CHAPTER 1

INTRODUCTION

Background Information

The investigation of physiological responses to exercise originated over a half a century ago (Hill and Lupton 1923; Margaria, Edwards and Dill 1933; Whipp and Wasserman 1972) and has become an important method in both clinical and exercise physiology research (Jones and Poole 2005a). Historically, the measurement of pulmonary oxygen consumption ($\dot{V}O_2$) in response to changes in work intensity has been of great interest to researchers as it provides a systemic measure of cardiorespiratory and metabolic functioning (Whipp and Wasserman 1972; Carter, Pringle, Jones and Doust 2002; Pringle, Doust, Carter, Tolfrey, Campbell and Jones 2003b). The use of such research also provides information as to systemic functioning of metabolic adaptations to exercise, but it has been proposed that the mechanisms regulating these responses lie within the working muscle and changes in oxygen (O_2) delivery and utilisation (Grassi 2005).

More recently, the instantaneous measurement of changes in the oxygen content or oxygenation (mOxy) within the working muscle has been made possible through the introduction of Near-Infrared Spectroscopy (NIRS) to exercise physiology research (Chance, Dait, Zhang, Hamaoka and Hagerman 1992; Belardinelli, Barstow, Porszasz and Wasserman 1995a; Turner, Cathcart, Parker, Butterworth, Wilson and Ward 2006). NIRS uses changes in specific physiological chromophores to monitor changes in the

metabolic environment of the working muscle in response to bouts of exercise (Bae, Tyasukochi, Kan, Sasaki, Koseki, Hamaoka, Iwane and Haga 1996; Mancini 1997; Ding, Wang, Lei, Wang, Huang, Xia and Wu 2001; Bhambhani 2004). The recent development of NIRS technology has limited the quantity of research that has reported on concurrent $\dot{V}O_2$ and mOxy responses to exercise (Belardinelli, Barstow, Porszasz and Wasserman 1995b; Bhambhani, Buckley and Susaki 1999; Demarie, Quaresima, Ferrari, Sardella, Billat and Faina 2001; DeLorey, Kowalchuck and Paterson 2004a; Turner et al. 2006).

Introduction to Metabolic Adaptation

Whipp and Wasserman (1972) originally reported that the $\dot{V}O_2$ response to moderate-intensity exercise could be fitted to a monoexponential function in order to quantify its speed and amplitude. Since this observation, numerous investigations have used similar modelling techniques to report upon metabolic adaptations in a number of conditions which may either enhance or retard cardiorespiratory adaptation to exercise (Xu and Rhodes 1999; Jones and Poole 2005a; 2005b). This broad research area has become known as $\dot{V}O_2$ kinetics and primarily focuses upon the speed and amplitude of $\dot{V}O_2$ adjustment in response to changes in work intensity. In their original investigation, Whipp and Wasserman (1972) identified that the metabolic and $\dot{V}O_2$ response consisted of three important phases of transition to a bout of constant-load exercise. These identified phases include:

1. *On-Transient Response (Primary Component)*

The on-transient response comprises two phases. Phase I encompasses the cardiodynamic phase where deoxygenated blood is returned to the lungs and a sharp linear increase in $\dot{V}O_2$ is observed. Phase II is the rapid exponential increase in $\dot{V}O_2$ or decrease in mOxy observed following the original Phase delay. This increase in $\dot{V}O_2$ continues until the energy requirements of the exercise are completely met through aerobic metabolism. The on-transient response demonstrates the Primary Component (Phase I and Phase II) of the overall $\dot{V}O_2$ response to a moderate (A) and heavy (B) intensity SWT as shown in Figure 1.1 over the page.

2. *Steady-State or Slow Component Responses*

During moderate-intensity (< Ventilatory Threshold (VT)) exercise and after the initial primary component, a steady-state in $\dot{V}O_2$ and mOxy is observed where aerobic energy production is equal to the energy requirements of the exercise intensity. During high-intensity (>VT) exercise, no steady-state in $\dot{V}O_2$ or mOxy is developed, and a decrease in muscular and metabolic efficiency is observed. The gradual increase in $\dot{V}O_2$ across high-intensity exercise has been termed the $\dot{V}O_2$ slow component. The corresponding decrease in mOxy within the muscle has been defined as the mOxy slow component. An example of the $\dot{V}O_2$ slow component is shown in Figure 1.1B.

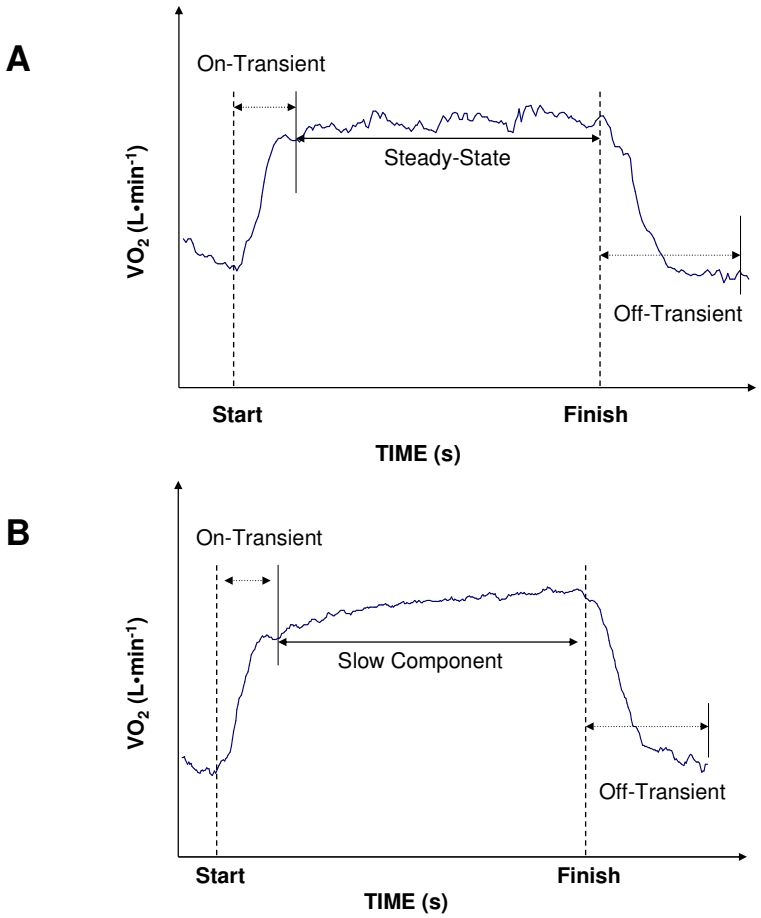

Figure 1.1: Typical $\dot{V}O_2$ responses to moderate (A) and heavy-intensity (B) exercise bouts

3. Off-Transient Response

The off-transient response is the recovery of $\dot{V}O_2$ and mOxy measures to resting baselines following the completion of an exercise bout. The nature of the off-transient response is influenced by both the intensity and duration of the exercise bout. Examples of the off-transient $\dot{V}O_2$ response to moderate (A) and high-intensity (B) exercise are shown above in Figure 1.1.

Previous investigations have reported that the magnitude and nature of these $\dot{V}O_2$ and mOxy responses vary significantly with differences in laboratories and measurement systems, aerobic capacity, disease states, training status, gender or other physiological factors, making the nature of these responses somewhat difficult to compare and contrast (Koga, Shiojiri and Kondo 2005; Whipp, Ward and Rossiter 2005). As such, the fitting of the metabolic response to exponential equations allows the quantification of speed and amplitude measures for each individual response (Koga et al. 2005; Whipp and Rossiter 2005). However, the methods used to model these kinetic responses rely ultimately on the intensity of the exercise bout. Moderate intensity (<VT) exercise is able to be modelled using a single function exponential component, whereas high-intensity (>VT) exercise requires a double exponential model, due to the development of the $\dot{V}O_2$ or mOxy slow component (Bearden and Moffat 2001). Each exponential component is fitted using a number of kinetic parameters to describe both the amplitude and speed of the metabolic responses. The exponential functions used to model the physiological responses consist of the following kinetic parameters, and are schematically represented in Figure 1.2.

- Amplitude (A): the absolute amplitude ($\dot{V}O_2$: $L \bullet min^{-1}$; mOxy: %) of each physiological phase (A_p: Primary component amplitude; A_s: Slow component amplitude; A_f: Off-transient amplitude);
- Time delay (TD): time taken (s) from SWT commencement or completion to beginning of exponential phase of the on- or off-transient response (TD_p: Primary component time delay; TD_s: Slow component time delay; TD_f: Off-transient time delay);

- Time constant (τ): time taken (s) to reach 63% of each individual exponential component (τ_p: Primary component time constant; τ_s: Slow component time constant; τ_f: Off-transient time constant); and,
- Weighted mean response time (wMRT): time taken (s) to reach 63% of the overall on- or off-transient response across multiple exponential components, and is weighted on both the TD and τ of each function (wMRT: On-transient weighted mean response time; $wMRT_f$: Off-transient weight mean response time).

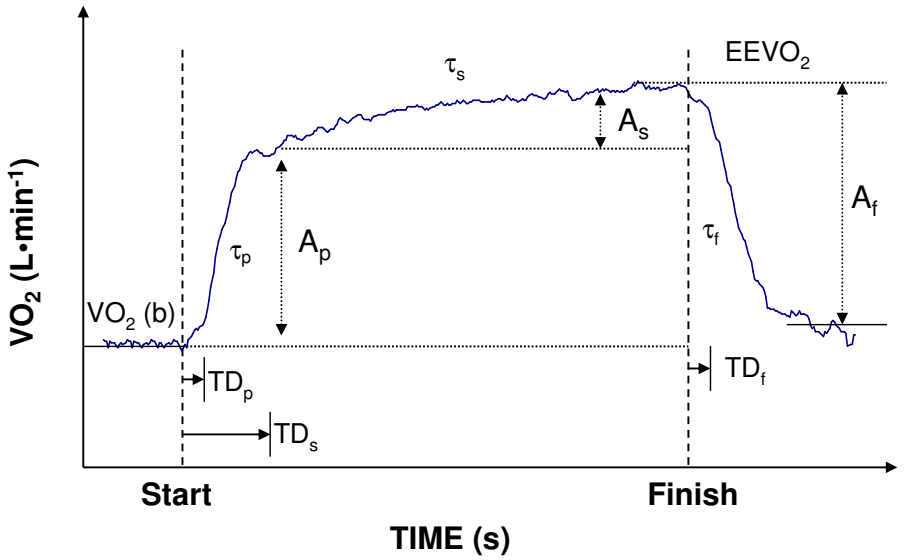

Figure 1.2: The kinetic markers used within the exponential functions to quantify the speed and amplitude of the on-transient Phase II and slow components as well as the off-transient response of $\dot{V}O_2$ adaptation to an exercise bout (see above for key).

In summary, the capacity to accurately describe and quantify the nature of the $\dot{V}O_2$ and mOxy responses across a constant-load exercise bout allows researchers to identify causal or influencing factors which may limit the rate of $\dot{V}O_2$ or mOxy adjustment in response to changes in work. The examination and quantification of $\dot{V}O_2$ and mOxy kinetics has applications within both clinical and athletic populations given the wide variety of conditions which affect the metabolic response and the proposed clinical and performance benefits of a speeded response.

Effects of Aging on Metabolic Adaptation

To date, research has observed that sedentary aging is related to significant declines in several physiological characteristics, such as VT and LT (Allen, Seals, Hurley, Ehsani and Hagberg 1985; Masse-Biron, Mercier, Collomp, Hardy and Prefaut 1992), $\dot{V}O_2$max (Babcock, Paterson and Cunningham 1992; Tanaka, Desouza, Jones, Stevenson, Davy and Seals 1997; Katzel, Sorkin and Fleg 2001; Tanaka and Seals 2006), muscle fibre composition and capillarisation (Frontera, Hughes, Krivickas and Roubenoff 2001; Andersen 2003; Deschenes 2004) and glycolytic or oxidative enzyme activities (Coggan, Spina, Rogers, King, Brown, Nemeth and Holloszy 1992; Russ and Kent-Braun 2004). Similarly, sedentary aging has also been shown to significantly attenuate the amplitude and speed of the $\dot{V}O_2$ on-transient kinetic response to various exercise intensities and incremental exercise tests (Babcock, Paterson, Cunningham and Dickinson 1994b; Chilibeck, Paterson, Petrella and Cunningham 1996a; DeLorey et al. 2004a). Sedentary aging has also been observed to improve the mOxy response and the relationship to the $\dot{V}O_2$ responses during moderate and heavy-intensity exercise (Stathokostas,

DeLorey, Kowalchuk and Paterson 2003; DeLorey, Kowalchuck and Paterson 2005). DeLorey et al. (2004a) reported that the on-transient response to moderate-intensity exercise was slower but demonstrated greater total O_2 extraction within the working muscle in older sedentary subjects compared to a similar young cohort. More recently, DeLorey, Kowalchuck and Paterson (2005) showed that in response to heavy-intensity exercise, older sedentary subjects demonstrated slower $\dot{V}O_2$ kinetics but faster mOxy kinetics than younger subjects. The investigators hypothesised that this may be suggestive of a slower adaptation of local muscle blood flow in the elderly subjects. However, to date no such data are available on trained older subjects.

Furthermore, a number of previous investigations have reported that the $\dot{V}O_2$ slow component is reduced with sedentary aging either as a result of a decrease in a number of factors including $\dot{V}O_2$max, changes in the peripheral muscle characteristics, or alterations in muscle fibre recruitment patterns (Rossiter, Ward, Kowalchuk, Howe, Griffiths and Whipp 2001; Sabapathy, Schneider, Comadira, Johnston and Morris 2004). DeLorey et al. (2005) observed the effect of age on the initial $\dot{V}O_2$ and mOxy primary components in untrained subjects in response to heavy-intensity exercise, but did not report upon any changes with relation to the development of the slow component.

To date, no research has investigated the effect of aging on the mOxy slow component during high-intensity exercise. The majority of the slow component has been identified to occur within the working muscle (Poole 1994) and therefore changes in the histochemical and enzymatic environment within the muscle are likely to influence its development. Such changes have been

reported to occur with sedentary aging (Frontera and Hughes 2000). While the $\dot{V}O_2$ and mOxy slow components have been shown to be significantly related to each other during high-intensity exercise in young trained individuals (Miura, Araki, Matoba and Kitagawa 1999; Demarie et al. 2001), no research has yet investigated this relationship in middle-aged individuals.

Lastly, the effect of aging on the off-transient $\dot{V}O_2$ and mOxy responses has yet to be fully investigated. It has been suggested that the off-transient $\dot{V}O_2$ response is significantly slowed with sedentary aging (Chick, Cagle, Vegas, Poliner and Murata 1991; Chilibeck, Paterson, Cunningham, Taylor and Noble 1997; Chilibeck, Paterson, McCreary, Marsh, Cunningham and Thompson 1998). No data exist on the age-related changes in the off-transient mOxy response in well-trained older subjects.

Statement of the Research Problem

At present, a small number of recent investigations have examined the nature of both the $\dot{V}O_2$ and mOxy kinetics during bouts of exercise at various intensities (Miura et al. 1999; Demarie et al. 2001; Grassi, Pogliaghi, Rampichini, Quaresima, Ferrari, Marconi and Cerretelli 2003). The effect of age on the $\dot{V}O_2$ and mOxy responses to both moderate and high-intensity cycling exercise in sedentary subjects has previously been investigated and described (DeLorey et al. 2004a; 2005). No data to date have described the effect of age on these responses in well-trained individuals. Given that a number of physiological capacities that influence metabolic adaptation can be maintained into older age (i.e. LT, $\dot{V}O_2$max, muscle fibre composition) with physical training (Pollock, Foster, Knapp, Rod and Schmidt 1987; Tanaka and Seals 2003), it is

of interest as to whether there is an effect of age on $\dot{V}O_2$ and mOxy responses in well-trained older athletes. Finally, while it appears that the relationship between the $\dot{V}O_2$ and mOxy responses is significantly changed with sedentary aging, no research has identified age-related mechanisms responsible for this effect of age.

Purpose of the Thesis

Therefore, the current series of research investigations has a number of purposes:

1. To investigate and describe the effect of age on physiological and peripheral muscle characteristics in well-trained cyclists.

2. To examine the effect of age on the on-transient $\dot{V}O_2$ and mOxy responses to moderate-, heavy- and severe-intensity SWT in well-trained cyclists.

3. To examine the effect of age on the development of the $\dot{V}O_2$ and mOxy slow components during heavy- and severe-intensity SWT in well-trained cyclists.

4. To investigate the relationships between the $\dot{V}O_2$ and mOxy responses and changes in hematological parameters across moderate-, heavy- and severe-intensity SWT in well-trained young and middle-aged cyclists.

5. To investigate the relationships between the $\dot{V}O_2$, mOxy kinetics across moderate-, heavy- and severe-intensity SWT and the peripheral muscle histochemical and enzymatic characteristics of well-trained young and middle-aged cyclists.

6. To investigate the role of changes in muscle electromyographic activity and fibre recruitment in the development of the $\dot{V}O_2$ and mOxy slow components during heavy- and severe-intensity SWT in well-trained young and middle-aged cyclists.

7. To examine the effect of age on the off-transient $\dot{V}O_2$ and mOxy responses following moderate- heavy- and severe-intensity exercise in well-trained cyclists.

Limitations and Assumptions

The following limitations and assumptions may apply to the present study:

1. *Specificity of the results*

   The data collected during the present study were obtained from well-trained young and middle-aged cyclists who were competitive during the twelve months prior to the study. The results may not be valid for all athletes of similar physiological capacities or different training modalities or performance levels.

2. *Maintenance of physiological capacities*

   All physiological testing detailed within the subsequent studies was completed within four weeks for each individual subject. It is assumed

that the research subjects maintained their physiological capacities throughout all testing.

3. *External lifestyle and genetic influences*

   Many of the physical and physiological characteristics reported within the present study may be influenced by lifestyle and genetic factors which cannot be controlled. As with most aging research, a large variation within the results is likely given the pronounced effect of long-term environmental and lifestyle influences on such a cohort (Shephard 2002). However, by setting specific inclusion criteria for participation, these influences were likely to be minimised.

4. *Representative nature of the muscle biopsy results*

   The muscle fibre composition, fibre cross-sectional area, capillarisation and enzyme activity data from the present study is representative of the whole VL at the standardised sampling site. It is known that such factors may change with sampling position and depth of the sample location within such peripheral muscles (Lexell, Taylor and Sjostrom 1985; Dwyer, Browning and Weinstein 1999; Porter, Koolage and Lexell 2002).

5. *Representative nature of the NIRS and sEMG results*

   The NIRS and surface Electromyography (sEMG) measures taken from the VL are representative of changes in the entire muscle. Both apparatus were placed over a motor point of the VL and therefore would be expected to represent whole muscle changes in metabolic and neuromuscular activity (Kendall, McCreary and Provance 1993).

6. *Subject compliance*

   All subjects completed all sessions within the present investigation. It was assumed that subjects followed standardised dietary and prior exercise guidelines for the 24 h prior to the commencement of each testing session.

7. Human ethics constraints

   The initial research design had proposed the inclusion of an untrained middle-aged group to allow the effect of training into middle-age to be examined. However, the CQU Human Research Ethics Committee reached the conclusion that the required exercise testing would not be safe in such a population and therefore the group was excluded from the present study.

8. Recovery between heavy and severe-intenstiy exercise

   In the current study, set criteria of a resting $\dot{V}O_2$ of 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$ was used to determine when each subject had adequately recovered from the heavy-intensity exercise bout. At the time of the research design, no data was available detailing the recovery duration required to restore normal on-transient responses to high-intensity exercises. Recently, Burnley, Doust and Jones (2006) produced data suggesting that 45 min of recovery is required to restore normal $\dot{V}O_2$ kinetics. Therefore, the methods of the current investigation do not meet these criteria and the data from the severe-intensity SWT may have been influenced by the lack of recovoey following the heavy-intensity SWT.

Delimitations

The following delimitations may apply to the present study:

1. *Limited sample size*

   Due to the time-demanding and invasive nature of the experiments conducted in this thesis, only a small number of well trained young (n=7) and middle-aged (n=7) cyclists were recruited. However, the sample size is typical of that seen in previous reports investigating kinetic responses to repeated exercise bouts and invasive needle biopsies (Barstow, Jones, Nguyen and Casaburi 1996; Pringle, Doust, Carter, Campbell, Tolfrey and Jones 2002; DeLorey et al. 2004a; DeLorey et al. 2005).

2. *Gender restriction of subjects*

   The subjects recruited within the present series of studies were restricted to males to avoid any effect of gender or hormonal changes due to menstruation or menopause in either age-group.

3. *Sport restriction of the subjects*

   The subjects recruited within the present study were restricted to competitive triathletes and cyclists currently in training. The results of the present study may therefore not apply to older athletes who are competitive in different sports or activities.

4. *Age restriction of subjects*

   The age of the well-trained cyclists recruited for the present series of studies were limited to young (18-25 y) and middle-aged (45-55 y) athletes.

5. *Sample Representation*

   The data contained within the present series of studies are based from a specific sample of subjects, and therefore might not be representative of similar populations.

6. *Dietary Guidelines*

   The cyclists were only given food and fluid intake instructions for the 12 h period prior to any exercise testing session. No attempt was made to restrict or monitor dietary intake outside of this time period.

7. *Representative nature of the NIRS and sEMG results*

   The NIRS and sEMG results are representative of the VL and VM, and other proximal muscles. During a crank cycle, all thigh and shank muscles are activated periodically at particular activation ranges (Jorge and Hull 1986; Raymond, Joseph and Gabriel 2005; Chapman, Vicenzino, Blanch, Knox and Hodges 2006). Therefore, VL and VM activity have been recorded as an indicator of changes in muscle activity and fibre recruitment within the thigh and shank.