forecasting and regression. Their practical success can be attributed to solid theoretical foundations based on VC-theory (Cherkassky & Ma 2004). The detailed in-depth theoretical background on SVM is introduced in (Vapnik 1995) (Vapnik & Lerner 1963) (Vapnik 1998) (Schlkopf & Smola 2002) (Cherkassky & Ma 2004) (Thissen, Pepers, Ustun, Melssen & Buydens 2004). In this section, only the essential basics of the so called ϵ-insensitivity SVR based static nonlinearity modelling (Vapnik 1998) is described. This describes in some detail the SVR method we used in this paper.

Let $\{u_i, y_i\}_{i=1}^N$ be a set of inputs and outputs data points ($u_i \in U \subseteq \mathcal{R}^d$, $y_i \in Y \subseteq \mathcal{R}$, N is the number of points). The goal of the support vector regression is to find a function $f(u)$ which has the following form

$$f(u) = w \cdot \phi(u) + b, \tag{2}$$

where $\phi(u)$ represents the high-dimensional feature spaces which are nonlinearly transformed from u. The coefficients w and b are estimated by minimizing the regularized risk function:

$$\frac{1}{2}\|w\|^2 + C\frac{1}{N}\sum_{i=1}^{N} L_\epsilon(y_i, f(u_i)). \tag{3}$$

The first term is called the regularized term. The second term is the empirical error measured by ϵ-insensitivity loss function which is defined as:

$$L_\epsilon(y_i, f(u_i)) = \begin{cases} |y_i - f(u_i)| - \epsilon, & |y_i - f(u_i)| > \epsilon \\ 0, & |y_i - f(u_i)| \leq \epsilon \end{cases} \tag{4}$$

This defines an ϵ tube. The radius ϵ of the tube and the regularization constant C are both determined by user.

By solving the above constrained optimization problem, we have

$$f(u) = \sum_{i=1}^{N} \beta_i \phi(u_i) \cdot \phi(u) + b. \tag{5}$$

where the coefficients β_i corresponds to each (u_i, y_i). The support vectors are the input vectors u_j whose corresponding coefficients $\beta_j \neq 0$.

By the use of kernels, all necessary computations can be performed directly in the input space, without having to compute the map $\phi(u)$ explicitly. After introducing kernel function $k(u_i, u_j)$, the above equation can be rewritten as follows:

$$f(u) = \sum_{i=1}^{N} \beta_i k(u_i, u) + b, \tag{6}$$

For linear support regression, the kernel function is thus the inner product in the input space:

$$f(u) = \sum_{i=1}^{N} \beta_i < u_i, u > +b. \tag{7}$$

For nonlinear SVR, there are a number of kernel functions which have been found to provide good generalization capabilities, such as polynomials, radial basis function (RBF), sigmoid. Here we give the polynomial and RBF kernel functions as follows:

- RBF kernel: $k(u, u') = exp(-\frac{\|u-u'\|^2}{2\sigma^2})$,
- Polynomial kernel: $k(u, u') = ((u \cdot u') + h)^p$.

Brief introduction of SVR regression can be found in papers (Su, Wang, Celler, Savkin & Guo 2007) (Su, Wang, Celler & Savkin 2007). Details about SVR, such as the selection of radius ϵ of the tube, kernel function, and the regularization constant C, can be found in (Vapnik 1998) (Schlkopf & Smola 2002) (Guo, Bartlett, Shawe-Taylor & Williamson 2002).

4.2. Model identification

Examining the relationships between central cardiovascular variables and oxygen uptake rate during exercise is fundamental to the study of exercise physiology. In this study, we applied both Support Vector Regression and traditional linear regression (we use Least-Square linear regression) to investigate the relationships between relative percentage change of cardiovascular variables (SV%, HR%, TPR% and CO%) and $\dot{V}O_2$ %. The measurement of model performance adopted throughout this paper is the Mean Square Error (MSE):

$$MSE = \frac{1}{n} \sum_{i=1}^{n} (x_i - \hat{x}_i)^2. \tag{8}$$

where x_i is the observed value and $\hat{x}_i$ is the predicted value.

Relation	SV%vs$\dot{V}O_2$%	HR%vs$\dot{V}O_2$%	TPR%vs$\dot{V}O_2$%	CO%vs $\dot{V}O_2$%
Kernel	Polynomial	Polynomial	RBF	RBF
Parameter	d=2	d=1	$\sigma = 400$	$\sigma = 300$
Constant C	50	30	5000	5000
ϵ-insensitivity	4.5	16	8	25
Support vectors number	8 (13.3%)	20 (33.3%)	17 (28.3%)	8 (13.3%)
Estimation error (MSE)	8	159	35	233

Table 2. Details about the estimation of the relationships between cardiovascular variables and oxygen uptake rate using SVR

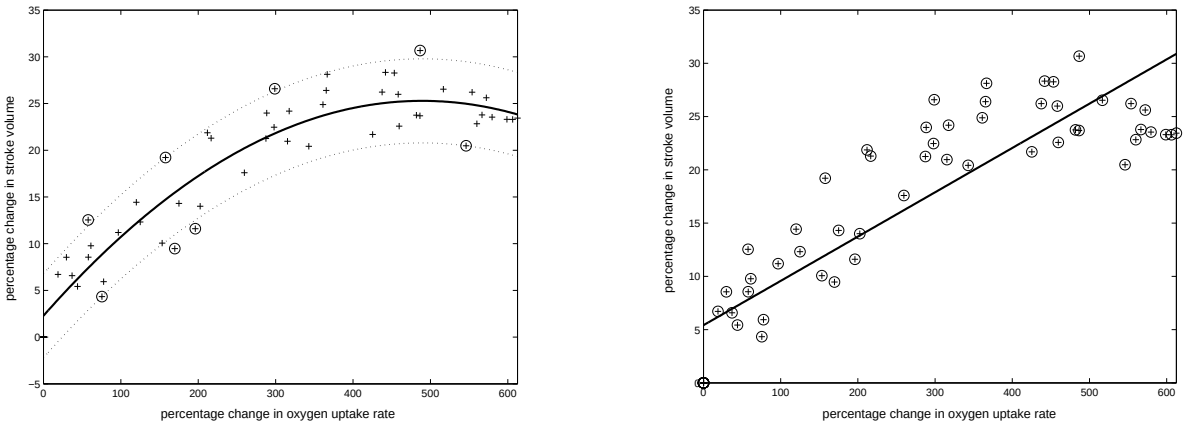

Figure 7. Comparison of the estimation of percentage change in SV from percentage change in $\dot{V}O_2$ between using SVR and LS: a) SVR (left). b) LS (right).

Relation	SV%vs$\dot{V}O_2$%	HR%vs$\dot{V}O_2$%	TPR%vs$\dot{V}O_2$%	CO%vs $\dot{V}O_2$%
Linear Regression	21	159	146	304
SVR	8	154	35	233

Table 3. Estimation errors comparison (MSE) between using SVR and using linear regression method

As discussed in Subsection 4.1, the performance of the model using SVR depends on the selection of kernel function and several design parameters including capacity (C) and insensitivity region (ϵ). To model the steady state relationship between SV % and $\dot{V}O_2$ % in graded exercises using SVR, the polynomial kernel is selected as its performance is comparable to that of the model using linear regression methods. The best setting obtained in the present study for the rest parameters was also found (see Table 2) and the comparison results between SVR and traditional linear regression in terms of MSE is shown in Table 3 and Figure 7. In Figure 7(a), the continuous curve stands for the estimated input output steady state relationship. The dotted lines indicate the ϵ-insensitivity tube. The plus markers are the points of input and output data. The circled plus markers are the support points. It is obvious that the use of SVR leads to performance improvement in terms of MSE which decreases from 21 to 8. Both the result in Table 3 and the regression figures in Figure 7 indicate that the relationship between SV% and $\dot{V}O_2$ % during steady state exercise is nonlinear. This result is consistent with the previous reports (Astrand et al. 1964) (Cautero, Prampero & Capelli 2003) (Knobloch et al. 2005).

Although other researchers (Freedman et al. 1955) (Reeves et al. 1961*b*) (Richard et al. 2004) (Rowland, Popowski & Ferrone 1997) (Reeves, Grover & Filley 1961) (Dexter et al. 1951) (Astrand et al. 1964) have described the nonlinear behaviour between stroke volume and $\dot{V}O_2$, they did not demonstrate the relationship from the viewpoint of modelling. We present here for the first time a nonparametric modelling method (that

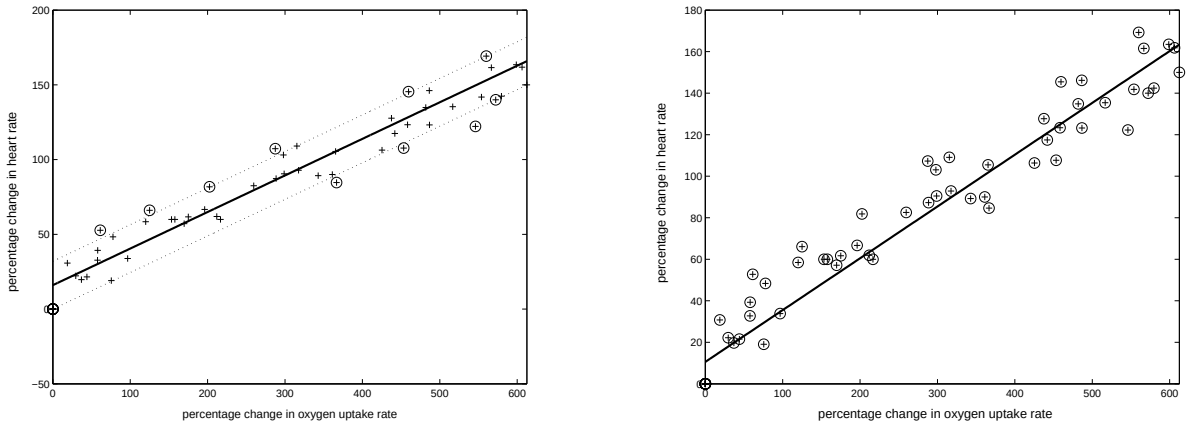

Figure 8. Comparison of the estimation of percentage change in HR from percentage change in $\dot{V}O_2$ between using SVR and LS: a) SVR (left). b) LS (right).

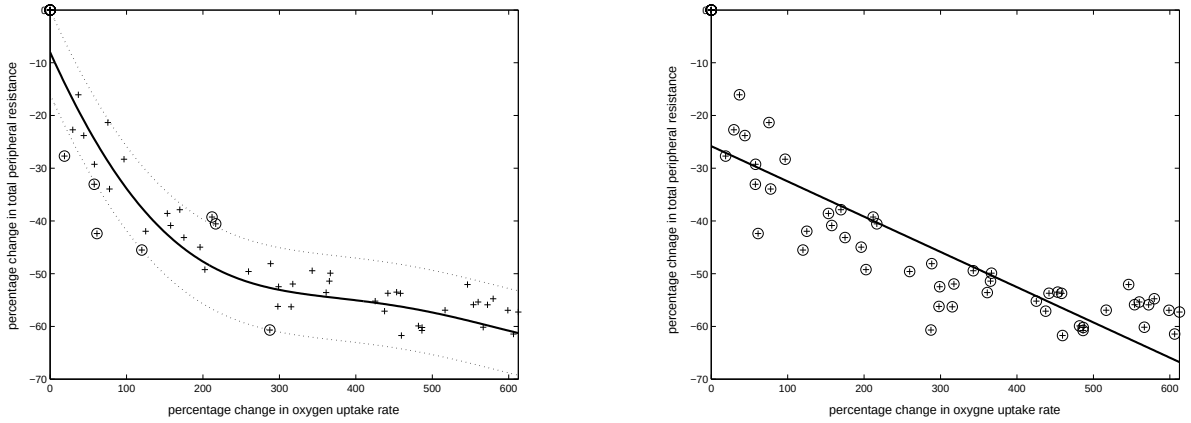

Figure 9. Comparison of the estimation of percentage change in TPR from percentage change in $\dot{V}O_2$ between using SVR and LS: a) SVR (left). b) LS (right).

is SVR) to model the relationship between SV% and $\dot{V}O_2$ %. The results (Table 2 and Table 3) show the advantages and efficiency of SVR. In SVR, the solution to the problem is only dependent on a subset of training data points which are referred to as support vectors. Using only support vectors, the same solution can be obtained as using all the training data points. To get the relationship between SV% and $\dot{V}O_2$ %, SVR uses just 13% of the total points available to model their nonlinear behaviour efficiently and decreases MSE by 62 % compared with that for linear regression.

In presenting the steady state relationship between variations of HR% to $\dot{V}O_2$ %, the results turn out that in all but one case to be an order 1 polynomial kernel, which implies a linear relationship (see Figure 8 and Table 3). This suggests that the percentage increase in HR indeed increases linearly as a function of $\dot{V}O_2$ %. This result agrees with the previous researchers (Turley & Wilmore 1997) (Vapnik 1998).

As shown in Figure 9, the SVR model describes how the TPR % fell with the lower workload and remained relatively constant even with the increasing workload. SVR uses

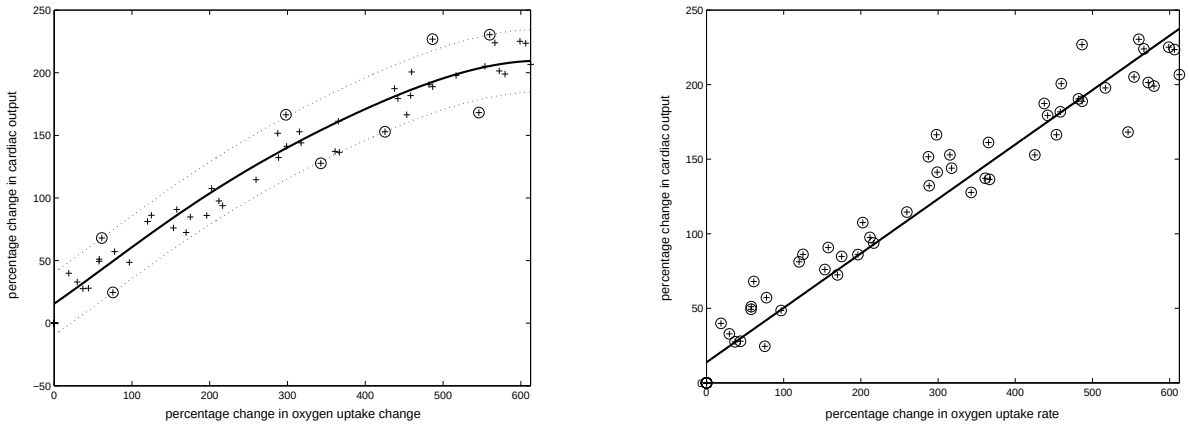

Figure 10. Comparison of the estimation of percentage change in CO from percentage change in $\dot{V}O_2$ between using SVR and LS: a) SVR (left). b) LS (right).

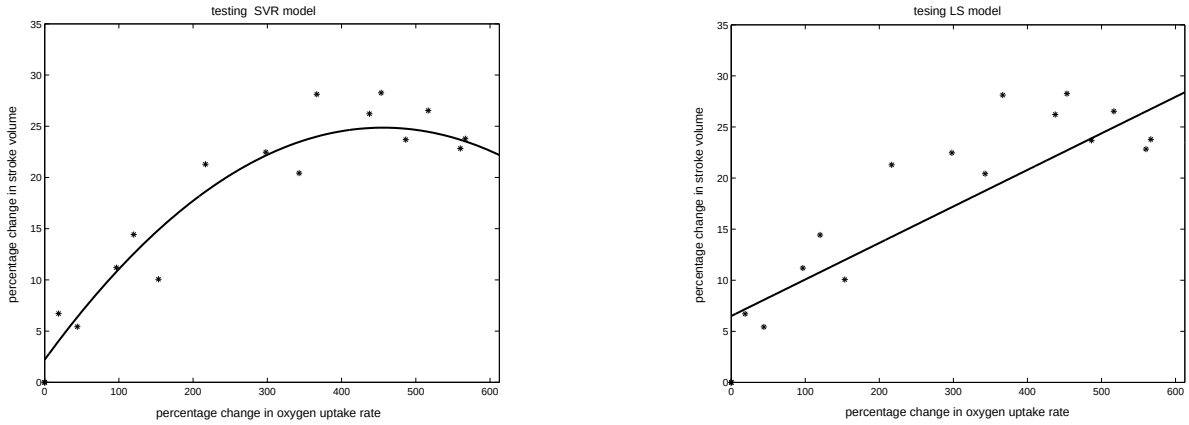

Figure 11. Comparison of the test results of estimating percentage change in SV from percentage change in $\dot{V}O_2$ between using SVR and using linear regression.

just 28 % of the total points to get an efficient nonlinear model. Compared with linear regression, the SVR model decreases MSE from 146 to 35, an improvement of 76 %.

Cardiac output has been widely demonstrated to increase as a linear function of oxygen uptake rate during steady state incremental exercise (Freedman et al. 1955) (Allor et al. 2000) (Astrand et al. 1964) (Capelli, Cautero & Prampero 2001). However, our results show that the increase in CO% with respect to $\dot{V}O_2$ % can be best described by a nonlinear model (that is SVR), which improves the MSE by 23% compared to linear regression.

4.3. Model verification

From the above analysis, we know that the relationship between HR% and $\dot{V}O_2$ % is linear and can be modelled using simple linear regression. So, the model verification excludes this model.

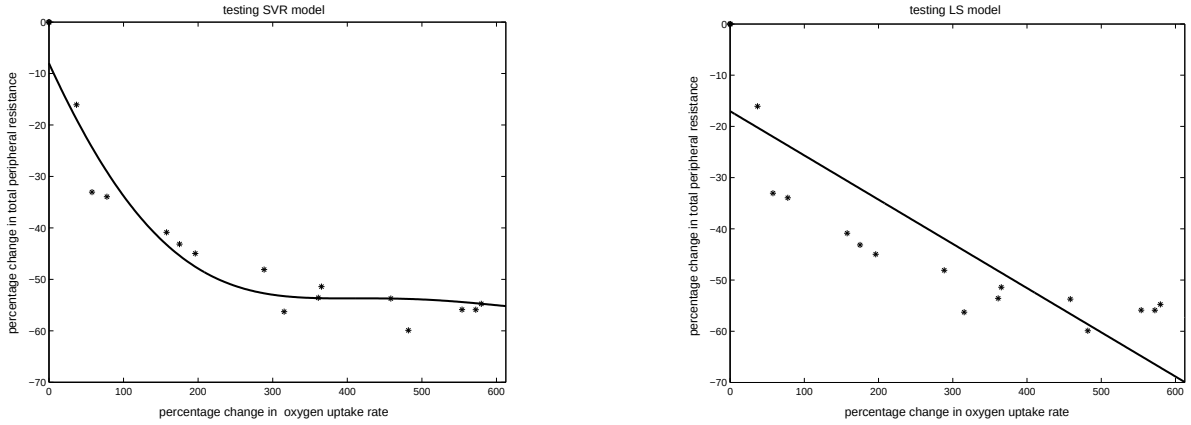

Figure 12. Comparison of the test results of estimating percentage change in TPR from percentage change in $\dot{V}O_2$ between using SVR and using linear regression.

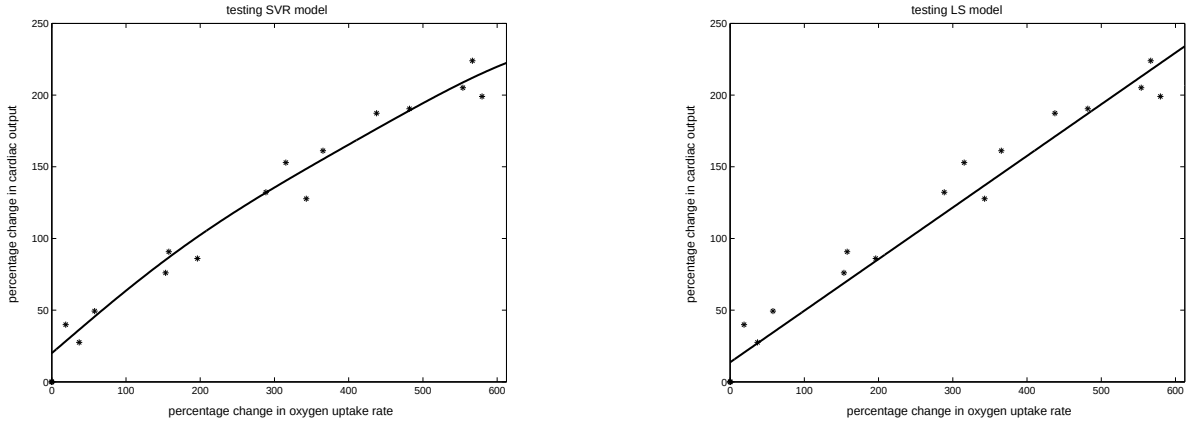

Figure 13. Comparison of the test results of estimating percentage change in CO from percentage change in $\dot{V}O_2$ between using SVR and using linear regression.

Relation	SV%vs$\dot{V}O_2$%	TPR%vs$\dot{V}O_2$%	CO%vs $\dot{V}O_2$%
Kernel	Polynomial	RBF	RBF
Parameter	d=2	σ= 400	σ= 350
Constant C	50	5000	5000
ϵ-insensitivity	3.5	8	20
Support vectors number	10 (24 %)	11 (27.6%)	10 (22.8 %)

Table 4. Details about the estimation of the relationship between cardiovascular variables and oxygen uptake rate based on training data (70% of the data)

To further evaluate the feasibility of SVR model, the whole data set is divided into two parts: the first part (70 % of the data) is used to design the model and the second part (30 % of the data) is used to test its performance. The SVR model was

established using the training data points through tuning of three design parameters (kernel function, loss function, and capacity value). In Figure 11 to Figure 13, we present the testing results for each situation. For each testing situation, selected parameters are shown in Table 4. Table 5 is the comparison of MSE between SVR and traditional linear regression.

Relation	SV%vs$\dot{V}O_2$%	TPR%vs$\dot{V}O_2$%	CO%vs $\dot{V}O_2$%
LR training error	18	127	272
LR test error	30	156	394
SVR training error	7	32	203
SVR test error	10	51	284

Table 5. Estimation error (MSE) comparison between using SVR and using linear regression for both the training and the test

The results obtained on the testing data indicate that the SVR model outperforms the traditional linear regression as indicated, by modelling the trend of the data more closely as well as obtaining a lower MSE. Even for the relationship of cardiac output and oxygen consumption, the testing error (MSE) of SVR (284) is very much less than that of traditional linear regression method (394), further indicating that the SVR model provides superior accuracy. Moreover, all the proposed models outperform the linear regression models in error reduction both in the training data set and the testing data set.

Both the comparison figures presented in Figure 11 to Figure 13 and MSE shown in Table 5 indicate that SVR compare favourably with traditional linear regression. One reason is that SVR are based on the structural risk minimization inductive principle, which seeks to minimize an upper bound of the generalization error consisting of the sum of the training error and a confidence level. As the structure of the model become more complex, the risk term decreases and the confidence interval increases. Therefore, SVR implements a right balance between the quality of the approximation of the given data and the complexity of the approximating function. Normally, for a given data set, a model with too complex a structure often results in poor generalization performance and over-fitting phenomena, despite having a good learning performance. However, a good SVR model can be obtained by selecting the three design parameters (kernel function, loss function, and capacity value). The best model can implement a trade-off between training errors and model complexity so as to achieve a high generalization performance and solve the over-fitting problem. Another key characteristic of SVR is that it applies the kernel methods implicitly to transform data into a feature space, and uses linear regression to get a nonlinear approximation function in the feature space (Vapnik 1995). Consequently, SVR is a convex optimization tool. It is very efficient in terms of speed and complexity (Guo et al. 2002).

5. CONCLUSIONS

This paper investigates experimentally the steady state relationships between key central cardiovascular variables and oxygen uptake during incremental exercise. Reliable data were collected and the experimental results demonstrate previously unknown nonlinear behaviour of some cardiovascular variables to exercise. A Support Vector Machine, a new powerful machine learning method based on statistical learning theory was introduced in the modelling of the cardiovascular system response.

When comparing the performance of SVR methods to simple linear regression methods for modelling the cardiovascular response to exercise, two conclusions can be drawn. Firstly, the increase in CO % as a function of $\dot{V}O_2$ % can be best described by a nonlinear model (SVR), although this relationship has been widely presented in the literature as a linear function during incremental steady state exercise. Secondly, for changes in stroke volume and total peripheral resistance during steady state incremental exercise, previous researchers described their nonlinear behaviour without attempting to present suitable models. In this paper we clearly demonstrate that changes of SV and TPR with $\dot{V}O_2$ are non linear.

This study demonstrates that SVR is a new and effective method that can be used satisfactorily to model cardiovascular responses to moderate exercise in normal subjects. Because SVR introduces regularization terms in the loss function, the over-fitting problem is successfully solved. That means that even if new subjects are recruited to carry out the experimental protocol, the regression models will still provide a reasonable dimension and maintain model robustness.

In this study, we estimate cardiovascular variables for moderate exercise only (less than 125 w). We believe that over a wider range of exercise intensity, the nonlinearities would become more evident, and the nonlinear modelling approach (Vapnik 1995) (Ruhe & P.Wedin 1980) (Su, Wang, Celler, Savkin & Guo 2007) (Su, Wang, Celler & Savkin 2007) (Su, Huang, Wang, Celler, Savkin, Guo & Cheng 2007) (Cheng, Savkin, Celler, Su & Wang 2008, will appear) would prove much more effective than the linear one.

Another important fact we found in this study is that relative responses (percentage changes with respect to rest value) of the cardiovascular system to exercise are more uniform than absolute responses (see Section 3). This would suggest that across individual subjects, the variability in baseline values, possibly related to basal metabolism, is greater than the variability in cardiovascular response to exercise.

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