**Physiological measurement**

**Dynamic control of breathing during exercise and hypercapnia**

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**Abstract**—The dynamic influences of end-tidal CO₂ and exercise on ventilation are compared when CO₂ and exercise are imposed separately and when they are imposed simultaneously. Five human subjects are studied. The subjects performed three trials: random work rate forcing, random CO₂ inhalation and their simultaneous loading. The work rate was varied between 20 and 80 W as a pseudorandom binary sequence. The concentration of inspired CO₂ was varied randomly between 0 and 7 per cent, adjusted so that it produced approximately the same amount of ventilatory fluctuations as the random work load. The relative contribution of each variable was analysed using multivariate autoregressive analysis at frequencies ranging from 0.1 to 1 cycle min⁻¹. The results show that the dynamics of the response to CO₂ inhalation, exercise and their combination are nonlinear and that the combination of CO₂ inhalation and exercise magnifies the nonlinear behaviour. Ventilation is largely unaffected by either work rate or end-tidal CO₂ at 1 cycle min⁻¹. During simultaneous CO₂ and work rate forcing, ventilation tends to follow the change in the end-tidal CO₂.

**Keywords**—Autoregressive model, Dynamic response, Exercise, Hypercapnia, Relative power contribution


1 Introduction

The dynamic ventilatory response to hypercapnia and exercise has been investigated by frequency responses (DAUBENSPEEK, 1973; CASABURI et al., 1977; SWANSON and BELLVILLE, 1974; WIGERTZ, 1970) and impulse responses (BENNETT et al., 1981; SOHAB and YAMASHIRO, 1980) as well as transient responses to various inputs. However, the dynamic response to their combination has not been analysed. Moreover, previous investigators seemed to pay relatively little attention to inherent system noise. (An exception is the issue of how it can be eliminated from the estimated ventilatory response.) As ventilation shows considerably irregular fluctuation, it is important to know the characteristics of noise as well as the system (plant and controller) for the analysis of dynamic ventilatory response. It is especially crucial in an attempt to predict and control the subject's ventilation. To accomplish this, it is necessary to decompose ventilatory fluctuation into the inherent noise and influences from other variables. Multivariate autoregressive modelling and relative power contribution analysis are useful methods of discriminating these components. The relative power contribution analysis decomposes the power spectrum of ventilation into the sum of the contributions from each variable at each frequency. The mathematical procedure is described in the Appendix. Decomposition is feasible even if the system includes multiple variables which interact with each other. This is an advantage over the cross-spectral method which gives a biased result for the analysis of the feedback system (AKAIKE, 1967).

In the present paper the dynamic influences of end-tidal CO₂ and exercise on ventilation are examined when their levels are perturbed separately and simultaneously. Work rate and end-tidal CO₂ gas concentration were changed quasirandomly, and the contributions of end-tidal CO₂ concentration (FETCO₂) and work rate (WR) on ventilation (Vₜ) were examined by the autoregressive model with the exogenous variable (ARX model). The power spectrum of ventilation was decomposed into the contributions from each variable and the residual power, which cannot be accounted for by the other variables.

2 Methods

The subjects were five healthy young adults ranging in age from 24 to 29 years. The subjects were familiar with the breathing apparatus, but were not informed about the experimental protocol beforehand. While in the supine position on a bicycle ergometer (Tatebe Seishudo EM-401), they placed their feet in the stirrups on the pedals and were instructed to pedal constantly at 60 rotation min⁻¹. Inspired and expired flow was measured by a hot-wire flowmeter. Gas fractions in the mouth were measured with a mass spectrometer (Perkin-Elmer MGA 1100). A low
dead-space oronasal mask, through which room air was breathed, was fitted on the face. The total dead space, including the breathing valve and the mask, was 30–35 ml. Minute ventilation \( (V_e) \), O\(_2\) uptake \( (V_{O_2}) \), CO\(_2\) output \( (V_{CO_2}) \), heart rate and \( F_{ETCO_2} \) were computed at intervals of 10 s by a respiromonitor (Minato RM300) using breath-by-breath estimations.

The study consisted of three trials: (a) random work rate forcing; (b) random CO\(_2\) inhalation; (c) random work rate forcing with random CO\(_2\) inhalation. Each subject performed only one trial per day, and the sequence of these trials was randomised among the subjects.

(a) Random work rate forcing: The work load was switched over between 20 and 80 W for all subjects. It was determined that this value did not exceed the anaerobic thresholds, which were estimated by a 2 min incremental work test in a manner similar to that described by Wasserman et al. (1973). The work load was maintained below this value because the ventilatory response for the work load is nonlinear beyond the anaerobic threshold. Anaerobic thresholds and physical characteristics for each subject are presented in Table 1.

(b) Random CO\(_2\) inhalation: Inhalation gas mixtures were prepared by a random gas generator (Respy Laboratory GASMIXER-002). Pure gas sources of N\(_2\), O\(_2\) and CO\(_2\) were connected to a gas mixing chamber through electromagnetic valves which were controlled by an 8-bit digital computer (Fujitsu FM-77). The system was capable of mixing gases to any desired final composition with a first-order delay of about 3 s. The gases were humidified at room temperature as they flowed to the chamber. The concentration of inspired CO\(_2\) was varied randomly for 30 min between 0 and 7 percent at random intervals from 10 to 90 s. The amplitudes of work rate forcing and inspired CO\(_2\) fluctuation were adjusted so that each produced approximately the same amount of ventilatory fluctuation. This CO\(_2\) random signal was generated so that there was no cross-correlation with the pseudorandom work rate sequence.

(c) Random work rate forcing with random CO\(_2\) inhalation: The same pseudorandom sequences as described above were imposed on each subject simultaneously.

The data obtained from the respiromonitor were analysed by a digital computer system (DEC VAX 11/750). The data obtained during the first 5 min of each trial were discarded and the data obtained during the subsequent 25 min. were analysed. The TIMSAC (time series analysis and control) computer program package written by Akaike and Nakagawa (1972) was used.

The frequency domain characteristics of work rate fluctuation are presented in Fig. 2. This figure shows the power spectral density for work rate fluctuation. The point at which the power dropped below the 3 dB level, i.e. the half-power point, was considered to represent the upper limit of useful frequencies. This point lies approximately at the frequency of 1 cycle min\(^{-1}\). The power band is slightly narrower than that of the pseudorandom sequence described by Bennett et al. (1981).

Analysis of the correlation coefficients of the residuals (innovation) is useful for the selection of system variables to be used eventually. Initially, we took ventilation \( (V_e) \), gas exchange variables \( (V_{O_2}, V_{CO_2}, F_{ETCO_2}) \), heart rate and work rate. Heart rate was chosen to examine the influence of cardiodynamic changes on ventilation. The cross-correlation coefficients of the residuals normalised by the autocorrelation of the residuals were as shown in Table 2. In all subjects, the residuals of \( V_e, V_{O_2} \) and \( V_{CO_2} \) showed a strong correlation. Several laboratories have taken the good correlation between \( V_e \) and \( V_{CO_2} \) as suggestive evidence of some underlying CO\(_2\) linked control mechanism that can operate independently of the mean level of \( P_{aCO_2} \). However, causality cannot be discriminated between them, and it is also possible that some of the apparent correlation is due to a common signal that drives

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**Table 1 Physical characteristics and anaerobic thresholds for each subject**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>AT (W)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. K.</td>
<td>25</td>
<td>65</td>
<td>170</td>
<td>&gt;100</td>
</tr>
<tr>
<td>O. N.</td>
<td>27</td>
<td>54</td>
<td>171</td>
<td>100</td>
</tr>
<tr>
<td>K. H.</td>
<td>25</td>
<td>73</td>
<td>170</td>
<td>140</td>
</tr>
<tr>
<td>N. M.</td>
<td>29</td>
<td>56</td>
<td>171</td>
<td>120</td>
</tr>
<tr>
<td>H. N.</td>
<td>27</td>
<td>65</td>
<td>174</td>
<td>120</td>
</tr>
</tbody>
</table>

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Fig. 1 Block diagram of system identification process

Fig. 2 Normalised power spectral density for the input signal (random binary work rate forcing). Upper limit of useful frequency content is that frequency at which the power falls below the 3 dB level.