A New Model for Oxygen Uptake Kinetics in Heavy Exercise

Tokuo YANO*1, Hisayoshi OGATA*2, Takahiro YUNOKI*3 and Masaki ABE*4

Background: We simulated the kinetics of oxygen uptake ($\dot{V}O_2$) in heavy exercise using the sum of slow and fast components of $\dot{V}O_2$ that are formed by the following model structure. After the onset of exercise, $\dot{V}O_2$ in subunits (sub-$\dot{V}O_2$) participating in work increases. When these subunits cease to take part in the work and other subunits become involved in the work, sub-$\dot{V}O_2$ gradually decreases in the subunits that have ceased to take part in the work and starts to increase in the subunits that have started to participate in the work. Sub-$\dot{V}O_2$ is added during this relay of subunits.

Methods: To form the fast component, the kinetics of sub-$\dot{V}O_2$ is assumed to be symmetric at the on- and offset of exercise. To form the slow component, the kinetics of sub-$\dot{V}O_2$ is assumed to be asymmetric. $\dot{V}O_2$ kinetics actually measured was analyzed using a mathematical model to obtain the basic parameters for the simulation. Since the structure of the model for the simulation differs from that of the mathematical model, we selected the values of parameters obtained in the mathematical model so as to fit to the present model structure.

Results: The $\dot{V}O_2$ kinetics simulated is coincident with the $\dot{V}O_2$ kinetics actually measured not only in exercise but also during recovery.

Conclusion: $\dot{V}O_2$ kinetics in heavy exercise can be constructed by the model structure proposed in the present study and by selecting the data analyzed by the mathematical model.

Key words: model, fast component, slow component, oxygen uptake, exercise.

In the moderate exercise, oxygen uptake ($\dot{V}O_2$) becomes constant after an initial rapid increase (fast component), whereas $\dot{V}O_2$ in the heavy exercise shows a gradual increase (slow component) after the initial rapid increase[1,2,3,4]. The $\dot{V}O_2$ kinetics in the heavy exercise has been studied using mathematical models. In one model, the gradual increase is usually expressed as an increase added the rapid increase, i.e., two components have time delay[1,2,3,4]. In another model, $\dot{V}O_2$ kinetics is separated into two components of fast and slow, i.e., two components start at the same time [5,6]. The former model is generally used in recent years. However, not all researchers agree with the concept of a delay onset[7]. There is still debate over whether the two phases are physiologically best described with common or independent time delay.

*1 矢野徳郎　北海道大学大学院教育学研究科　教授
*2 尾方寿好　北海道大学大学院教育学研究科　博士課程３年
*3 柚木孝敬　北海道浅井学園大学生涯学習システム学部　講師
*4 阿部匡樹　国立身体障害者リハビリテーションセンター研究所　研究員

We used the mathematical model with common time delay and examined the relation between the magnitude of the slow component and the muscle fatigue[8]. It was found that maximal power output (MPO) exerted immediately after the end of the exercise reduced from resting level due to muscle fatigue during heavy exercise and the reduction of MPO was significantly related to the magnitude of the slow component of $\dot{V}O_2$. The results were interpreted as follows: Phosphocreatine (PCr) re-synthesis would be slow in fast twitch fibers[9] and newly working muscle fibers instead of fatigued muscle fibers (fast muscle fibers) would start to consume PCr, resulting in accumulation of creatine (Cr). Since Cr is thought to be a controller of $\dot{V}O_2$[10], the increased level of Cr would cause an increase of $\dot{V}O_2$.

Although mathematical expressions in the models inherit the structure of $\dot{V}O_2$ kinetics, its structure is different from that of the above-mentioned interpretation. However, we do not have a mathematical model with the structure proposed in the present study. Therefore, we made the simulation instead of the mathematical model. The simulated $\dot{V}O_2$ kinetics was, then, compared with actual data so as to examine whether the structure of the model proposed in the present study is proper in quantity.

Methods

Analysis of actual data of $\dot{V}O_2$

We analyzed the $\dot{V}O_2$ kinetics in heavy exercise using the mathematical model to obtain the values of parameters for the simulation. For this purpose, we selected a typical result of $\dot{V}O_2$ kinetics from our experiments. In this experiment, a cycle ergometer was used for the load, with work at zero watts before and after the main exercise and at 170

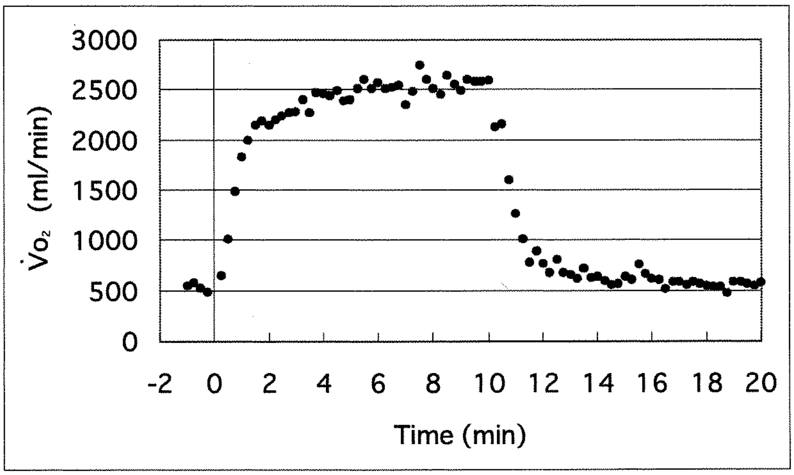

Fig. 1. Oxygen uptake measured in heavy exercise. Exercise before and after the main exercise was performed at zero watts. Main exercise was performed at 170 watts.

watts during the main exercise. This load corresponded to VT + 0.25 · ($\dot{V}O_2$peak - VT), where VT is the value of $\dot{V}O_2$ at ventilatory threshold and $\dot{V}O_2$peak is the peak value determined in incremental exercise. $\dot{V}O_2$ kinetics is shown in Figure 1. Data are output every 15 sec. $\dot{V}O_2$ at work above zero watts was approximated by the following equation[5,6]:

$$\dot{V}O_2\ (t) = A_1 \cdot (1-\exp(-(t-TD)/\tau_1)) + A_2 \cdot (1-\exp(-(t-TD)/\tau_2)) \quad (1)$$

where A is the amplitude of the system, TD is time delay, τ is the time constant of the system and t is the time.

$\dot{V}O_2$ after the loaded cycling was approximated by the following equation[11]:

$$\dot{V}O_2\ (t) = \dot{V}O_2\text{end} - (A_1 \cdot (1-\exp(-(t-TD)/\tau_1)) + A_2 \cdot (1-\exp(-(t-TD)/\tau_2))) \quad (2)$$

where $\dot{V}O_2$end is the above-zero-watts $\dot{V}O_2$ just before completion of exercise at 170 watts.

$\dot{V}O_2$ kinetics for 3 min after start of the exercise was also approximated by the following equation.

$$\dot{V}O_2\ (t) = A_1 \cdot (1-\exp(-(t-TD)/\tau_1)). \quad (3)$$

The initial $\dot{V}O_2$ values in the main exercise and recovery periods were not included in the approximation data in order to eliminate the effect on approximation of the initial cardiodynamic phase of $\dot{V}O_2$ response[3,12].

As shown in the simulation results of Figures 3 and 4, there is a fluctuation in $\dot{V}O_2$ kinetics corresponding to delay interval (see detail in results). Therefore, we determined the fluctuation in $\dot{V}O_2$ kinetics actually measured. First, the differences between the values of $\dot{V}O_2$ during exercise and the values obtained by Eq.(1) were calculated (residual). Second, three-points moving average was obtained to smooth data of residuals (Fig. 2). A power spectrum of the residuals before averaging was also obtained by fast Fourier transformation (FFT: Fig. 2).

Simulation

We hypothesized that the oxygen uptake not only consists of the oxygen uptake related to work but also the oxygen debt during recovery from fatigue occurring in some muscle fibers (subunit) during exercise. The following simulation was performed: Exercise was assumed to continue by a relay of subunits. The oxygen uptake kinetics in a subunit was assumed to exponentially increase for on-transition and to exponentially decrease for off-transition (sub-$\dot{V}O_2$). When a subunit is relayed, sub-$\dot{V}O_2$ at the offset of the preceding subunits is added to sub-$\dot{V}O_2$ at the onset of the on-going subunit (relay-$\dot{V}O_2$). Based on these serial summations, we calculated the kinetics of relay-$\dot{V}O_2$ shown as open triangles in the upper panel of Figure 3. Exercise duration was set at 10 min. Therefore, relay-$\dot{V}O_2$ kinetics after 10 min expresses the recovery phase (lower panel of Fig. 3). The relay-$\dot{V}O_2$ during recovery was calculated by summing the sub-$\dot{V}O_2$ at the offset of each subunit at a given recovery time.

The quantitative calculation is as follows: It was assumed that the sub-$\dot{V}O_2$ kinetics of a subunit increases for on-transition as represented by the following equation:

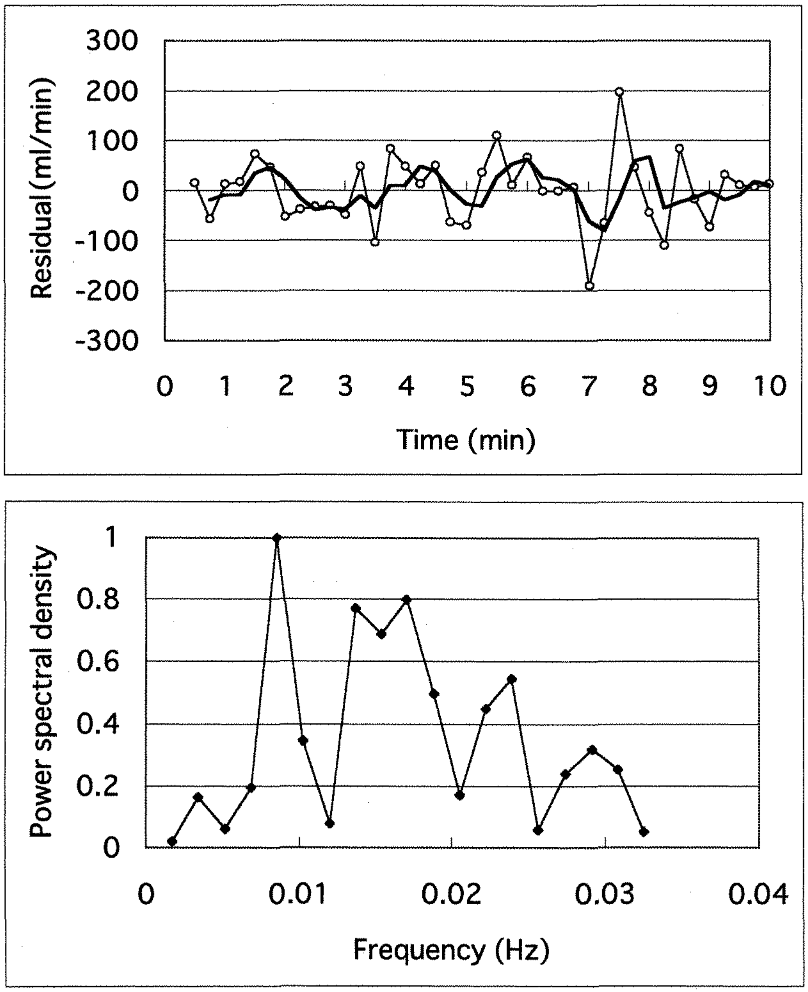

Fig. 2. Differences between values of oxygen uptake obtained by the approximation equation and measured values (residual). Three-pointmoving averages are connected by a thick line (upper panel). Power spectrum is normalized by maximal value (lower panel).

$$\text{Sub-}\dot{V}o_2\ (t) = A \cdot (1 - \exp(-(t - D \cdot (n-1)/\tau)) \tag{4}$$

$D \cdot (n-1) < t < D \cdot n$

where A is the amplitude of the system, τ is the time constant of the system, D is the relay interval, n is the number of subunit order and t is time. $D \cdot (n-1)$ is a parameter for converting the real time to the time in the subunit. For example, if the relay interval is 0.5 min and the order of subunit is the 5th, the working time of the 5th subunit ranges from 2 min to 2.5 min and Eq.(4) becomes $A \cdot (1 - \exp(-(t-2)/\tau)$. When the time passing from the start of the exercise is 2 min, the time passing within the 5th subunit becomes 0 min.

Sub-$\dot{V}o_2$ kinetics for off-transition is represented by the following equation:

$$\text{Sub-}\dot{V}o_2\ (t) = \dot{V}o2end \cdot \exp(-(t - D \cdot n)/\tau) \tag{5}$$

$D \cdot n < t$

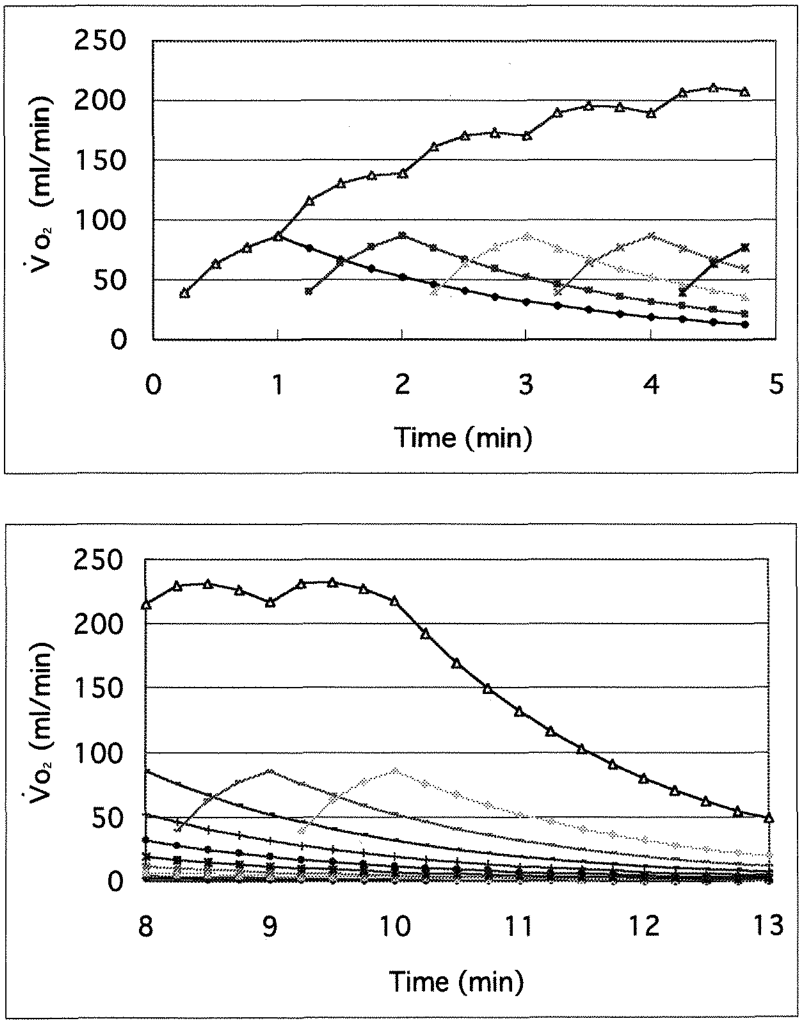

Fig. 3. Kinetics of oxygen uptake at the on- and offset of subunit. The subunit is relayed at 1-min intervals. The upper panel shows simulation at the beginning of exercise. Oxygen uptake kinetics at the onset of subunit ends at 1 min and enters the recovery phase. The oxygen uptake kinetics in the next subunit starts from the beginning of this recovery phase. At this time, summation of oxygen uptake of subunits occurs. The totals of these serial summations are shown by open triangles as the relay oxygen uptake. The lower panel shows simulation at the ending of exercise and simulation during the recovery phase after 10 min exercise. Note that only oxygen uptake at the offset of subunit is summed during the recovery.

where $\dot{V}o_2$end is the value of $\dot{V}o_2$ at the end of exercise in the subunit. D・n is also a parameter for converting the real time to the recovery time in the subunit. Sub-$\dot{V}o_2$ for off-transition starts at the end of the subunit's activity and continues until its value becomes zero.

Figure 3 shows the sub-$\dot{V}o_2$ kinetics when the amplitude is 100 ml/min, the time constant at the onset of subunit is 0.5 min, the time constant at the offset of subunit is 2.0

min and the relay interval is 1.0 min. Relay-$\dot{V}O_2$ at a given time is the sum of sub-$\dot{V}O_2$ for on-transition of the ongoing subunit and sub-$\dot{V}O_2$ for off-transition of the preceding subunits.

Parameter values used in the simulation for basic kinetics

The amplitude of $\dot{V}O_2$ kinetics for the subunit was 100 ml/min. The time constant at the onset of subunit was set at 0.5 min in the simulation. We referred to the time constant actually determined for the initial 3 min (Table 1). Time constants at the offset of subunit were set at 0.5, 1.0 and 2.0 min in the simulation. We referred to the actual time constants of fast and slow components at the offset of exercise (Table 1).

Figure 2 shows the residuals. The moving average of the residuals between these values appears to fluctuate periodically (at approximation 2-min intervals). The lower figure shows a power spectrum obtained by FFT. The peak appears when the wavelength is about 2 min. Shorter wavelengths can be seen. Therefore, three intervals of subunit relay (0.5, 1.0 and 2.0 min) were used in the simulation. Exercise duration which is the sum of relay intervals was set at 10 min. Therefore, kinetics after 10 min expresses the recovery phase.

Parameter values used in simulation for fast and slow components

The amplitude of subunit was 1400 ml/min. The time constant was set at 0.5 min at the onset of subunit and at 0.5 min at offset of subunit. Using these values, sub-$\dot{V}O_2$ kinetics for on- and off-transitions was calculated. Then, relay-$\dot{V}O_2$ kinetics was calculated by summation of sub-$\dot{V}O_2$. Relay-$\dot{V}O_2$ during exercise was defined as the fast component for on-transition (fast on-component) and relay-$\dot{V}O_2$ during recovery was defined as the fast component for off-transition (fast off-component).

The amplitude of subunit was 300 ml/min. The time constant of subunit was set at 0.5 min at the onset of subunit and at 2 min at the offset of the subunit. Using these values, sub-$\dot{V}O_2$ kinetics was calculated. Then, relay-$\dot{V}O_2$ kinetics was calculated by summation of sub-$\dot{V}O_2$. Relay-$\dot{V}O_2$ during exercise was defined as the slow component for on-transition (slow on-component) and relay-$\dot{V}O_2$ during recovery was defined as the slow component for off-transition (slow off-component).

Table 1. Parameters obtained from oxygen uptake kinetics measured in exercise and recovery.

	fast component		slow component		
	A_1	t_1	A_2	t_2	TD
	l/min	min	l/min	min	min
Exercise	1.76	0.48	—	—	0.34
	1.38	0.34	0.72	2.75	0.36
Recovery	1.67	0.44	0.36	1.98	0.37

Three relay intervals were used (0.5, 1.0 and 2.0 min) to compare the fitting for $\dot{V}O_2$ kinetics actually measured.

Results

Effects of time constant at the offset of subunit and relay interval.

Figure 4 (upper figure) shows the kinetics of relay-$\dot{V}O_2$. The amplitude of sub-$\dot{V}O_2$ was set at 100 ml/min and the time constant for on-transition was set at 0.5 min. The effects of the time constant of sub-$\dot{V}O_2$ for off-transition (0.5, 1.0 and 2.0 min) on relay-$\dot{V}O_2$ are shown in each panel. The upper, middle and lower panels show the relay-$\dot{V}O_2$ in the cases of an interval of 0.5, 1.0 min and 2.0 min, respectively. When the time constants of sub-$\dot{V}O_2$ for on- and off-transitions were the same, the relay-$\dot{V}O_2$ kinetics was the same as the originally assumed sub-$\dot{V}O_2$ kinetics. However, when the time constant for sub-$\dot{V}O_2$ for off-transition was longer than that for on-transition, the relay-$\dot{V}O_2$ kinetics was greater than the amplitude of the originally assumed sub-$\dot{V}O_2$ kinetics (100 ml/min). Moreover, the relay-$\dot{V}O_2$ increased rapidly when the relay interval was short. Fluctuation in relay-$\dot{V}O_2$ was observed. When the interval became longer, both the wavelength and wave-amplitude of relay-$\dot{V}O_2$ fluctuation increased.

The relay interval of subunit did not affect the recovery time. The recovery time of relay-$\dot{V}O_2$ was related to the value of the time constant assumed in sub-$\dot{V}O_2$ for off-transition. When time constants of sub-$\dot{V}O_2$ for off-transition were 0.5 1.0 and 2.0 min, the recovery times were 2.0, 4.0 and 8.0 min, respectively.

Simulation for fast and slow components

Figure 5 shows $\dot{V}O_2$ kinetics for the fast component, slow component and sum of their components. The approximated values at the end of exercise decreased as the relay interval increased. Flexion points were recognized when intervals were one or two min. Thereafter wave appeared. Its wavelength was interval dependent. Thus, in the graphs, it seems that the $\dot{V}O_2$ kinetics before and after 2 min are different. The recovery times for the fast and slow off-components were 2 and 8 min, respectively.

Figure 6 shows the sum of the slow and fast components obtained from the simulation and the actually measured values of $\dot{V}O_2$ kinetics. Since the measured values include a time delay from active muscles to the lungs, the simulation values were plotted with 15 sec delay after the onset of exercise. In the initial stage of exercise, the values obtained under the three simulation conditions were coincident with the measured values. In the latter half of the exercise period, the approximated values obtained from the simulation were higher than the measured values when the relay interval was 0.5 min, almost the same as the measured values when the relay interval was 1.0 min, and lower than the measured values when the relay interval was 2.0 min. When simulated $\dot{V}O_2$ at 10 min during the exercise was high, the simulated $\dot{V}O_2$ in the first half of the recovery was high, and when

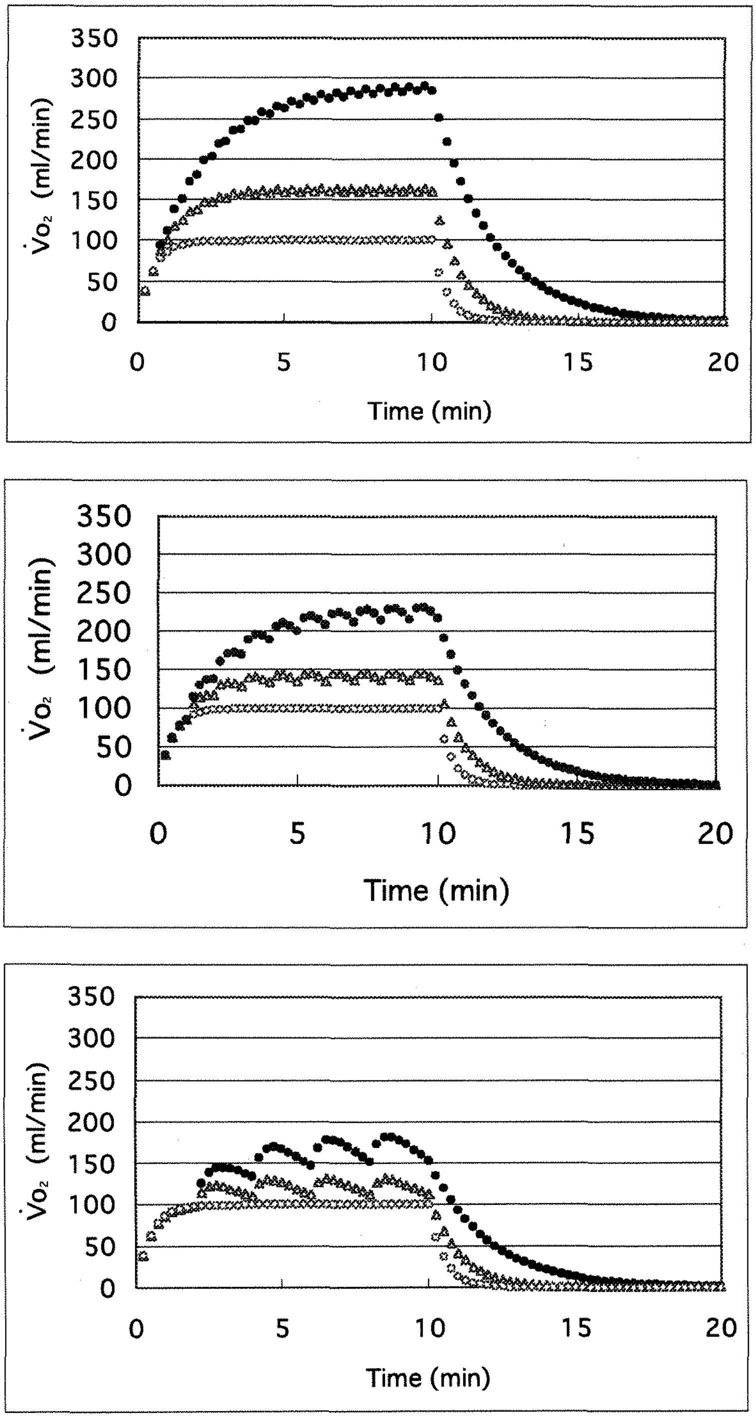

Fig. 4. Effects of the relay interval and time constant at the offset of subunit on relay oxygen uptake. The relay oxygen uptake kinetics calculated with the time constant of subunit for off-transition set at 0.5 (○), 1.0 (△) and 2.0 min (●) are shown. The upper, middle and lowerpanels show the oxygen uptake kinetics when the relay interval was set at 0.5, 1.0 and 2.0 min, respectively.

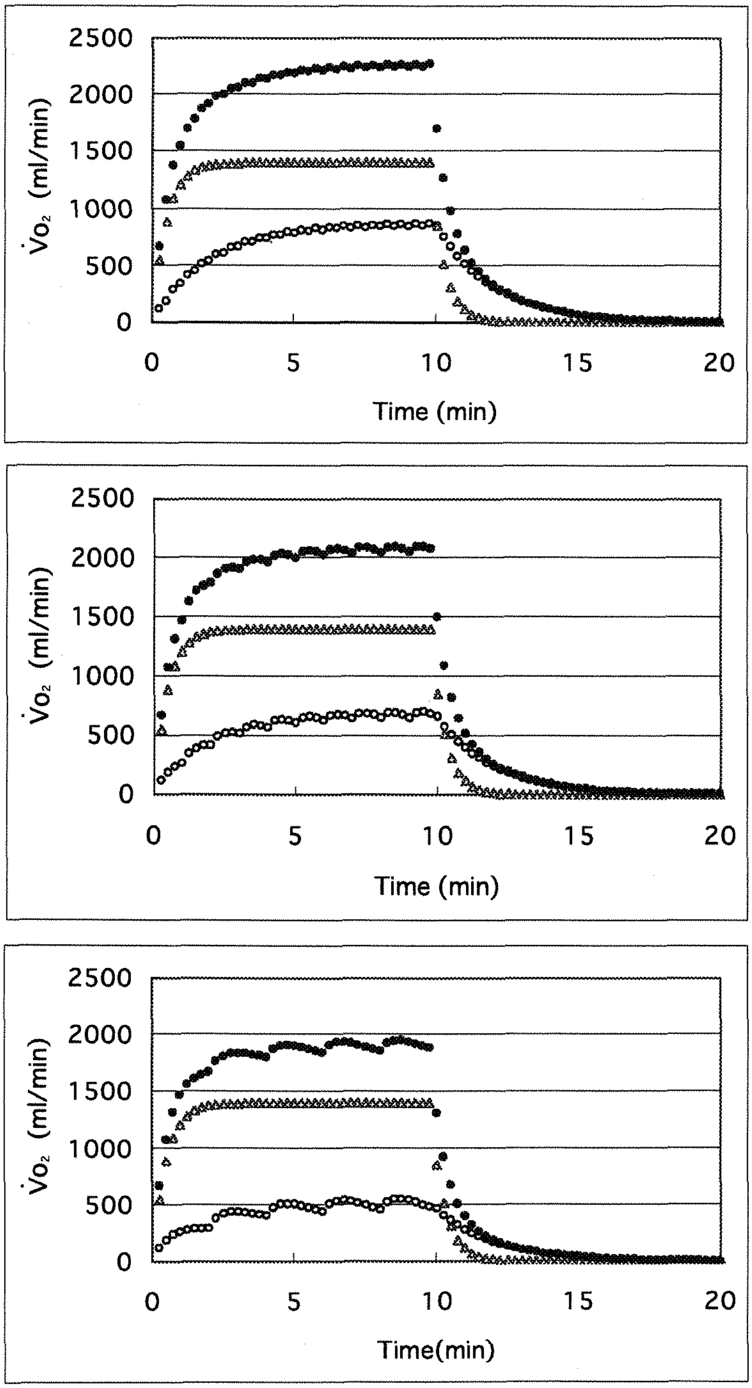

Fig. 5. Simulatd values of oxygen uptake kinetics in the slow component (○) and fast component (△). The solid circles show the summed values of oxygen uptake kinetics in the slow and fast components. The oxygen uptake kinetics for the slow component was calculated with a time constant of 2 min for offset of subunit. The oxygen uptake kinetics calculated with relay intervals of 0.5, 1.0 and 2.0 min are shown in the upper, middle and lower figures, respectively (See text for details.).

it was low, the value of the first half was low. However, in the latter half of the recovery period, the simulated values were almost the same as the measured values in all cases.

Discussion and conclusions

As the structure of the present model is different from that of the mathematical model concerning the beginning of exercise, the time constants obtained by separation using the mathematical model were not used in the present study. Instead, we adapted the time constants of 0.5 min to form slow and fast on-components. As the time constant at the onset of moderate exercise is reported to be around 0.5 min[3], this value is acceptable for the fast component. In the present study, the time constant was determined at the onset of exercise for 3 min. This value was around 0.5 min. Therefore, we selected the value of 0.5 min to form the slow on-component. Otherwise, the time constant to form the sum of the fast and slow on-components becomes a different value from 0.5 min.

In the present study, simulation of the $\dot{V}O_2$ kinetics was carried out with amplitudes to form the fast and slow on-components set at 1400 ml/min and 300 ml/min, respectively. The amplitude of the fast on-component determined using the mathematical model was used as the amplitude of sub-$\dot{V}O_2$ while the time constant determined was not used as the time constant of sub-$\dot{V}O_2$. We considered that kinetics of the fast on-component estimated using the mathematical model is misleading at the beginning of the exercise but becomes the proper value at the end of exercise. The amplitude of 300 ml/min was obtained by subtracting the amplitude (1400 ml/min) of the fast on-component from the amplitude (1700 ml/min) estimated in actual $\dot{V}O_2$ kinetics for the initial 3 min. The estimated amplitude was used because the gain that is obtained by dividing the amplitude estimated by the work rate performed is coincident with the reported ones[3,13].

The time constant at the offset of subunit to form the slow on-component was set at 2 min. This was derived from the values determined in recovery $\dot{V}O_2$ using the mathematical model. It has been reported that the slow off-component is not observed in the recovery period following moderate or heavy exercise but the slow off-component can be observed in the recovery period following exercise of greater intensity[3]. On the other hand, it has been reported that the slow off-component appears in the recovery period following heavy exercise[1,11], although the range of time constants obtained in those studies is large. The time constants used in the present study are not as long as those obtained in early studies but are not exceptionally short compared to those obtained in recent studies[14].

The fast on-component was obtained using the same time constants at the on- and offset of subunit. Therefore, relay-$\dot{V}O_2$ is not affected by the relay. Since the slow on-component was obtained using different time constants at the on- and offset of subunit, relay-$\dot{V}O_2$ can be affected by the relay. A relay interval of 1-2 min seemed appropriate for comparison of the measured and simulated values. Moreover, in the measured values of

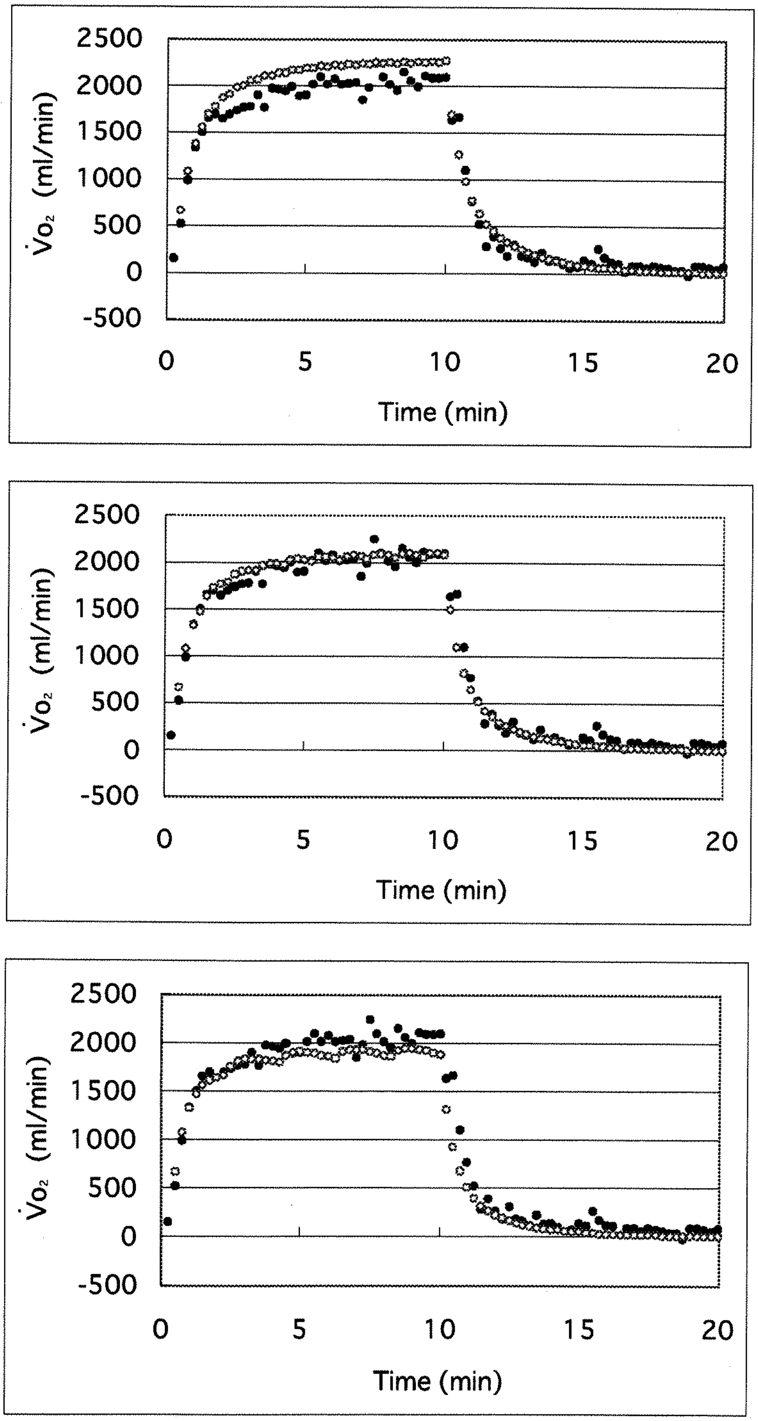

Fig. 6. Comparison of measured values and values obtained by simulation. The values obtained by simulation are the same as those shown in Fig. 5. The values calculated with relay intervals of 0.5, 1.0 and 2.0 min are shown in the upper, middle and lower figures, respectively. Talking into account the time delay included in the measured values, the simulation values were plotted from 15 sec after the onset of exercise.

$\dot{V}O_2$ kinetics, a flexion point was observed at 2 min (Fig. 1). In previous reports, this flexion point was regarded as the point of increase in additional $\dot{V}O_2$ or, in other words, the starting point of the slow on-component although this is not clearly referred to in the literature[1,2,11]. Judging from the results of the simulation, this view may have arisen because the time when the first or second relay occurred was regarded as the starting point of the slow on-component.

To form the fast on-component, the kinetics of sub-$\dot{V}O_2$ was assumed to be symmetric at the on- and offset of exercise. To form the slow on-component, the kinetics of sub-$\dot{V}O_2$ was assumed to be asymmetric. Time constants at the offset of subunits to form the fast and slow on-components were the same. Relay of subunit was taken into the present model. We selected some of the parameter values obtained using the mathematical model to simulate $\dot{V}O_2$ kinetics in heavy exercise. None of the values of parameters obtained using the mathematical model were used for the simulation since the structure of the present model was different from that of the mathematical model. The $\dot{V}O_2$ kinetics simulated was coincident with the $\dot{V}O_2$ kinetics actually measured not only in exercise but also during recovery. $\dot{V}O_2$ kinetics in heavy exercise can be constructed by the model structure proposed in the present study and by selecting the data analyzed by the mathematical model.

References

1. Barstow TJ, Jones AM, Nguyen PH, Casaburi R. Influence of muscle fiber type and pedal frequency on oxygen uptake kinetics of heavy exercise. J Appl Physiol 1996; 81: 1642-1650.
2. Barstow TJ, Mole PA. Linear and nonlinear characteristics of oxygen uptake kinetics during heavy exercise. J Appl Physiol 1991; 71: 2099-2106.
3. Ozyener F, Rossiter HB, Ward SA, Whipp BJ. Influence of exercise intensity on the on- and off-transient kinetics of pulmonary oxygen uptake in humans. J Physiol (Lond) 2001; 533: 891-902.
4. Scheuermann BW, Hoelting BD, Noble ML Barstow TJ. The slow component of O_2 uptake is not accompanied by changes in muscle EMG during repeated bouts of heavy exercise in humans. J Physiol (Lond) 2001; 531: 245-256.
5. Casaburi R, Barstow TJ, Robinson T, Wasserman K. Influence of work rate on ventilatory and gas exchange kinetics. J Appl Physiol 1989: 67; 547-555.
6. Capelli C, Antonutto G, Zamparo P, Girardis M, diPrampero PE. Effects of prolonged cycle ergometer exercise on maximal muscle power and oxygen uptake in humans. Eur J Appl Physiol 1993: 66; 189-195.
7. MacDonald M, Pedersen PK, Hughson RL. Acceleration of $\dot{V}O_2$ kinetics in heavy submaximal exercise by hyperoxia and prior high-intensity exercise. J Appl Physiol 1997; 83: 1318-1325.
8. Yano T, Yunoki H, Ogata H. Relationship between the slow component of oxygen uptake and the potential reduction in maximal power output during constant-load exercise. J Sport Med Phys Fitness 2001; 41: 165-169.
9. Kushmerick MJ, Meyer RA, Brown TR. Regulation of oxygen consumption in fast- and slow- twitch muscle. Am J Appl Physiol 1992: 263 (Cell Physiol 32); C598-C606.
10. Mahler M. First-order kinetics of muscle oxygen consumption and an equivalent proportionality between QO_2 and phosphorylcreatine level. J Gen Physiol 1985: 86; 135-165.
11. Bearden SE, Moffatt RJ. $\dot{V}O_2$ kinetics and the O_2 deficit in heavy exercise. J Appl Physiol 2000; 88: 1407-

1412.
12. Whipp BJ, Ward SA, Lamarra N, Davis JA, Wasserman K. Parameters of ventilatory and gas exchange dynamics during exercise. J Appl Physiol: Respirat Environ. Exercise Phyiol 1982; 52: 1506-1513.
13. Henson LC, Poole DC, Whipp BJ. Fitness as a determination of oxygen uptake response to constant-load exercise. Eur J Appl Physiol 1989; 58: 21-28.
14. Cunningham DA, St Croix CM, Paterson DH, Ozyener F, Whipp BJ. The off- transient pulmonary oxygen uptake ($\dot{V}o_2$) kinetics following attainment of a particular $\dot{V}o_2$ during heavy-intensity exercise in humans. Exp Physiol 2000; 85: 339-347.