Comparisons of VO₂ Kinetics in Moderate-Intensity Exercise Transitions in Highly-Trained and Untrained Subjects

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ABSTRACT

McNulty CR, Robergs RA. Comparisons of VO₂ Kinetics in Moderate-Intensity Exercise Transitions in Highly-Trained and Untrained Subjects. JEPonline 2017;20(1):249-263. The purpose of this study was to assess measures of the time taken for subjects of different training status to reach steady-state VO₂, using a traditional data processing model and a new model. Two groups of subjects were recruited: an untrained (UT) (n = 7), and a highly-trained (HT) cyclist group (n = 9). Following a maximal cycling test to exhaustion to ascertain ventilation threshold (VT), each subject underwent two cycling trials. Trial 1 consisted of an exercise transition to 85% VT. Trial 2 involved a transition to 35% VT for 6 min, followed by a 2nd transition to 85% VT. 3-breath averaged data were fit using the traditional mono-exponential model to ascertain both tau and 4xtau, and using a new method (TTSS) to derive the time taken to reach steady-state. 4xtau (4τ) and TTSS values were statistically analyzed for comparison and validity of tau. As well, differences in tau and TTSS values between the groups were assessed. There were significantly lower values for TTSS compared to 4τ for all trials. For the 85% VT exercise transitions, TTSS remained invariant between both trials. However, 4τ increased significantly for the transition from a baseline compared to the transition from unloaded cycling. These results indicate a necessity to propose new methods of VO₂ kinetics data processing.

Key Words: Mono-Exponential, Trained, Untrained, VO₂ Kinetics
INTRODUCTION

The kinetic response of oxygen uptake (VO$_2$) following an exercise transition to steady-state has been routinely modelled using a mono-exponential equation, which incorporates a time constant [tau; τ] (42-46). The equation is as follows:

\[ VO_2(t) = VO_2(ss)(1 - e^{-kt}) \]

Regarding the equation, \( VO_2(t) \) represents oxygen uptake above resting value at any time \( t \) after the onset of exercise, \( VO_2(ss) \) is the steady state value (above rest) for oxygen consumption, and \( k \) is the rate constant of the reaction with the dimension of time. Here, the rate constant denotes the inverse of \( \tau \) – that is, \( \frac{1}{k} \times 60 = \tau \) (32). From this equation, \( \tau \) is 63% of the overall VO$_2$ response amplitude (19,29,32,44). It is also commonly agreed that the time taken for an individual to reach a steady-state VO$_2$ following an exercise transition is equal to \( 4\tau \) (26). Figure 1 represents multiples of \( \tau \) as subsequent gains of \(~63\%\) of the remaining amplitude. That is, \(~63\%, ~86\%, ~95\%,\) and \(~98\%\) of the response accounts for \( \tau \), \( 2\tau \), \( 3\tau \), and \( 4\tau \), respectively.

[Figure 1. Graphical Representation of the Multiple \( \tau \) Values as They Account for \(~63\%\) of the Remaining Amplitude of the Response Over Time. It is commonly agreed that \( 4\tau \) is the completion of the response, and therefore equates to time take to reach steady state VO$_2$ (26).]

Generally, the mono-exponential model is applied to the phase-II VO$_2$ response of sub-threshold exercise transitions. However, some studies (especially those using supra-threshold exercise transitions, which exhibit a phase-III slow component) have used a two-
component model (31,33,37) or a three-component model (28,29,33) to include either phase-I or a phase-III slow component or both. As well, some researchers have applied a time delay component to the mono-exponential function to account for the phase-I response (24,45). Clearly, the mono-exponential model has been modified (or had additions made) in order to suit differing VO$_2$ kinetic responses. However, even with its versatile use over the past four decades, the mono-exponential model has yet to be explicitly validated. This is all the more problematic when past research exists that questions the validity of using a simple mono-exponential model to explain the behavior of VO$_2$ kinetics (9,25,30,32,34,35,41).

Past research has examined the VO$_2$ kinetic differences between differing training statuses of groups of subjects (10,11,18,22,23,30,36,38,48). Hickson et al. (23) and Hagberg et al. (22) described a more rapid VO$_2$ kinetics response in trained subjects for a relative workload, compared with less-trained subjects. Morgan et al. (36), following the discussion of some past research of the time, concluded that less-trained individuals will incur an increased relative aerobic demand than higher trained subjects, resulting in a slower VO$_2$ kinetic response to exercise. Casaburi et al. (10), Zhang et al. (48), and Phillips and colleagues (38) demonstrated that endurance exercise training has a positive effect on the reduction of time taken to reach steady state, per the application of a mono-exponential model. Phillips et al. (38) further demonstrated that increases in the rapidity of the VO$_2$ kinetic response can occur in as early as a week in a 30-day endurance training study, and is therefore not reserved for experienced athletes.

The non-homogeneity and small sample sizes ($n = \sim 4$ to 7) of past VO$_2$ kinetics research was addressed by Koppo et al. (30). They set out to investigate the interaction of exercise intensity and training status in the determination of $\tau$, specifically using a homogenous subject cohort of eight trained and seven untrained subjects. There were two key findings in their paper. First, and supporting the above-mentioned literature, $\tau$ became progressively slower as exercise intensity increased. Again, the mono-exponential model was traditionally built on the basis that it behaves as a linear first order system, where the increase in $\tau$ should not occur. Second, it was shown that the VO$_2$ kinetic response was faster in the trained group compared with the untrained group.

McNulty et al. (35) designed a custom computer program intended to quantify a true time to steady-state (TTSS) for sub-threshold exercise transitions. The software used a method of back-extrapolation of the phase-III steady-state value for an exercise transition (using the final $\sim 3$ min of the response), with the application of a 2nd order polynomial function from the onset of an increase in workload to a user-defined endpoint. This endpoint was computer calculated as the final data point (using breath by breath data) of phase-II, which was defined as the closest point (along the $y$-axis) to the linear steady-state response. The time (measured from the $x$-axis) required to reach steady-state was calculated at this point. See Figure 2 for a visual representation of the TTSS application.
Figure 2. Application of TTSS Software to the Breath by Breath VO₂ Kinetic Response of a Subject Cycling at 75% of Ventilation Threshold. The exercise transition begun at 200 sec, following baseline measures. Note that “a” represents the time taken for a subject to reach state, which is indicated with the intersection of the back-extrapolated linear regression and the 2nd order polynomial, and “b” represents an overlay of the traditional mono-exponential model to the same data set.

It is evident that current methods of VO₂ kinetics data processing are in need of validation and, if necessary, reconstructing. The aims of this study were to: (a) compare values of τ and 4τ to those of TTSS for a group of highly-trained cyclists and a group of untrained subjects; and (b) assess the speed of the VO₂ kinetics response of all subjects while making mean comparisons between the highly-trained and untrained groups. We hypothesized that: (a) 4τ would not be representative of TTSS and would in-fact be an over-estimation; and (b) as a mean, highly-trained subjects will have a faster VO₂ kinetic response to an identical relative increment in intensity than untrained subjects.

METHODS

Subjects
Sixteen male subjects (mean age = 26 ± 7.3 yrs; height = 178 ± 8.2 cm; weight = 78 ± 12.1 kg) were recruited and completed the exercise trials of this study. The criteria for recruitment were healthy males aged between 18 and 45 yrs who were free from musculoskeletal injury, the presence of cardio-pulmonary and/or metabolic disease or more than two risk factors for sedentary lifestyle diseases. Recruitment occurred at a country NSW university, local gymnasiums, and through the local cycling and running clubs. All subjects were asked to complete an Exercise and Sports Science Australia: Adult Pre-Screening System (16) tool to verify that they were in good physical health. Written informed consent was obtained from each subject prior to data collection. All methods were approved by the institution’s Human Research Ethics Committee.

The subjects were assigned to either a highly-trained group (HT) or an untrained group (UT). Subjects in the HT group were required to be active cyclists, preferably at competition level with a VO₂ max >60 mL·kg⁻¹·min⁻¹. Subjects in the UT group were not trained cyclists with a
VO₂ max <45 mL·kg⁻¹·min⁻¹. Following the VO₂ max testing, 9 subjects were recruited into the HT group (mean age = 24 ± 6.5 yrs; height = 180 ± 8.4 cm; weight = 73 ± 9.5 kg; VO₂ max = 67 ± 7.9 mL·kg⁻¹·min⁻¹; VT watts = 282 ± 29.8 W). Seven subjects were recruited into the UT group (mean age = 29.6 ± 7.9 yrs; height = 176 ± 7.8 cm; weight = 85 ± 12.1 kg; VO₂ max = 40 ± 4.6 mL·kg⁻¹·min⁻¹; VT watts = 182 ± 28 W).

Procedures
After completion of the informed consent, a familiarization session and a VO₂ max ramp protocol cycle ergometer test were administered for each subject. During the familiarization session, the subject’s height and mass were recorded. Also, the cycle ergometer’s seating and handle bar arrangement were adjusted for each subject’s preference and biomechanical needs. The adjustments were recorded and maintained for future exercise bouts. Before exercising, each subject was asked to remain seated for 5 min to get a resting heart rate (HR) measure. Then, the subject was asked to cycle at 50 W and 100 W (for UT and HT, respectively) for several minutes to establish a comfortable and constant pedalling cadence. The cadence was the set point for all testing per individual subject.

Prior to conducting the VO₂ ramp test and for all subsequent trials as well, the subject was fitted with a multiple one-way valve mouthpiece system supported by an acrylic head unit. Electrocardiography (ECG) was used to acquire heart rate throughout the VO₂ max test and steady state exercise trials using a 5-lead ECG configuration (CASE, GE Healthcare, Waukesha, USA). The ECG leads were attached using gel electrodes placed over the spine of both scapulae, the iliac crest of both ilia, and between the 4th and 5th intercostal space along the mid-axillary line of the left side of the torso.

For indirect calorimetry, expired gas analysis was acquired using a 3 L latex compliant and elastic mixing bag placed on the expired port of the mouthpiece. Mixed expired air was sampled continuously and pumped to rapid response oxygen and carbon dioxide gas analyzers (AEI Technologies, Pittsburgh, PA, USA). During and following each breath, the elastic recoil of the mixing bag caused air to be vented through a 1 cm diameter hole in the inferior end of the mixing bag. Expired gas signals were acquired from the latex mixing bag for 100 ms at the start of each inspired breath and aligned to the timing of end expiration based on a pre-determined measured time-delay. Ventilation was measured by a flow turbine (UVM, VacuMed, Ventura, CA, USA) connected to the inspired side of the mouthpiece. All data were acquired using custom developed software (LabVIEW™, National Instruments, Austin, TX) and commercial electronic acquisition devices (National Instruments, Austin, TX). The breath-by-breath system was calibrated before the ramp test and before each bout in both trials using a 3 L syringe and commercial medical grade calibration gas (16.00% oxygen and 5.00% carbon-dioxide). These methods are validated and described in more detail by Kim and Robergs (27).

Administration of the VO₂ ramp test had the subjects’ cycle at their predetermined cycling cadence, for which they were asked to maintain for the entire test. The ramp function was 20 W·min⁻¹ for the UT group, and 30 W·min⁻¹ for the HT group due to the need to keep the test between 8 and 12 min (2,6,47). The VO₂ ramp protocol consisted of 2 min of breathing while at rest to attain a baseline reading, followed by 2 min at double the ramp function Watts, and then followed by a near continuous ramp function (increment at 0.5 Hz). The subjects were
also instructed to continue cycling until volitional exhaustion (1). The test was terminated once the subject could no longer maintain a pedalling frequency of >40 rev·min⁻¹ (1).

Using the breath-by-breath VO₂ data collected from the ramp test, the VT of each subject was determined objectively by the ventilatory equivalent method (20) using a custom designed computer program (LabVIEW™, National Instruments, Austin, TX, USA). The VT was detected by the program through the user directed application of three linear segments to the data. The VT was computed as the time of the intersection between segment 1 (baseline response, slope ~ 0) and segment 2 (initial deviation from baseline). The detection of the VT required agreement between two investigators (agreement was set at ± 10 sec). Where there was opposing detection, a third researcher was asked to interpret the data. The VT was then used to determine the cycle ergometer power output required for the subsequent exercise trials.

Since this study focused on the comparison of less-trained subjects and highly-trained cyclists, two cycling trials were administered. The first exercise trial (T1) involved seated rest for 2 min, then 2 min of unloaded (0 W) cycling, followed by an increase to 85% VT for 6 min (ample time for the subject to reach steady state VO₂). The second trial (T2) involved seated rest for 2 min, then 2 min of unloaded (0 W) cycling, then an increase to 35% VT for 6 min, and finally an increase to 85% VT for 6 min. Throughout this paper, the initial 35% VT 6-min segment, and the following 85% VT 6-min segment of T2 will be referred to as T2a and T2b, respectively.

Each subject was fitted for indirect calorimetry and ECG prior to commencement of the exercise trial. A minimum time frame of 48 hrs separated the completion of the VO₂ ramp test and each subsequent trial day. The subjects remained seated on a chair between bouts, and only begun the next cycling bout once their HR had returned to within 10 beats·min⁻¹ of its rested value, and after at least 15 min had passed. This time frame was chosen since past research (8,21) has indicated that there is no significant effect of prior moderate intensity exercise on VO₂ kinetics in subsequent trials.

### Statistical Analyses

The raw breath-by-breath data, which included absolute and relative VO₂, respiratory exchange ratio (RER), and the ventilatory equivalent ratios for oxygen (O₂) and carbon dioxide (VE/VO₂ and VE/VCO₂ respectively) were processed using a 3-breath average from custom designed software (LabVIEW™, National Instruments, Austin, TX). Each trial text file was imported into a commercial graphics and curve fitting program (Prism, GraphPad Software, La Jolla, CA, USA), and data were removed for the initial rest data collection of each trial. The data were then graphed and the phase-I data were identified and removed for each trial. Initially, the whole data sets (phase-II and -III) were fit using the mono-exponential equation. From here, τ and 4τ values were recorded.

TTSS was quantified using custom software (LabVIEW™, National Instruments, Austin, TX). The breath averaged data for each exercise trial were first fit with linear regression over the last 3 min of data for each 6-min transition. A 2nd order polynomial function was then applied iteratively to the initial nonlinear phase of the VO₂ response. The program allowed a user controlled continuous data point increment for this data phase and the intersection of
the nonlinear function and the linear regression of steady state was detected (time with the lowest residual for VO$_2$ nonlinear – VO$_2$ linear) as the TTSS.

Statistical analysis of the data was performed using SPSS (IBM Corporation, New York, NY, USA). The subjects of this study completed two cycling trials. T1 involved a transition to 85% VT for 6 min, and T2 involved two consecutive transitions of 35% VT and 85% VT for 6 min each. The data was processed to ascertain time values (s) for $\tau$, 4$\tau$, and TTSS. To compare the time value of $\tau$ to TTSS, an analysis of variance (ANOVA) was used. A three-way mixed-design ANOVA (GROUP [2] x METHOD [2] x TRIAL [3]) was implemented to analyze 4$\tau$ and TTSS for both subject groups, in T1, T2a, and T2b. Following this, the two 85% VT increments of T1 and T2b were statistically analyzed using both modelling methods (4$\tau$ and TTSS) and no division between the HT and UT groups (data was reported as a mean value for both subject groups for each method). For this, a two-way ANOVA (METHOD [2] x TRIAL [2]) was used. Significance was set at P<0.05. All data are presented as mean ± SD.

RESULTS

For the mean 4$\tau$ and TTSS data for both HT and UT subject groups for all trials (T1, T2a, and T2b) in Figure 3, time was significantly lower for the TTSS values (main effect, P<0.001) compared with the 4$\tau$. There was a significant main effect (P<0.001) difference between the three trials for both 4$\tau$ and TTSS, as well as a significant interaction (P = 0.003) between trial and method. Overall, there was a decrease in time for both 4$\tau$ and TTSS for all three trials (T1, T2a, and T2b). There was no significant difference of the groups (HT and UT) for the 85% increment in T1 and T2b.

Figure 3. 4$\tau$ and TTSS Data for Both Subject Groups for All Three Trials (T1, T2a, and T2b). * = P<0.05 for 4 tau vs. TTSS; # = P<0.05 for trials 1 vs. 2 for TTSS.
Given the non-significant group effect, the group data were combined. For the mean combined group data \((n = 16)\) 4τ and TTSS comparisons between the two 85% VT exercise transitions (T1 and T2b) in Figure 4, there was no significant difference for TTSS. However, T2b was significantly larger \((P = 0.043)\) than T1 for the 4τ method. As well, there was a significant interaction \((P = 0.032)\) between methods and trials. Finally, there was also a significant \((P < 0.001)\) between the two methods.

**Figure 4. Mean Combined Groups Data for 4τ and TTSS for Both 85% VT Exercise Transitions (T1 and T2b).** * = P<0.05 for trials 1 vs. 2b for 4 tau; # = P<0.05 for main effect for method (4 tau vs. TTSS).

Displayed in Table 1 are the τ, 4τ, and TTSS data variables for the subjects completing all the exercise transitions. Although the results were not significant in analyzing comparisons of VO₂ kinetics speed between the HT and UT groups, the data does exhibit a notable trend for the HT group to have faster kinetics using measures of τ and TTSS.

**DISCUSSION**

In this study, we compared temporal values for two methods of calculating the time taken for a subject to reach steady state VO₂ following an exercise transition. One method involved the traditional use of a mono-exponential to derive a value for τ. Then, τ was multiplied by 4 to give a value 4τ, which is generally considered to be the completion of the mono-exponential model response and, therefore, is a good approximation of the time taken to reach steady state (26). The second method involved using a custom designed model that is applied as two separate components to the VO₂ kinetics data. There were three main findings in our results. First, and in line with our hypotheses, the calculation of 4τ in all trials revealed an over-estimate of the time taken to reach steady state VO₂ in both HT and UT groups. This is especially apparent in T2b, although it is still significant in all trials. Second, and also in line with our hypotheses and the results of past research, the speed of VO₂ on-kinetics was...
increased for the HT group compared with the UT group for all trials. Lastly, the 85% VT exercise transition times in both trials (T1 and T2b) for 4τ (which is said to follow linear first order mechanisms) varied significantly. However, the times for the TTSS method were very similar.

Traditionally, sub-threshold VO$_2$ kinetics to steady state data is fit using a mono-exponential equation of which τ is derived to measure the rate of phase-II kinetics (3,5,25,40,43). In the context of the model, τ is representative of the attainment of ~63% of the phase-II amplitude following an exercise transition (19,32,39,44). From this, an estimate of the time taken to reach steady state can be made by the calculation of 4τ.

To date, there has been minimal constructive investigation of the use of a mono-exponential model, despite its initial acceptance more than four decades ago (43). While there have been several studies (5,25,30,34,41) with some empirical evidence to oppose the use of τ, they are limited and there lacks any strong empirical validation of the methods. Therefore, it was felt necessary to reassess the pre-defined concepts of τ and 4τ as they apply to two contrasting subject groups, highly-trained and untrained. With the pre-existing acceptance within the literature of training status and its effect on the rapidity of VO$_2$ kinetics (10,11,18,22,23,30,36,38,48), it seemed a logical area to assess the newly defined method of TTSS.

**TTSS vs. 4τ**

This study used the TTSS method (35) to quantify the time taken for a subject to reach steady state VO$_2$ following an exercise transition. As discussed, the literature states that τ is also a valid measurement of VO$_2$ on-kinetics. Therefore, it would be assumed that the values of both TTSS and 4τ would be quite similar for each subject in both trials. However, our results indicated that there is a significant distinction between both these methods of data modelling. For both subject groups in all trials, 4τ was significantly higher than the TTSS values. This may be considered a clear indication of the error of using a mono-exponential model to fit VO$_2$ kinetics. Defining the time taken to reach steady state VO$_2$ with something as simplistic multiplying the time constant by 4 is unreasonable. τ accounts for ~63% of the total response time of the model. Therefore, according to the model (see Figure 1) ~86%, ~95%, ~98%, and >99% of the response accounts for 2τ, 3τ, 4τ, and 5τ, respectively. If we considered a calculated τ following an exercise transition to be 30 sec, then, 3τ would equal 90 sec and 5τ would equal 150 sec. That is a 60-sec difference between 3τ and 5τ, however, it is less than a 5% difference in the total response amplitude of the model. Again, as a mono-exponential model has been shown to not adhere well to the phase-II VO$_2$ response (35), using a simplistic time constant multiplication method to calculate the time take to reach steady state VO$_2$ is a vast oversimplification. This can also lay argument as to why the results of this study indicated an overestimation when using 4τ, compared with TTSS.

**Highly-Trained vs. Untrained Response**

The results of this study (Table 1) suggest that subject cardiovascular fitness has strong implications for both 4τ and TTSS measures. In both modelling methods, there was a marked increase in the rapidity of the VO$_2$ kinetics for the HT group compared to the UT group for the same relative intensity exercise increment. This can be argued in favour of cardiovascular training adaptations that allow for a trained individual to better adjust to the required energy demands due to being more economical (22,36).
Table 1. Mean and SD Data for All Subject Variables (τ, 4τ, and TTSS) for Both the HT Group and the UT Group for All Trials (T1, T2a, and T2b). Note the overall faster kinetic response to each exercise transition for the HT group vs. UT group, which has been shown in previous research.

### HIGHLY-TRAINED

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<td>40.9</td>
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<td>60.7</td>
</tr>
</tbody>
</table>

**Comparison of T1 and T2b**

A secondary result of this study showed there to be a large discrepancy for calculations of the 85% trials (T1 and T2b) for 4τ compared to TTSS. As seen in Figure 4 and shown statistically, the mean 85% VT (including both the HT and the UT subject groups) exercise transition times for the TTSS method are relatively similar. However, there is a significantly larger 4τ response time for T2b compared with T1. As well, and as discussed earlier, the overall the 4τ response was larger than the TTSS for both trials.

There have been numerous studies comparing VO₂ kinetics of moderate, heavy, and severe exercise following transitions from a baseline intensity above rest or an unloaded output, or from prior priming exercise (4,7,12-15,17,25,33,40). Of these, Hughson and Morrissey (25) and Bowen et al. (4) calculated values for τ for baseline intensities above unloaded exercise and successive transition increases. DiMenna et al. (14) examined heavy intensity VO₂ kinetics following a moderate intensity baseline, but they failed to report the τ values for the baseline intensity.
Hughson and Morrissey (25) studied the VO$_2$ kinetics of 6 healthy, untrained subjects who completed two cycle ergometer protocols. The first was from rest to 80% of their gas exchange threshold (GET) for 10 min. The second protocol was from rest to 40% GET for 10 min, followed by a second transition to 80% GET for 10 min. Mean $\tau$ results were calculated at 37.8 ± 7.2 sec for the first protocol, and 30.0 ± 7.8 sec for the 40% GET transition, and 60.6 ± 10.8 sec for the 40 to 80% GET transition of the second protocol. There is a clear increase in $\tau$ for the 2nd transition following initial baseline exercise in the second protocol, as well as an increase in $\tau$ for the same relative intensity between both protocols. From a theoretical perspective, the mono-exponential model of VO$_2$ kinetics should behave as a linear first order system. Therefore, the same relative exercise transition (that is, 40% GET) within the moderate intensity domain of the second protocol should be relatively invariant. As well, under the same principles it would be expect that both 80% GET transitions of the two protocols would be similar.

Given the results of Hughson and Morrissey (25) study, it can be concluded that either the basis of the model is incorrect, or it did not properly account for changes within the VO$_2$ kinetics response following a baseline transition. Interestingly, our study indicated a similar result to that of Hughson and Morrissey (25) in that there was a significant increase in 4$\tau$ (and therefore, $\tau$) for the 85% VT transition compared to the same power output transition without an elevated baseline. Hence, based on these results, it could be concluded that the VO$_2$ kinetic response is slowed following an elevated baseline transition and yet, our TTSS results indicated the contrary. The similarity of the mean TTSS values for both exercise trials (T1 and T2b) further sustains the argument that a simple mono-exponential function misinterprets VO$_2$ kinetics data. It is seems clear that to continue to base data processing and interpretation from such a misinterpretation would likely hinder scientific progression in the field.

Bowen et al. (4) reported similar variation in $\tau$ values following an exercise transition to 90% of lactate threshold (LT) from a ~45% LT baseline intensity. Again, $\tau$ increased following the second exercise transition, compared to the initial transition from a 20 W baseline.

**CONCLUSIONS**

Our investigation supports previously documented findings that indicate a clear increase in the speed of VO$_2$ kinetics to steady state for trained subjects compared with less or untrained subjects. As well, the results of this study have shown two major inadequacies with the use of a mono-exponential model to fit phase-II VO$_2$ kinetics data. That is, calculations of the VO$_2$ kinetic time course using $\tau$ are largely overestimated, and, there are differences in $\tau$ for the same relative intensity transition where the TTSS method has been shown there are minimal. The results demonstrate a strong necessity to re-evaluate the elements of the VO$_2$ kinetic response, both physiologically and mathematically. Using a mono-exponential function to model such a response appears to be an oversimplification, which is misleading of the underlying kinetics as well as for the estimate of time to steady state.
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