A detailed comparison of oxygen uptake kinetics at a range of exercise intensities

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Abstract

It is believed that exercise performed in the heavy intensity exercise (above Gas Exchange Threshold (GXT)) domain will reach a steady state (albeit delayed). However reported modelled time constants for the slow component indicate the $\dot{V}O_2$ response would not be complete within the duration of the exercise performed. This raises important questions regarding the concept of heavy intensity exercise and the suitability of current exponential models to describe the slow component of $\dot{V}O_2$. .The purpose of this study was; to comprehensively describe the relationship between exercise intensity and the slow component of $\dot{V}O_2$, and to investigate whether a steady-state in $\dot{V}O_2$ was achieved during constant work-rates above the gas exchange threshold (GXT). Eight recreationally active male participants volunteered for this study (age: 24±8 y; Stature: 1.78±0.09 m; mass: 76.5±10.1 kg; $\dot{V}O_{2peak}$: 3.89±0.72 $L \cdot min^{-1}$). The participants were required to visit the laboratory on nine occasions for testing. The first visit involved determination of GXT and $\dot{V}O_{2peak}$ with a progressive ramp exercise test. The following tests involved multiple laboratory visits, with the participants performing a square wave transition from rest to one of eight exercise intensities; -20%Δ (minus 20% of the difference in $\dot{V}O_2$ between that at GXT and VO_{2peak}), -10%Δ, GXT, 10%Δ, 20%Δ, 30%Δ, 40%Δ and 50%Δ. The $\dot{V}O_2$ response was modelled using both mono and bi exponential non-linear regression techniques. Difference in the SEE for the mono and bi exponential models were analysed using a paired samples *t*-test, and the slope of $\dot{V}O_2$ vs Time (for the final minute of exercise) was analysed using a one-sample *t*-test. A slow component of $\dot{V}O_2$ was found for all exercise intensities. The SEE's were significantly lower in the bi vs. mono exponential model across all exercise intensities ($p<0.05$). The slope was not different from 0 ($p<0.05$) for the final minute of any exercise intensity, indicating that a steady-state was achieved. The modelled slow component time constants are typical of literature reported values, but would indicate that $\dot{V}O_2$ would not be achieved during the duration of the exercise. These findings demonstrate that $\dot{V}O_2$ was in steady-state for all exercise intensities for the final minute of exercise. These findings also demonstrate that using a bi exponential model, a slow component can be modelled even below GXT and that the time constant of the slow component would be too long to result a steady-state.

Declaration

I declare that the work in this thesis was carried out in accordance with the regulations of the University of Gloucestershire and is original except where indicated by specific reference in the text. No part of this thesis has been submitted as part of any other academic award. The thesis has not been presented to any other education institution in the United Kingdom or overseas.

Any views expressed in the thesis are those of the author and in no way represent those of the University.

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Abbreviations

$\dot{V}O_{2max}$	-	Maximal oxygen uptake
%	-	Percentage
$\dot{V}O_2$	-	Oxygen uptake
GXT	-	Gas exchange threshold
WR	-	Work rate
$\dot{V}O_{2peak}$	-	Peak oxygen uptake
O_2	-	Oxygen
ATP	-	Adenosine Tri-Phosphate
AT	-	Anaerobic threshold
BLa^-	-	Blood lactate
LT	-	Lactate threshold
FE_{O2}	-	Fraction of expired oxygen
CO_2	-	Carbon dioxide
$\dot{V}_E$	-	Pulmonary ventilation
VT	-	Ventilatory threshold
V-slope	-	Ventilatory slope
$\dot{V}CO_2$	-	Volume of carbon dioxide
MLSS	-	Maximum lactate steady state
CP	-	Critical power
RCP	-	Respiratory compensation point
PCO_2	-	Partial carbon dioxide
Δ	-	Delta
BxB	-	Breath by breath
$t - \delta$	-	Time delay
$\dot{Q}$	-	Cardiac output
(a-v) O_2 diff	-	Difference in oxygen content between arterial-to-venous
τ	-	Time constant
MRT	-	Mean response time
RER	-	Respiratory exchange ratio
TCA	-	Tri-Carboxylic Acid
$MexpO_2$	-	Mixed Expired O_2
$MexpCO_2$	-	Mixed Expired CO_2

pH - The negative decimal logarithm of the concentration of hydrogen

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1.0 Review of Literature

1.1 $\dot{V}O_2$ kinetics

1.1.1 Historical background

Oxygen uptake kinetics is the study of the rate of change in pulmonary oxygen uptake ($\dot{V}O_2$) at the on- or off-set of exercise (Hughson and Morrissey, 1982; Hughson, 1990; Barstow, 1994; Jones and Poole, 2005). It is shown to respond differently above and below the gas exchange threshold (GXT) and to respond in phases, dependent upon relative exercise intensity (Whipp *et al*, 1982; Whipp and Ward, 1990; Barstow, 1994).

In experimental studies conducted up until ~1980, the majority of studies still characterised the $\dot{V}O_2$ response to exercise as a single exponential function beginning at the onset of exercise (Hagberg *et al*, 1978; Hagberg *et al*, 1980). The postulation of this response was evidently appropriate in studies that had used the Douglas bag method of indirect calorimetry (Hill and Lupton, 1923; Henry, 1951), where the number of data points in the transient phase were relatively few, and the duration of each sample, by comparison, reasonably long (~30 s). The development of tools designed to measure $\dot{V}O_2$ on a breath-by-breath basis, coupled with repeated bouts of the same exercise test being averaged (Whipp and Wasserman, 1972; Linnarsson, 1974; Whipp *et al*, 1982), led to the demarcation of three discrete phases in the gas exchange response profiles.

Following this, the analyses of various authors (Whipp *et al*, 1982; Beaver, Wasserman and Whipp, 1986; Barstow and Mole, 1991) cemented the concept of a three-phase gas exchange response: the initial cardiodynamic phase (phase 1), the primary exponential component (phase 2), and the steady state (phase 3).

1.1.2 Three phase response

The influential work of Whipp and colleagues (1982) demonstrated a three-phase $\dot{V}O_2$ response when averaging several repetitions of moderate intensity exercise (i.e. below GXT) in order to reduce the influence of inter-breath fluctuations on the $\dot{V}O_2$ signal. Whipp *et al* (1982) proposed that an abrupt rise in $\dot{V}O_2$ (phase 1) was mediated through an increased cardiac output ($\dot{Q}$) (and hence pulmonary blood perfusion) since an altered mixed venous PO_2 would not influence $\dot{V}O_2$ at the lung due to the muscle to lung transit delay at the onset of exercise. This is demonstrated using the Fick equation (Equation 1.1).

$$\dot{V}O_2 = \dot{Q} \cdot C_{(a-\overline{v})}O_2$$

Equation 2.1. Fick equation.

Where $\dot{Q}$ represents cardiac output (stroke volume (SV) x heart rate (HR)) and $C_{(a-\overline{v})}O_2$ represents the arterial oxygen content minus the venous oxygen content, otherwise termed the arteriovenous oxygen difference.

So, the initial phase 1 response has therefore been termed the cardiodynamic phase, as the rise in $\dot{V}O_2$ (~15 s) reflects an increased $\dot{Q}$ that will occur irrespective of any changes in muscle O2 utilisation at the onset of exercise. During phase 1, demonstrably slower changes in $\dot{V}O_2$ are apparent during exercise that may constrain or restrict the initial SV response, i.e. starting exercise transitions from a higher work rate or from a supine position, thereby supporting the above assertion (Karlsson, Lindborg, and Linnarsson, 1975; Hughson and Morrissey, 1982). The influence of an expanded $C_{(a-\overline{v})}O_2$, reflecting muscle O_2 utilisation, is not signalled at the pulmonary capillaries until the muscle to lung transit delay has concluded. The increased end tidal carbon dioxide (CO_2) pressure (PCO_2) and reduced oxygen (O_2) pressure (PO_2) signals the onset of phase 2 toward the steady state $\dot{V}O_2$ requirement (phase 3) (Whipp and Ward, 1990; Whipp, *et al*, 1982). Figure 1.1 depicts a graphical representation of the three-phase response.

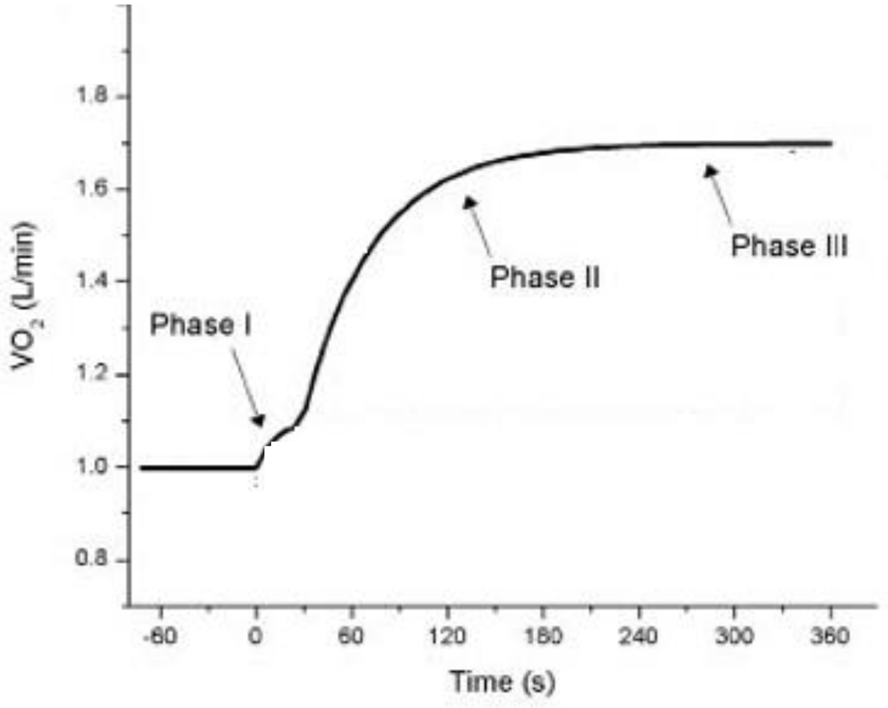


Figure. 2.1. Schematic of the pulmonary oxygen uptake vs. Time profile. A typical rest-work three phase $\dot{V}O_2$ response is illustrated above.

To further clarify, at the onset of exercise, below the GXT, $\dot{V}O_2$ increases rapidly due to an increase in venous return (Whipp *et al*, 1982). Phase 1, generally lasting ~15 s, is a function of an increased return of venous blood, most of which was pooled in the periphery prior to exercise (Casaburi *et al*, 1989b). Because phase 1 is mainly a result of increased venous return, independent of muscle metabolism, as noted above, it is often referred to as the cardiodynamic phase (Whipp *et al*, 1982).

Phase 2 or the primary component represents an exponential increase in $\dot{V}O_2$ related to the continued increase in pulmonary (and muscle) blood flow along with the return of deoxygenated blood (reflecting venous blood from the active muscles arriving to the lungs). This phase has been shown to closely reflect the adjustments of oxidative metabolism at the active skeletal muscle level (Grassi *et al*, 1996; Rossiter *et al*, 1999). During phase 2, several authors have demonstarted that $\dot{V}O_2$ will increase in an approximately mono exponential fashion (Whipp *et al*, 1982; Hughson, Sherrill and Swanson, 1988; Whipp, 1994; Barstow *et al*, 1996) to attain a new steady-state within ~3 minutes (phase 3) (Whipp *et al*, 1982; Whipp and Ward, 1990; Whipp, 1994).

However, unlike the response to sub-GXT intensity exercise, during exercise intensities performed above the GXT, the $\dot{V}O_2$ response is assumed by many to become more complicated (Barstow and Mole, 1991; Barstow *et al*, 1996; Engelen *et al*, 1996). This due to the notion that $\dot{V}O_2$ does not attain a steady state after the primary $\dot{V}O_2$ response, so is no longer be said to increase in a simple mono exponential manner. However, $\dot{V}O_2$ will continue to increase for several minutes, an additional component that is believed to cause $\dot{V}O_2$ to rise above the predicted value (Whipp and Wasserman, 1972; Paterson and Whipp, 1991; Whipp, 1994). Whipp and Mahler (1980) demonstrated that the $\dot{V}O_2$ value attained at the end of constant load exercise lasting ~10 min increased significantly above that predicted from incremental exercise as the work rate was increased above the GXT. In support of this it has been noted that sub-GXT, $\dot{V}O_2$ increases linearly with work rate at ~10 $ml \cdot min^{-1} \cdot W^{-1}$. However supra-GXT, $\dot{V}O_2$ has commonly been reported to increase at ~13 $ml \cdot min^{-1} \cdot W^{-1}$ (Pearce and Milhorn, 1977; Barstow, 1994; Poole *et al*, 1994; Whipp, 1994; Whipp, 1987). This observable and quantifiable delayed $\dot{V}O_2$ response is termed slow component (Casaburi *et al*, 1989; Poole *et al*, 1994; Whipp, 1994). This slow component has been characterised as a delayed response becoming superimposed on the abrupt rise in $\dot{V}O_2$ at the onset of exercise, and is different to O_2 drift (Barstow and Mole, 1991). The aforementioned phenomenon, O_2 drift, should not be confused with slow component. The O_2 drift is typically seen during moderate intensity exercise (<GXT) of a prolonged duration (Kalis *et al*, 1988). In these instances, the gradual rise in $\dot{V}O_2$ is generally below ~200ml of O_2. This rise is not associated with elevated, nor increasing arterial [BLa^-]. Whereas the slow component of $\dot{V}O_2$ is generally of much greater magnitude, with values often greater than 1.0 $L \cdot Min^{-1}$ being reported (Whipp, 1987; Whipp and Ward, 1990) and is often quantified for empirical convenience as the $\dot{V}O_2$ difference between the sixth minute (or the end-exercise) and the third minute of exercise [$\Delta\dot{V}O_2$ (6-3)] (Whipp and Wasserman, 1972; Barstow, 1994).

1.2 Exercise Intensity Domains

1.2.1 Moderate Intensity Exercise

Within the moderate intensity exercise domain it is widely believed pulmonary $\dot{V}O_2$ rises in a mono exponential manner and attains a new steady-state within ~3 minutes (Whipp *et al*, 1982; Hughson, Sherrill and Swanson, 1988; Whipp, 1994) giving a time constant of 25-35 s with a time delay of 15-20 s (Whipp and Wasserman, 1986, Burnley *et al*, 2000, Wilkerson *et al*, 2004). The $\dot{V}O_2$ response to moderate intensity exercise is thought to display three distinct responses: a slowly developing response (also called cardiodynamic), the primary response, and the steady state. The $\dot{V}O_2$ is shown to increase linearly with work rate at ~10 $ml \cdot min^{-1} \cdot W^{-1}$, and once the new steady-state is attained, adenosine tri-phosphate (ATP) re-synthesis within the myocytes and the rate of ATP re-synthesis from oxidative phosphorylation are in equilibrium. Furthermore, whilst exercising at this intensity there is assumed to be no significant rise in arterial $[BLa^-]$ (Kindermann, Simon and Keul, 1979; Faude, Kindermann and Meyer, 2009).

The first response effectively represents a time delay of ~20 s which reflects the transit time that pooled deoxygenated blood takes to travel from the working muscles to the lungs, i.e. venous return (Casaburi, Daly, Hansen, and Effros, 1989; Hughson, O'Leary, Betik, and Hebestreit, 2000; Whipp, 1994). The increases in $\dot{V}O_2$ within the early delay component have been largely attributed to the augmented cardiac output and the sudden increase in venous return (Bell, Paterson, Kowalchuk, Padilla, and Cunningham, 2001; Faisal, Beavers, Robertson, and Hughson, 2009). Smaller contributions have also been ascribed to changes in lung gas stores and mixed venous O_2 content (Casaburi *et al*, 1989). The primary response reflects an exponential rise in $\dot{V}O_2$ and achieves steady state in ~ 3 min (Deley, Millet, Borrani, Lattier, and Brondel, 2006; Obert *et al*, 2000). This exponential response is understood to be initiated by the arrival venous blood from the working muscles at the lungs and represents augmented muscle O_2 utilisation and continued rise in pulmonary blood flow (Whipp, 1994). The time constant for the rise in $\dot{V}O_2$, otherwise termed tau (t), is thought to be relatively invariant across the range of moderate intensity work rates (Hagberg, Hickson, Ehsani, and Holloszy, 1980; Whipp and Ward, 1990). However some contentions have been reported (Hagberg *et al*, 1980; Phillips *et al*, 1995; Chilibeck *et al*, 1996; Brittain *et al*, 2001). The notion that pulmonary $\dot{V}O_2$ in this response reflects closely the muscle $\dot{V}O_2$ (Grassi *et al*, 1996) is supported by modelling studies and additionally the temporal correspondence between changes in $\dot{V}O_2$ and breakdown of phosphocreatine (Rossiter *et al*, 1999; Whipp *et al*, 1999).

The modelling of $\dot{V}O_2$ kinetics within this exercise intensity domain has conventionally been achieved in a number of ways, primarily as a mono exponential function (Equation 1.2). Pulmonary oxygen uptake has been shown to behave exponentially following step changes in external work rate and the amplitude of the response may be expressed as a function of time (Henry and DeMoor, 1956; Whipp and Wasserman, 1972; Linnarsson, 1994). The mean response time (MRT) represents the time required for the O_2 transport-utilisation system to reach 63% of the metabolic requirement (asymptote). Therefore, MRT is defined as time delay and time constant of the exponential at 63% of the asymptote of the steady state response (Linnarsson, 1974; Sietsema, Daly, and Wasserman, 1989). The MRT can therefore be used for comparisons of the overall rate of change between responses (Cerretelli, Shindell, Pendergast, DiPrampero, and Rennie, 1977; DiPrampero, Davies, Cerretelli, and Margaria, 1970).

It has been recognised that it is necessary to account for the time delay, if pulmonary $\dot{V}O_2$ kinetics are to be used in estimation of $\dot{V}O_2$ kinetics at a muscular level, meaning that incorporating all data points when using a monoexponential function has ceased (Barstow, Buchthal, Zanconato, and Cooper, 1994; Whipp, Ward, Lamarra, Davis, and Wasserman, 1982). This appreciation has led to the use of a technique that has become commonplace i.e. the removal of the first 20 seconds of data to time align pulmonary and muscle $\dot{V}O_2$ responses (Lamarra *et al*, 1987; Gerbino *et al*, 1996; Grassi *et al*, 1996; Krustrup *et al*, 2004).

1.2.2 Heavy Intensity Exercise

Heavy intensity exercise has been described by some authors as exercise supra-GXT but below critical power (CP) (Hill, 1993), with CP, or maximal steady state, being demarcated the cut-off point for severe intensity exercise. The basis of the CP concept is that there is thought to be a hyperbolic relationship between power output and the time that the power output can be sustained. The relationship can be described based on the results of a series of work rates performed to exhaustion and will represent the highest sustainable work rate (Moritani *et al*, 1981; Hill, 1993; Poole, 1988; Vanhatalo, Doust and Burnley, 2007). During heavy exercise, there is a greater oxidative cost and steady-state attainment is thought to be delayed due to the presence of the $\dot{V}O_2$ slow component. The O_2 cost associated with this type of exercise is generally reported to increase to ~13 $ml \cdot min^{-1} \cdot W^{-1}$ (Whipp and Wasserman, 1972; Pearce and Milhorn, 1977; Whipp and Mahler, 1980; Poole, 1988; Barstow and Mole, 1991). Additionally, arterial [BLa^-] will increase above baseline values, but does, however, reach equilibrium (at an elevated level), this may range from 2-5 mmol·L^{-1} (Billat *et al*, 2003), and although there is a greater O_2 cost associated with this exercise intensity $\dot{V}O_2$ will still reach a steady state. (Whipp and Wasserman, 1972; Pearce and Milhorn, 1977; Whipp and Mahler, 1980; Barstow and Mole, 1991; Whipp, 1994).

The characteristics of the on-transient $\dot{V}O_2$ kinetic response to heavy exercise are shown to take on a more complicated description than the simple mono exponential model (Barstow, 1994; Linnarsson, 1974; Whipp and Wasserman, 1970). The delayed onset of steady state caused by the slowly developing excess $\dot{V}O_2$, has led to it being termed the slow component of $\dot{V}O_2$ (Billat, Richard, Binsse, Koralsztein, and Haouzi, 1998; Poole, Barstow, Gaesser, Willis, and Whipp, 1994; Sloniger *et al*, 1996). Evidence for the existence of a slow component during heavy intensity cycle ergometry exercise has been reported as far back as the 1960's (Astrand and Saltin, 1961; Margaria, Cerretelli, Aghemo, and Sassi, 1963). Following these initial reports, the slow component of $\dot{V}O_2$ has been more extensively described with the excess $\dot{V}O_2$ driving the overall $\dot{V}O_2$ requirement over and above that would be predicted from the $\dot{V}O_2$-WR relationship (Paterson and Whipp, 1991; Whipp and Ward, 1990).

1.2.3 Modelling heavy intensity

Research is equivocal as to whether primary response $\dot{V}O_2$ kinetics are slowed in heavy intensity exercise, as compared to moderate intensity exercise. This may be a reflection of a greater time constant in the primary component, or an additional slow component in $\dot{V}O_2$ that will reach a delayed steady state at a level above that predicted from a sub-GXT $\dot{V}O_2$/work rate regression, or, potentially both (Paterson and Whipp, 1991). This additional requirement has been shown to demonstrably slow the MRT (Paterson and Whipp, 1991). When investigators have modelled the heavy intensity exercise $\dot{V}O_2$ response, determining the primary and slow components separately; it has been shown the time constant in heavy intensity exercise was systematically slowed due to the additional slow component (Barstow *et al*, 1993). However, further research has demonstrated varying results, with Paterson and Whipp (1991) noting that the time constant increased with exercise intensity; whereas Barstow and Mole (1991) reported no change. Although these studies utilised slightly different mathematical models, both utilised a two-component model, with phase-1 regarded as a time delay. In the domain of heavy intensity exercise a second exponential term is used to characterise the slow component. This term, which tends to a higher asymptote, has a separate time delay and time constant to characterise the delayed onset. Although results differed between Barstow and Mole (1991) and Paterson and Whipp (1991), data from the aforementioned study demonstrated the longest time constant was noted in the highest work rates.

More recently, Carter *et al.* (2002), whilst attempting to systematically characterise the $\dot{V}O_2$ response across multiple exercise intensities, utilised a three-compartment model, representing phase I, phase II and the slow component, and demonstrated that the primary response time constant was increased in the heavy exercise intensity domain, as compared to the moderate exercise intensity domain (Barstow, Cooper, Sobel, Landaw, and Epstein, 1990).

An exponential function has been widely employed to describe the slow component of $\dot{V}O_2$ (Equation 1.2) (Bearden and Moffatt, 2000; Camus, Atchou, Bruckner, Giezendanner, and DiPramero, 1988; Linnarsson, 1974). However, there is some contention as to whether the slow component is an exponential or a linear function (Barstow and Mole, 1991; Paterson and Whipp, 1991). Some studies, albeit a minority, have modelled the slow component rise as a linear function (Armon, Cooper, Flores, Zanconato, and Barstow, 1991), whilst others have simply expressed the magnitude of the slow component as the difference between the $\dot{V}O_2$ at exercise cessation and the $\dot{V}O_2$ at three minutes (Billat, Mille-Hamard, Petit, and Koralsztein, 1999; Jones and McConnell, 1999). A widely reported criticism of this simplified approach is that it underestimates the magnitude of the slow component (Bearden and Moffatt, 2001).

Therefore, the $\dot{V}O_2$ response to heavy intensity exercise may be characterised by a number of occurrences, including, the slowing of phase II time course (Paterson and Whipp, 1987); an additional $\dot{V}O_2$ requirement of delayed onset (Linnarsson, 1974; Paterson and Whipp, 1987), with the slow component causing $\dot{V}O_2$ to increase to greater values than that predicted from the extrapolation of sub-GXT work rates (Poole, Ward, Gardner, and Whipp, 1988; Whipp, 1987).

1.2.4 Severe Exercise Intensity

The severe intensity domain has been described as exercise performed above the maximal lactate steady state, or Critical Power, as within this domain both $\dot{V}O_2$ and arterial [BLa$^-$] do not reach a steady state (Gaesser and Poole, 1996). It has generally been shown that both $\dot{V}O_2$ and arterial [BLa$^-$] rise inexorably until fatigue ensues, at which point maximum values of $\dot{V}O_2$ are attained (Wasserman and Whipp, 1975; Gaesser and Poole, 1996). Evidently, maintenance of exercise duration in this domain is finite, in cases where the exercise is sustained long enough, this domain is also characterised by the manifestation of a slow component (Poole, 1994; Poole *et al*, 1994; Gaesser and Poole, 1996; Pringle and Jones, 2002).

A key postulation that exists surrounding the $\dot{V}O_2$ response to exercise in the severe intensity exercise domain is that, at a constant work rate, a slow component will be present and of a greater magnitude than that seen in heavy intensity exercise (Billat *et al*, 1998; Hill and Stevens, 2001). However, the difference in the response is that $\dot{V}O_2$ is unable to reach a steady state and instead rises inexorably until either $\dot{V}O_{2max}$ is attained or exhaustion ensues (Hill, Halcomb, and Stevens, 2003; Whipp, 1994). It has been supposed that the slow component will drive $\dot{V}O_2$ to $\dot{V}O_{2max}$ instead of a delayed steady state, encompassing all work rates above critical power (Poole *et al*, 1988; Poole *et al*, 1990).

1.3 Thresholds

1.3.1 Gas Exchange Threshold

The conventional measure of GXT has been defined as the breakpoint in the slope of the relationship between CO_2 output and O_2 uptake (Beaver, Wasserman and Whipp, 1986; Gaskill *et al*, 2001). Below the GXT, it is demonstrated by many that oxygen uptake ($\dot{V}O_2$) increases in a mono exponential manner, attaining steady-state within ~3 minutes during constant work-rate exercise (Whipp *et al*, 1982; Whipp and Ward, 1990; Whipp, 1994). For exercise intensities that are above GXT, it has been suggested that $\dot{V}O_2$ no longer increases in a simple mono exponential manner and could be underestimated due to a delayed response, termed the slow component (Casaburi *et al*, 1989a; Poole *et al*, 1994; Whipp, 1994).

GXT is often cited as a putative measure for slow component emergence (Whipp and Wasserman, 1972; Whipp *et al*, 1982), despite a lack of empirically driven research at sub-threshold intensities (Barstow and Mole, 1991; Xu and Rhodes, 1999). It is often referred to as the point at which ventilation increases disproportionately to oxygen consumption. This is linked to HCO_3^- buffering of H^+ necessitates non-metabolic CO_2 production (Beaver, Wasserman and Whipp, 1986), thereby resulting in an increase in arterial blood lactate concentration ($[BLa^-]$). This may be expressed as;

$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO3^- + H^+$

Equation 2.2. Carbonic acid-bicarbonate buffering system

Essentially, as exercise continues this will result in an increase in blood lactate concentration, causing blood pH will lower due to the increase in hydrogen concentration ([H+]), bicarbonate (HCO_3^-) is able to combine with H^+, to form carbonic acid (H_2CO_3), thereby acting as a buffer and raising pH levels, then finally expelling this in the form of excess CO_2. It is also considered to be a viable non-invasive alternative to LT (Beaver, Wasserman and Whipp, 1986; Gaskill *et al*, 2001).

1.3.2 Anaerobic Threshold

Wasserman and McIlroy (1964) originally developed the concept that a critical threshold exists where the metabolic needs for O_2 in the muscle exceed the capacity of the cardiopulmonary system to supply them; a systematic increase in anaerobic metabolism and lactate is thereby formed in the muscle. The term anaerobic threshold (AT) was used to describe this transitional point where there is a systematic rise in blood Lactate during exercise (Davis *et al*, 1976, Brooks, 1985). This concept however, has been criticised on many fronts. Evidence has amassed that dissociates lactate production from anaerobiosis, suggesting that muscles can release lactate even when the O_2 supply is more than adequate (Brooks, 1991). These issues have led to vast controversy over the definition, and the techniques used for detection and the resultant measurements vary widely.

Despite contentions the term AT has been used to illustrate the demarcation of moderate to heavy intensity exercise (Gaesser and Poole, 1996, Xu and Rhodes, 1999). Moderate intensities have been described as those that do not result in an increased (above resting levels) metabolic acidemia (Whipp, 1994). However, controversy still surrounds the calculation of the AT; as there are various methods used, both from the measurement of blood lactate (Hughson *et al*, 1987, Green and Dawson, 1993) and from respiratory data (Beaver *et al*, 1985, Beaver *et al*, 1986). The AT has previously been used as an effective gauge of physical fitness in patients with cardiorespiratory complications, as well as healthy individuals and elite athletes (Beaver, Wasserman and Whipp, 1986; Wilmore, Costill and Kenney, 2008).

1.3.3 Lactate Threshold

Many researchers have since adopted the term Lactate threshold (LT), which some describe as the highest $\dot{V}O_2$ that can be achieved without a sustained increase in blood Lactate concentration and decrease in pH (Wasserman *et al*, 1994). Since the pivotal work conducted by Hill and colleagues (1924), it has been well established that lactate increases in the blood during heavy exercise. As exercise increases above a certain work rate threshold, an anaerobic component of metabolism causes lactate to increase markedly. This increase is accompanied by an almost equal reduction in bicarbonate concentration in the blood (Beaver, Wasserman and Whipp; Faude, Kindermann and Meyer, 2009), causing carbon dioxide (CO_2) production to accelerate, evidenced by an increased respiratory CO_2 output (Whipp, 1987; Gaskill *et al*, 2001).

Classically, identification the LT, was achieved by measuring arterial lactate at frequent intervals during a period of increasing work rate and determining where it begins to increase, i.e., a direct lactate threshold (Beaver, Wasserman and Whipp, 1986). This traditional method of using lactate concentration is based upon the idea that blood lactate concentration ($[BLa^-]$) increases systematically with exercise intensity (Haverty, Kenney and Hodgson, 1988). Visual inspection of graphical plots of lactate levels are then relied upon to determine the threshold. However, there are clear issues with this, objectivity is of paramount importance and using visual detection does not always provide this (Faude, Kindermann and Meyer, 2009). Furthermore, applying this to a wider population, the invasive nature and comparable cost inefficiency of this method are not desirable; meaning the production and utilisation of an accurate, non-invasive method of threshold determination was of importance.

The LT has also been subject to scrutiny, it is argued by some authors, as Noakes (2003) described, that arterial $[BLa^-]$ does not show a clearly defined, abrupt threshold response during exercise of progressively increasing intensity. Some authors contend arterial [BLa^-] begins to rise as soon as progressive exercise commences. However, at lower exercise intensities, the rate of the increase is so low that it is barely noticeable. Only when the exercise becomes more intense does the rise become apparent. This has been corroborated in previous literature, by researchers such as Yeh *et al* (1983) who reported that they found no observable LT due to arterial [BLa^-] increasing continuously from the start of exercise during ramp testing protocol, however this is widely disputed. Further issues with LT are evident amongst literature as inconsistent blood sampling methods, including; venous, arterial and arterialised venous samples, have been reported, making comparisons between studies difficult (Haverty, Kenney and Hodgson, 1988). Further confounding the situation is the site blood is extracted from ranges, whether it is; earlobe, fingertip or toe pin-prick samples or blood extracted from the median cubital vein. In addition to blood site, the laboratory analysis methods will also affect the test result (Faude, Kindermann and Meyer, 2009). It has been shown that earlobe samples are uniformly lower than that of samples measured at the fingertip or toe, with Forsyth and Farrally (2000) demonstrating that arterial [BLa^-] differed across all three sites. With regard to blood analysis, plasma values are demonstrably higher than whole venous lactate concentrations, with capillary samples measuring between the two (Faude, Kindermann and Meyer, 2009).

The identification of an accurate, non-invasive method was based upon the postulation that bicarbonate (HCO_3^-) buffering of hydrogen (H^+) necessitates non-metabolic CO_2 production (Beaver, Wasserman and Whipp, 1986). Bicarbonate is said to be a major buffer of metabolic acids in the body fluids and therefore an increase in arterial [BLa^-] causes an obligatory increase in CO_2 production, affecting both pulmonary gas exchange and ventilation (Beaver, Wasserman and Whipp, 1986). There had been attempts to improve the accuracy of a non-invasive method, aside from using arterial [BLa^-], visual inspection of graphical plots of ventilatory equivalents, end-tidal gas concentrations, and respiratory exchange ratio (RER) have also been utilised (Wasserman *et al*, 1973; Orr *et al*, 1982). However Beaver, Wasserman and Whipp (1986) utilised a method that involves the analysis of the behaviour of $\dot{V}CO_2$ as a function of $\dot{V}O_2$ during progressive exercise tests when exceeding the LT is accompanied by the buffering of lactic acid by HCO_3^- with a consequential increase in $\dot{V}CO_2$. This results in a transition in the relationship between the $\dot{V}CO_2$ and $\dot{V}O_2$, which is considered the underlying element in all methods of AT/LT detection by gas exchange. $\dot{V}O_2$ is utilised as an independent variable as it is the direct index of metabolism. This method was coined the 'V-slope' method as, utilising computerised regression, they analysed the slopes of gas volume curves ($\dot{V}CO_2$ vs. $\dot{V}O_2$ plot, which detects the beginning of the excess CO_2 output generated from the buffering of H^+) (Orr *et al*, 1982; Smith and O'Donnell, 1984; Beaver, Wasserman and Whipp, 1986).

1.3.4 Critical Power

The CP concept was originally developed as a model derived from a series of exhaustive, constant-load, exercise bouts (Poole, 1988; Hill, 1993). All-out exercise testing has made quantification of the parameters for the two component model easier to ascertain (Vanhatalo, Doust and Burnley, 2007; Poole, 2009; Pettitt, 2012). Critical power is thought to represent an exercising intensity that can be performed, theoretically, without exhaustion occurring and represents the maximal steady state for lactate and O_2 uptake (Moritani *et al*, 1981; Poole *et al*, 1988). Conversely, when intensities exceed CP, expenditure of the finite anaerobic capacity ensues concurrently with the accumulation of metabolites known to have deleterious effects on skeletal muscle contractions (Jones *et al*, 2008). Coupled with the expenditure of anaerobic capacity is the augmentation in pulmonary $\dot{V}O_2$ towards $\dot{V}O_{2max}$ (Hill, 1993; Hill, Poole and Smith, 2002). The higher the work rate above CP, the more rapid the expenditure of the anaerobic capacity and achievement of $\dot{V}O_{2max}$ occurs (Poole, 1988; Poole and Smith, 2002; Vanhatalo, Jones and Burnley, 2011).

1.4 Mechanism of the Slow Component of $\dot{V}O_2$

1.4.1 Overview

There have a number of postulations that have attempted clarify the physiological cause for the slow component of $\dot{V}O_2$. The putative effect of lactate on slow component is, perhaps, the most well documented (to be discussed below); however, there have been a number of postulations made for the mechanism of the slow component. Some of which include; epinephrine, catecholamines, cardiac and ventilatory work, Inspiratory resistance and fatigue, temperature, mitochondrial phosphorus-oxygen (P-O) coupling, muscle fibre type recruitment, recruitment of lower efficiency fast-twitch motor units, priming exercise, physical training status and age (Poole *et al*, 1991; Poole, 1994; Poole *et al*, 1994).

1.4.2 Lactate and the slow component

At exercise intensities above GXT, there is an increased production and removal of lactate (Barstow, 1994; Poole, 1994). This has, however, led to the postulation of a causal relationship between slow component and arterial [BLa^-] (Xu and Rhodes, 1999). It is important to acknowledge that although the two are in fact closely correlated (Whipp, 1987; Barstow, 1994), it has never been shown that they do actually coincide and lactate has been shown not to mandate an additional $\dot{V}O_2$ requirement (Poole, 1994). In an attempt to clarify the putative causes of the slow component, Poole (1994) demonstrated, using surgically isolated, electrically stimulated canine gastrocnemius, that increasing arterial [BLa^-] by ~10 mmol, did not increase muscle $\dot{V}O_2$, meaning that although there is a close temporal association between changes in arterial [BLa^-] and $\dot{V}O_2$ during heavy exercise, lactate itself does not mandate an additional $\dot{V}O_2$ demand. Engelen *et al* (1996) also established that a 57% elevation of blood lactate levels, induced by hypoxic breathing during heavy exercise, did not affect the time constant or the amplitudes of the slow component $\dot{V}O_2$.

The increase in the slow component of $\dot{V}O_2$, and its relationship with arterial [BLa^-], has previously been postulated to be caused by metabolic acidosis; by increasing the oxygen supply, and therefore Haemoglobin concentration, increasing oxygen transportation to the working muscles and thus aiding aerobic metabolism (Stringer *et al*, 1994). However, due to underling physiological implications, this has remained a postulation. Another suggested putative measure for the slow component/blood lactate relationship is that accumulation of intramuscular Hydrogen ions (H^+) may be responsible, by altering the equilibrium of the creatine kinase reaction and generating free creatine concentration (Mahler, 1985, Capelli *et al*, 1993). A perhaps more compelling putative hypothesis is that the associated acidosis, mediated by the Bohr effect, is the contributing factor in the slow component of $\dot{V}O_2$ (Wasserman *et al*, 1991, Stringer *et al*, 1994). It has been further suggested by Stringer *et al* (1994) that up to 62% of the slow component of $\dot{V}O_2$ can be induced by the onset of lactic acidosis. This, however, does not explain why $\dot{V}O_2$ exceeds values predicted from sub-maximal work rates (Whipp, 1994, Gaesser and Poole, 1996).

Despite the observation that the presence of the slow component is primarily accompanied by an increased arterial [BLa^-], it is extremely contentious as to what extent it is a putative measure for the slow component. As outlined above, it has never been shown that the two physiological mechanisms do actually coincide and lactate has been shown not to mandate an additional $\dot{V}O_2$ requirement (Poole, 1994).

1.4.3 Contracting muscles and the slow component

Using simultaneous measurement of both pulmonary and leg $\dot{V}O_2$ during cycle ergometry, Poole *et al* (1991) demonstrated that ~80% of the increase in pulmonary $\dot{V}O_2$, beyond the 3rd minute of exercise, could be accounted for by the increase in leg $\dot{V}O_2$, meaning that ~80% of the slow component arises from within the contracting muscles. This determination was affirmed by Rossiter *et al* (2002), who showed, using ^{31}P magnetic resonance spectroscopy, that the $\dot{V}O_2$ slow component was associated with a slow component of muscle phosphocreatine concentration ([PCr]), indicating that the slow component is linked to a greater ATP cost of force production, rather than elevated $\dot{V}O_2$ cost of ATP production. There is numerous evidence to suggest that fast-twitch fibres (type II), compared with slow-twitch fibre (type I), have a greater ATP cost for contractile activity owing to different chemical to mechanical coupling efficiencies, quicker actomyosin turnover, faster calcium pump activity and inefficient flavin adenine dinucleotide (FAD) versus nicotinamide adenine dinucleotide (NAD) linked α-glycerophosphate shuttle activity (Poole *et al*, 1994; Willis and Jackman, 1994). Demonstrating that exercise, which recruits a greater proportion of type II fibres, requires greater ATP, and thus $\dot{V}O_2$, cost (Poole *et al*, 1994; Jones *et al*, 2011). Barstow *et al* (1996) also reported a negative correlation between the magnitude of $\dot{V}O_2$ slow component and the percentages of type I fibres in exercising muscles (Vastus Lateralis), indicating that fibre type distribution has a great influence on the slow component of $\dot{V}O_2$ during exercise.

1.4.4 Muscle fibre type recruitment and the slow component

The human body skeletal muscular system exhibits two types of muscle fibres, both of which demonstrate many different structural, histochemical and behavioural characteristics. The two muscle types, as noted above, are referred to as slow (type I) or fast (type II) twitch; this is due to the speed at which maximum tension can be achieved. Due to a higher concentration of myosin ATPase in fast twitch fibres, they can achieve peak tension much faster than the slow twitch fibres. The fast twitch fibres may be further segmented based upon their affinity for aerobic capacity; i.e. type IIa and type IIx (Xu and Rhodes, 1999). The differential characteristics of the fibre types are; contraction speed, fatigability, [ATPase], mitochondrial and glycolytic concentrations (Salmons and Vrbova, 1969; McArdle, Katch and Katch, 2009).

As discussed above, the general consensus is that around 80% of the value for the slow component of $\dot{V}O_2$ can be accounted for by the working muscles (Poole *et al*, 1991). The manifestation of the slow component is primarily due to the recruitment of fast type II fibres, which have around an 18% lower phosphate-oxygen ratio than type I fibres, this is postulated to be due to a greater reliance on the α-glycerophosphate shuttle as opposed to the malate-aspartate shuttle. It has previously been demonstrated that type IIx muscle fibre recruitment increases proportionately to exercise intensity (Vollestad, 1985). The extent to which muscle fibre distribution affects the slow component of $\dot{V}O_2$ has been investigated by many authors (Vollestad, 1985; Barstow *et al*, 1996; Pringle, 2003). It has been previously noted that the higher the type I muscle fibre involvement, will directly correspond to a greater initial rise in $\dot{V}O_2$ (Barstow *et al*, 1996).

Subjects with a high percentage of the low efficiency (type II) fibres are shown to have a high phosphate cost of force production, which in turn generates a greater slow component of $\dot{V}O_2$ (Rossiter *et al*, 2001). A progression from one fibre type to the next is what incurs an additional increase in $\dot{V}O_2$, due to inefficiency of type II fibres (Coyle *et al*, 1992). The reasons for this were argued to be associated with early recruitment of type II fibres, more metabolite accumulation and muscle membrane excitability which may all contribute to eventual neuromuscular fatigue. Therefore, an alternative explanation for the emergence of the slow component has been postulated to be the fatigued muscle becoming less efficient (Poole *et al*, 1991).

1.4.5 Ventilatory and cardiac work and the slow component

The rest of the excess in $\dot{V}O_2$ (~20%) has been truncated to 'rest of body' (Poole *et al*, 1994; Jones *et al*, 2011). Within this, the O_2 cost of ventilation and cardiac work are purported to make the most significant contributions. As exercise intensity increases, there is an obligatory rise in ventilation in order to maintain effective gas exchange in the lungs; this increased ventilation is reported to contribute to the slow component. Despite this general agreement, the estimation of the O_2 cost between studies has varied, as Shephard (1966) noted an O_2 cost of 4.3 mL when the ventilation was >89 $L{\cdot}Min^{-1}$. Contrastingly, Aaron *et al* (1992) reported an O_2 cost of 3 mL. Despite the lack of conformity between studies, it is suggested the O_2 cost of the increase in ventilation could account for ~18-23% of the $\dot{V}O_2$ slow component (Aaron *et al*, 1992; Gaesser and Poole, 1996; Jones *et al*, 2011).

1.4.6 Adrenaline and the slow component

As with lactate, a number of other factors were postulated to mediate slow component and shown, either to have no effect, or a negligible effect. Turner *et al* (1995) demonstrated that the thresholds for lactate and epinephrine occur at similar workrates, this coupled with evidence that epinephrine infusion increases $\dot{V}O_2$ by ~20% in individuals at rest (Sjostrom *et al*, 1983), resulted in epinephrine being considered a mediator of slow component. The $\dot{V}O_2$ increase is due to the effect of epinephrine on the circulatory, respiratory and metabolic systems. However the putative mediation of epinephrine on the slow component was shown to be fallacious, as epinephrine elevations of 4 to 6 fold, by infusion, resulted in negligible changes in $\dot{V}O_2$ (Gaesser *et al*, 1994; Gaesser and Poole, 1996).

1.4.7 Muscle temperature and the slow component

Muscle temperature during exercise has also been postulated as a possible mediator of slow component, that is to say, during exercise increased metabolic activity within working muscles will result in an increase in muscle temperature and may also lead to an increase in O_2 consumption due to the Q_{10} effect. The Q_{10} effect represents the factor by which the rate of a reaction increases for every 10-degree rise in the temperature (Whipp, 1987). This possible effect was shown to be true during *in vitro* studies, as Willis and Jackman (1994) demonstrated that increasing muscle temperature by 6ºC resulted in the efficiency of mitochondrial respiration decreasing by ~20%. However human based studies were not supportive, as Koga *et al* (1997) demonstrated that directly increasing muscle temperature had no significant effect on the amplitudes of the primary component or slow component of $\dot{V}O_2$. Although there are many putative mechanisms for the slow component of $\dot{V}O_2$, the fundamental determination of where it actually emerges is still to be investigated.

1.4.8 Prior exercise and the slow component

As noted above, there have numerous studies conducted in order to try and elucidate contributing factors to the slow component of $\dot{V}O_2$. The effect of prior exercise, or exercise priming, has been studied widely with attempts to identify any limitations to muscle or pulmonary $\dot{V}O_2$ increases (Barstow *et al*, 1990b; Gerbino *et al*, 1996; Burnley *et al*, 2000; Burnley *et al*, 2002). It has been shown that the effect of prior exercise may significantly change the metabolic and gas exchange responses to subsequent exercise. An initial performance of heavy intensity exercise, but not moderate intensity exercise, has been shown to speed overall $\dot{V}O_2$ kinetics during subsequent heavy intensity exercise (Gerbino *et al*, 1996; Burnley *et al*, 2000). This has the effect of reducing the slow component amplitude, whilst the time constant remains the same (Bearden and Moffatt, 2001a; Koppo and Bouckaert, 2001; Scheuermann *et al*, 2001). Research into the effect of priming exercise has been of interest due to the potential prior exercise has to enhance or improve subsequent performance (Jones *et al*, 2003b; Raymer *et al*, 2007). The change in metabolic and gas exchange responses to subsequent exercise has been attributed to multiple reasons; ATP turnover is performed at a higher percentage by aerobic contribution, increased blood flow and oxygen extraction by the muscle, sparing of phosphocreatine and a reduction in lactic acid production (Jones *et al*, 2003a). It has been demonstrated that the $\dot{V}O_2$ response of both the primary and slow component amplitudes to heavy exercise are shown to be related to muscle fibre type recruitment, it is therefore suggested that performance of a priming exercise changes the muscle metabolic factors thereby changing the muscle fibre recruitment order (Burnley *et al*, 2002).

1.4.9 Other factors and the slow component

A number of postulated mediators of the slow component of $\dot{V}O_2$ have been discussed above, there are however further factors that may affect the slow component. One key parameter that has been shown to affect the slow component is exercise modality. There have been a number of studies looking at slow component, utilising different exercise modalities; cycling (Hagberg *et al*, 1980; Henson *et al*, 1989; Casaburi *et al*, 1992), running (Nagle *et al*, 1970; Costill *et al*, 1971) and arm cranking (Cerretelli *et al*, 1977; Casaburi *et al*, 1992). It has been uniformly shown that in comparison to cycling exercise of equivalent intensity, the slow component amplitude found in running was smaller. Dependent upon the exercise modality performed, when exercising at an absolute intensity, there is a significantly different effect of the $\dot{V}O_2$ kinetic response to heavy intensity exercise and the slow component magnitude (Billat *et al*, 1998b). The pulmonary oxygen uptake profile for a number of exercise modalities has been abundantly described;

arm cranking (Casaburi *et al*, 1992; Koga *et al*, 1996); leg extension (MacDonald *et al*, 1998, Koga *et al*, 2005); swimming (Demarle *et al*, 2001); running (Jones and McConnell, 1999; Carter *et al*, 2000b; Carter *et al*, 2002); and cycling (Linnarsson, 1974; Barstow and Mole, 1991; Ozyener *et al*, 2001). It has been suggested that this difference between exercises could be due to muscular contraction and fibre recruitment differences between the aforementioned exercises (Perrey *et al*, 2001).

The two most studied exercise modalities are comfortably cycling and running and there are notable biomechanical differences between the two that might account for differences noted in the slow component amplitude. Mechanical efficiency is one consideration as cycling is shown to less efficient, mechanically, than running (Whipp and Wasserman, 1969). Cycling generally demonstrates a more pronounced slow component magnitude than running (See Table 1.1), this is thought, in part, to be due to the effect muscle contraction has on phosphocreatine dephosphorylation (Billat *et al*, 1999b).

The $\dot{V}O_2$ response differs significantly between running and cycling. The overall $\dot{V}O_2$ response is shown to be comparable between the exercise modalities; however, there are some key differences that have been noted. Firstly, the amplitude of the overall $\dot{V}O_2$ response is significantly greater in running than cycling. In addition, cycling has been shown to demonstrate significantly higher slow component amplitude than running. Although these two modalities are the most frequently utilised, cycling or cycle ergometer exercise studies far outweigh those utilising running, Table. 1.1. details a plethora of literature studying the slow component of $\dot{V}O_2$, the difference in many variables between running and cycling is evident, as is the fact the majority of studies are utilising cycle ergometry.

1.5 Contentions in the literature

1.5.1 Overview

Table 1.1. details a comprehensive chronological list of studies that have conducted research that both; refers to the slow component of $\dot{V}O_2$ and reports slow component values. It is evident from this collection of literature that this area of physiology and more specifically, $\dot{V}O_2$ kinetics has received a lot of attention. The slow component of $\dot{V}O_2$ has been an issue of contention for some time, with reports originating from the early 90’s with Barstow and Mole (1991), and Paterson and Whipp (1991), being among the first to discuss this additional component of

$\dot{V}O_2$. As noted above, there have however been contentions regarding the modelling of slow component data. Key contentions originate from the assumptions that have previously been made, notably the inference that the additional 'slow' component of VO_2 is only evident >GXT, and that exercise performed >GXT, but <CP, will reach a steady state given sufficient time. Further to this the treatment of data and how it is modelled has also provided some basis for contention (Stirling and Zakynthinaki, 2009; Stirling, Zakynthinaki, and Billat, 2008; Stirling, Zakynthinaki, and Saltin, 2005).

1.5.2 Slow component, Gas exchange threshold and Lactate threshold

It is contended by many authors that the disproportionate increase in $\dot{V}CO_2$ versus $\dot{V}O_2$ above the GXT in ramp exercise are due to the production of non-metabolic CO_2 in muscle because of lactic acid buffering by plasma bicarbonate entering the cell in exchange with lactate (Wassermann, 1967; Wasserman, 1982). According to Wasserman's (1982) original model, plasma bicarbonate concentration decreases in an approximately 1:1 ratio with the increase in plasma lactate concentration, 1 mmol of CO_2 is generated above that produced by aerobic metabolism for each mmol of lactic acid buffered, and non-metabolic CO_2 produced in the muscle is partly responsible for hyperventilation because of the resulting increase in the CO_2 flow to the lungs. However, this concept has received some criticism. Peronnet and Aguilaniu (2006) argue that experimental data is not supportive of this model. They assert; bicarbonate is not the main buffer within the muscle; the decrease in standard bicarbonate concentration is not the mirror image of the increase in lactate concentration; buffering by bicarbonate does not result from an increased CO_2 production in muscle (no non-metabolic CO_2 is produced in tissues); and the CO_2 flow to the lungs, which should not be confused with $\dot{V}CO_2$ at the mouth, does not increase at a faster rate above than below GXT. The disproportionate increase in $\dot{V}CO_2$ at the mouth above GXT is due to hyperventilation (not the reverse) and to the low plasma pH which both reduce the pool of bicarbonate readily available in the body (Peronnet and Aguilaniu, 2006). This is however widely disputed.

Despite the observation that the presence of the slow component is primarily accompanied by an increased arterial [BLa^-], many experimental data are not supportive of a causal link. Given the lack of data support demonstrating a causal link between LT and the slow component it is contentious as to what extent it may be regarded a putative measure for the slow component and its emergence. As outlined above, it has never been shown that the two physiological mechanisms do actually coincide and lactate has been shown not to mandate an additional $\dot{V}O_2$ requirement (Poole, 1994). Furthermore, rarely do studies explore the oxygen uptake kinetics at exercise intensities close to GXT. There are well established reports above GXT, but limited reports below GXT. Even when the kinetics below the GXT are explored, the relative exercise intensity tends to be well below the threshold (i.e. 80%GXT). This indicates that there may not be a strong rationale in using GXT as the cut off point for bi exponential versus mono exponential mathematical modelling.

1.5.3 Modelling the data

The use of an exponential function to characterise the slow component is widely utilised (Bearden and Moffatt, 2000; Camus *et al*, 1988; Linnarsson, 1974). There has however been some contention noted as to whether the slow component is an exponential or a linear function (Barstow and Mole, 1991; Paterson and Whipp, 1991). There have been a number of attempts to model and characterise the slow component of $\dot{V}O_2$, including; modelling the slow component as a linear function (Armon *et al*, 1991), expressing the magnitude of the slow component as the difference between the $\dot{V}O_2$ at exercise cessation and the $\dot{V}O_2$ at three minutes (Billat *et al*, 1999; Jones and McConnell, 1999), employing non-linear least squares regression and applying a bi exponential equation (Carter *et al*, 2000; Carter *et al*, 2002) and in recent times Stirling and colleagues (2004; 2007; 2008; 2009) have asserted that a number of underlying principles in $\dot{V}O_2$ kinetics could be mistaken.

1.5.4 Time delayed phases

Stirling and colleagues (2004; 2007; 2008; 2009) assert that the existence of time-delayed phases is not supported by oxygen uptake kinetics data. They contend that, despite many attempts for a number of years, no convincing physiological mechanism for such behaviour has been proven to exist.

The time series for the $\dot{V}O_2$ is generally averaged before modelling the data. It has been suggested that in order to reduce noise and enhance the basic response pattern, repeated, identical experiments should be averaged (Linnarsson, 1974). This technique is used extensively in modelling oxygen uptake or heart rate kinetics particularly when focusing on modelling a phase which is of short time duration, such as phase 2 in these models (Linnarsson, 1974; Lamarra *et al*, 1987; Barstow and Mole, 1991). It is after this averaging that the features that are termed the three phases are visible. Particular the time delay for the third phase can only be seen clearly after such averaging, as prior to the averaging there exist too many fluctuations in the signal to identify the separate phases. Some previous works which modelled data focusing more on a phase which lasts for a longer duration (i.e. the slow component) have used only a single transition as they were able to obtain enough data to fit the parameters in their respective models (Langsetmo *et al*, 1997; Bernard *et al*, 1998; Langsetmo and Poole, 1999; Bearden and Moffatt, 2000; Obert *et al*, 2000; Borrani *et al*, 2001). In Bearden and Moffatt (2000) this data was then averaged using a rolling three-breath average before a three-phase model was fitted, whilst in Borrani *et al* (2001), the data was edited with outliers removed and then the three phase model was fitted. It has been asserted (Stirling, Zakynthinaki and Saltin, 2005; Stirling and Zakynthinaki, 2009) that in these instances, due to the spread of the data it is not obvious that three phases are required in the model or, that there exist different time delays for the second and third phases. Both models (Bearden and Moffatt, 2000; Borrani *et al*, 2001) include these features, however it is argued that the exponentials used for curve fitting fit better statistically with a time delay. It has been pointed out, however, that the improvement in fit following the introduction of a time delay is marginal and, bearing in mind that only a specific family of exponentials were used to model real noise-containing data, the existence of time delays in the time series of a single bout of exercise could be debatable (Stirling, Zakynthinaki and Saltin, 2005; Stirling and Zakynthinaki, 2008; Stirling and Zakynthinaki, 2009).

Further rationale that they put forward for the assertion of no time delayed phases is based upon the consideration that time-delayed phases are a figment of the incorrect treatment of the data and the overly simple curve fitting of the, usually, averaged data. The reported problems regarding high levels of uncertainty in slow component time delay or insufficient clarity in the drop in the respiratory exchange ratio (RER) defining primary component time delay are due to trying to fit time-delayed phases to data with no such features. Due to the poor data handling and curve fitting the time constants are also physiologically irrelevant. Breath-by-breath recordings exhibit spontaneous fluctuations (Linnarsson, 1974; Lamarra *et al*, 1987). A number of different algorithms with different assumptions are therefore used to estimate the breath-by-breath $\dot{V}O_2$, resulting in notable differences observable throughout the whole on/off transient, most notably so in the initial response (Koga, Shiojiri and Kondo, 2005). These algorithms can also affect the three-phase curve parameters estimates (Cauterro *et al*, 2002; Gimenez and Busso, 2008). Breath-by-breath variability may have biological significance (Borrani *et al*, 2001) as nonlinear systems such as those governing the respiratory and circulatory functions can produce signals that look like random noise but are in fact not stochastic (random values with normal distribution) (Kantz and Kurths, 1998; Belair and Glass, 2003; Kantz and Schreiber, 2003; Ellner and Guckenheimer 2006; Shelhamer, 2007). Therefore part of what is attributed to noise can contain inherent features and vital information (Zakynthinaki *et al*, 2007). For example, in both constant and free-paced 10,000-m runs the $\dot{V}O_2$ has a scaling exponent above 0.5, the value for white noise (Borrani *et al*, 2001). Noise reduction is commonly achieved through ensemble averaging the responses of multiple identical exercise bouts (Lamarra *et al*, 1987). This may only be justified when the noise is Gaussian and stochastic (Whipp and Rossiter, 2005) and the basic response pattern of each bout is identical, which in general is not the case (Bearden *et al*, 2004). Lamarra *et al* (1987) and Rossiter *et al* (2000) have previously reported that the noise is white, however, only the last 120s of non-slow component data were analysed. Whereas many previous studies have shown that some breath-by-breath algorithms may produce data with non-white noise (Capelli, Cautero and Di Prampero, 2001; Cauterro *et al*, 2002; Billat *et al*, 2006). In particular, in Potter *et al* (1999), a large number of data points were used and they found the noise to be non-random (although this was in children). Therefore averaging several repetitions may be considered methodologically unjustified (Cauterro *et al*, 2002).

1.5.5 Ensemble averaging of data

Zakynthinaki *et al* (2007) have demonstrated a possible issue with ensemble averaging. They display four on-transient data sets that correspond to identical velocities and identical work load changes, it is noted that they are very similar but not identical. This is also the case in the literature (Linnarsson, 1974; Xing *et al*, 1991), where such data sets are characterized as identical, despite observable fluctuations of high frequency and amplitude. The aforementioned authors surmised from the study that the averaging procedure introduces features not included in the original data sets (Zakynthinaki *et al*, 2007).

It is contended that an ensemble average could either underestimate, or overestimate, the basic response pattern, depending on whether the amplitude and/or concentration of the high frequency fluctuations is larger below, or above, the basic response pattern (Zakynthinaki *et al*, 2007). When the purpose of the study is to find the underlying dynamics, methods of treating the data such as averaging over repeated bouts of exercise, may cause a problem as they can introduce features not existing in the raw data set. Also much confusion could arise, as averaging over repeated experiments may lead to the introduction of sharp deviations from the underlying curve. This has important implications when deciding on the smoothness of a model and the underlying physiological reasons for non-smooth behaviour. A good example of such implications is that the three phases of the so called 3-phase model may only be clearly seen following averaging over multiple data sets, as in a single raw un-averaged data set the spread of individual time series data is too large to identify such features (Borrani *et al*, 2001).

Further to this due to variation in parameter values, particularly in the time constants, between exercise bouts when ensemble averaged, it may be considered debatable whether ensemble averaging is accurate and appropriate (Bearden *et al*, 2004; Zakynthinaki *et al*, 2007). A model that is fit to the features of averaged data is not necessarily a good model of the raw un-averaged data of a single exercise bout. A curve without time-delayed phases has previously been demonstrated to fit the data Stirling and Zakynthinaki, 2008; Stirling, Zakynthinaki and Billat, 2008). It is further contended that the basic response pattern should be modelled, not the ensemble average, which in general is a different curve (Zakynthinaki *et al*, 2007).

1.5.6 Parameter interdependency

The phase 1/2 components are interconnected, complicating the time delay interpretation (Whipp and Rossiter, 2005). Theoretically, the commencement of phase 2 (i.e., the first time delay) should be signalled by a fall in the RER, however, this decrease may not be sufficiently clear for this purpose and a value of at least 20s is commonly utilised (Whipp and Rossiter, 2005). Bearden and Moffat (2001) have noted that the use of a predetermined time frame for estimation of the amplitude of the slow component is not supported by their work.

Multiple research groups have attempted to improve the phase 2 of the mathematical modelling process fit by constraining the fitting window to start once exercise has commenced (Whipp and Rossiter, 2005). Due to the observation that there exists a high degree of interdependency in the parameters (Koga, Shiojiri and Kondo, 2005) arbitrarily cutting data affects all the parameter values. As a result τ_2 will be dependent on the amount of data removed, making it of limited use physiologically. For the phase 1 and slow component, the best fit to the data can result in unrealistically large values of the amplitude and/or time constant i.e. the model is producing time constants that predict completion long after the exercise bout is finished (Koga, Shiojiri and Kondo, 2005). The above rationale underpins Stirling and colleagues (2002; 2007; 2008; 2009) contention as to whether the exponential is a good model for these phases and how parameter interdependency can dramatically affect parameter estimates, and therefore confidence (Engelen *et al*, 1996; Casaburi *et al*, 1998; Whipp and Rossiter, 2005).

The extent to which parameters are interdependent has been broached in previous work (Koga, Shiojiri and Kondo, 2005), despite this finding it not been universally reported. However, as Table 1.1 demonstrates, compiling literature reported parameter values for Baseline $\dot{V}O_2$; Primary component magnitude, time constant and time delay; and Slow component magnitude, time constant and time delay, shows that there is a an aspect of parameter variability, not just within studies, but across studies.

1.5.7 No slow component below GXT

As a number of authors have contended, current conventions such as the current modelling process, ensemble averaging of data and assumptions/ignorance's regarding parameter variability, demonstrate a number of contentions. However, one convention that should be addressed is the acceptance that the slow component emerges only at exercise intensities above GXT (Whipp and Wasserman, 1972; Kalis *et al*, 1988; Ozyener *et al*, 2001). Although there are numerous reports in the literature of the slow component emerging exclusively at work rates >GXT (Whipp and Wasserman, 1972; Kalis *et al*, 1988; Henson, Poole and Whipp, 1994; Ozyener *et al*, 2001), the evidence for this could be viewed as insubstantial.

Many studies have investigated the slow component at relative intensities below and above GXT, however, this does not necessarily provide compelling evidence for the slow component emerging at GXT. Firstly, as mentioned above, the potentially tenuous link between LT, GXT, the slow component and its emergence at these, apparently, analogous demarcations is contentious. Furthermore, rarely does any study explore the oxygen uptake kinetics at exercise intensities close to GXT. There are well established reports above GXT, but limited reports below GXT (Carter *et al*, 2000, Carter *et al*, 2002; Wilkerson *et al*, 2004). Even when the kinetics below the GXT are explored, the relative exercise intensity tends to be well below the threshold (i.e. 80%GXT), and reports of a slow component magnitude below GXT are not entertained. Further to this, it is evident that across the literature very high exercise intensities are being selected to represent the heavy intensity exercise domain e.g. 50%Δ (or in some cases, higher) is commonly used, meaning the exercise may not be of a heavy intensity (Carter *et al* 200; Burnley, 2002; Pringle, 2002; Deley *et al*, 2005; Malek *et al*, 2008; Bosquet *et al*, 2011) (Henson, Poole and Whipp, 1989; Whipp, 1994; Poole, 1994; Carter *et al*, 2000; Carter *et al*, 2002).

1.5.8 Steady state assumption

Clearly there are a number of contentions with regards to the modelling of $\dot{V}O_2$ kinetics data, primarily focused around the treatment of collected data. However a further issue with regards to the modelling of slow component data is much more fundamental. There are a number of assumptions made within the field of $\dot{V}O_2$ kinetics, not least of which is the assumption that exercise performed supra-GXT, but sub-CP, will result in a steady state (Barstow and Mole, 1991; Whipp, 1994).

The time course of any exponential process may be characterised by the time constant (τ) and should be complete after 5 x τ has elapsed (Figure. 2.2) (Jones and Poole, 2005). In reality, however, slow component magnitudes for, apparently, steady-state heavy intensity exercise that have been universally reported demonstrate an issue of contention. As compiled literature (See Table. 2.1) demonstrates, values reported for 1τ show that the $\dot{V}O_2$ response would not be complete within the exercise protocol.

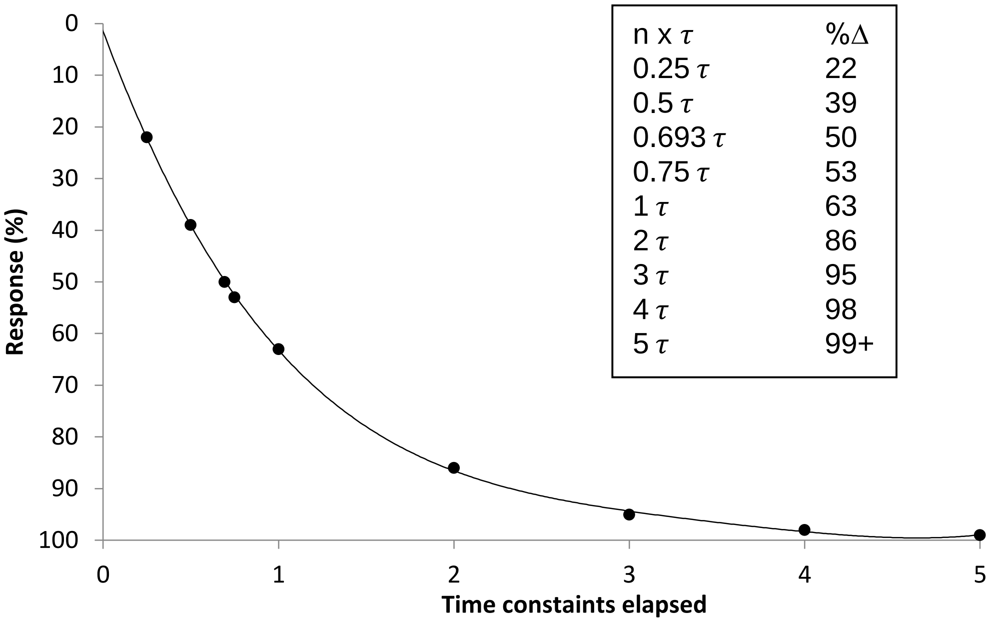


Figure. 2.2 Schematic representation of the time course of an exponential process that is a function whose instantaneous rate of change is proportional to ‘how far’ it currently is from its ‘target’. The time course can be characterised be the time constant (τ). After 1τ has elapsed the response will have attained 63% of its final value. The inset shows the percentage of the final value attained after nτ has elapsed. Graph reproduced from Jones and Poole (2005).

After 1τ has elapsed the response will have attained 63% of its final value, with the response complete in 5 x τ (Jones and Poole, 2005). However there are clear examples of inappropriate inferences being made from the aforementioned mathematical models in previous literature. For example, Carter *et al* (2002) provided a comprehensive examination of the oxygen uptake kinetics across exercise intensities, performing exercises on a treadmill of 6 minute (360s) duration. There were no reported values for; slow component magnitude, time delay or time constant for exercise intensities; 80% LT and 100% LT. However for 20%Δ (20% of the difference in $\dot{V}O_2$ between that at GXT and $\dot{V}O_{2peak}$), 40%Δ, 60%Δ, 80%Δ and 100%Δ they reported time constants of 221.7, 289.4, 247.1, 255.3 and 224 s, respectively. Based upon these reported time constants, the earliest the response would be complete is 1108.5s (for 20%Δ), well beyond the 360s test duration. Within this paper it was considered appropriate to only use a 2 component model above GXT (as convention has dictated), however no attempt was made to try and fit the 2 component model below threshold. A further example is evident in Pringle (2002), similar to above, no slow component magnitude, time delay or time constant was reported below GXT, whereas at 50%Δ and 70%Δ, time constants were 242.3 and 269.4 s respectively for a 360 s test protocol, meaning the $\dot{V}O_2$ response would not be complete until 1211.5s (for 50%Δ), again, long after test cessation. The reported time constants clearly demonstrate that none of the $\dot{V}O_2$ responses would be complete within the 360 s test duration. Even in instances heavy intensity exercise is performed prior to an exercise bout, overall $\dot{V}O_2$ kinetics have been shown to speed during subsequent heavy intensity exercise (Gerbino *et al*, 1996; Burnley *et al*, 2000), reducing the slow component amplitude, whilst the time constant remains the same (Bearden and Moffatt, 2001a; Koppo and Bouckaert, 2001; Scheuermann *et al*, 2001). In either case, the response would not be complete. The conclusions made in the aforementioned papers contradict their own data i.e. the reported time constants contradict the conclusion that there is a steady state. Meaning, subjects performing, so called, heavy intensity exercise >GXT but <CP, may not actually be reaching a steady state, which has clear implications for the current modelling process. This may be attributed to a failing/inability of the models used or inappropriate intensities being used for heavy intensity exercise, meaning $\dot{V}O_2$ hasn't stabilised. This may suggest that there is good reason to doubt the achievement of a steady state This could be further investigated by way of comparing the mean slopes of $\dot{V}O_2$/time for the final part of steady-state exercise bouts and assessing the differences from zero (if the exercise elicits a steady-state response, there would be no significant difference from zero) However, to the author's knowledge, this has not been previously reported. Further, it is also evident that these studies make an assumption that the slow component is a first-order process and therefore, for step exercise, exponential. This assumption has not been extensively evaluated and has the further implicit assumption that the process is singular and recruited in an abrupt step-wise fashion.

1.5.9 Reporting of the data

Within previous literature there is an evident trend in the reporting of data. The tendency of much previous literature (Carter *et al*, 2000; Carter *et al*, 2002) is to present average data in a tabular format, which is useful. However, many studies then choose to graphically depict this data, not as an average, but as a 'typical subject' response. The issue with this is that the typical response shown is not necessarily representative of the average data. Although presentation of individual data can be useful, without graphical depiction of an average response it makes it very difficult to compare individual or typical responses to a mean response. One further concern is that, in many cases, no residual data is presented with the models, meaning no comparison of the fit of the models can be made (Carter *et al*, 2000; Carter *et al*, 2002).

1.6 Summary

Within the field of $\dot{V}O_2$ kinetics there are some well-established conventions that are continually observed. The conventions for modelling oxygen uptake data that have emerged are scarcely questioned. Firstly, as some authors have contended, the treatment of $\dot{V}O_2$ kinetics data may be questioned. It has been argued by some authors whether ensemble averaging is accurate and appropriate (Bearden *et al*, 2004; Zakynthinaki *et al*, 2007). Some authors regard that an ensemble average will either underestimate, or overestimate, the basic response pattern, depending on whether the amplitude and/or concentration of the high frequency fluctuations is larger below, or above, the basic response pattern (Zakynthinaki *et al*, 2007). Averaging over repeated bouts of exercise may cause a problem as they can introduce features not existing in the raw data set leading to the introduction of sharp deviations from the underlying curve (Zakynthinaki *et al*, 2007). It is suggested that one must ensemble average repeated, identical exercise bouts to reduce noise (Lamarra *et al*, 1987). This can only justified when the noise is Gaussian and stochastic (Whipp and Rossiter, 2005) and the basic response pattern of each bout is identical, which in general is not the case (Bearden *et al*, 2004).

Further, once data has been fit to an exponential model it has been observed that there exists a high degree of interdependency in the parameters (Koga, Shiojiri and Kondo, 2005). It has been shown that cutting data points will affect parameter estimates, resultantly the phase 2 time constant will be dependent on amount of data removed and this may affect the amplitudes and/or time constants of the first phase and slow component, presenting unrealistically high values of the amplitude and/or time constant (for example, time constant values that mean the response would not be complete within the test duration) (Koga, Shiojiri and Kondo, 2005; Zakynthinaki *et al*, 2007). To the authors' knowledge, the extent to which parameters are interdependent has not been properly investigated and collected literature (Table 1.1) indicates that there may be an aspect of parameter variability, not just within single studies, but across multiple studies.

In addition to the aforementioned contentions, there are more issues of fundamental importance that may be questioned. Firstly, the conventional wisdom is that modelling of the slow component should only start at GXT or LT and although at exercise intensities above GXT, there is indicatively an increased Lactate turnover (Barstow, 1994; Poole, 1994). It has not been shown that they do actually coincide and lactate has been shown not to mandate an additional $\dot{V}O_2$ requirement (Poole, 1994). An assumption made by many is that there is no slow component below the GXT, which feeds into the premise of only applying a biexponential model above GXT. Despite varied reports in the literature of the slow component emerging exclusively at work rates >GXT (Whipp and Wasserman, 1972; Kalis *et al*, 1988; Henson, Poole and Whipp, 1994), the evidence for this could be viewed as insubstantial. This assertion is based on the knowledge that rarely do studies explore the oxygen uptake kinetics close to the GXT (Carter *et al*, 2000; Carter *et al*, 2002; Pringle *et al*, 2002), however these studies make an assumption that the slow component is a first-order process and therefore, for step exercise, exponential. This assumption has not been extensively evaluated and has the further implicit assumption that the process is singular and recruited in an abrupt step-wise fashion and given the lack of association between the LT to the slow component, assuming that the slow component is not present below GXT should be considered tenuous and warrants investigation.

A fundamental belief in the measurement of oxygen uptake kinetics is that exercise performed above the GXT, but below CP (i.e. heavy intensity exercise), will result in a steady state (Barstow and Mole, 1991; Whipp, 1994). However, within the literature, published slow component time constants demonstrate that the $\dot{V}O_2$ response would not be complete within the time frame of an exercise bout, meaning that the presence of a steady state is an assumption rather than a demonstrable feature of the data. The time constants reported demonstrate a contradiction, as $\dot{V}O_2$ should reach a steady state (Whipp, 1994) and the modelling process used assumes a steady state has been reached. However, the reported time constants demonstrate that none of the $\dot{V}O_2$ responses would be complete within 5 x τ, leading to doubt of the suitability of the model to describe the response and/or the exercise intensities being used to represent heavy intensity exercise (i.e. 50%Δ or in some cases higher) are too high and don’t elicit a steady state response.

Therefore the aims of this study are to comprehensively describe the relationship between exercise intensity and the slow component of $\dot{V}O_2$, sub- and supra-GXT, and to conduct a systematic investigation into whether a steady-state during constant work-rate exercise (>GXT) is achieved. The hypotheses explored in this study are; exercise performed in the heavy exercise intensity domain may not reach a steady-state of oxygen uptake, parameters of the exponential modelling process are interrelated, the monoexponential model will produce a significantly lower standard error of the estimate in sub-GXT exercise intensities compared to the biexponential model, based upon modelled slow component time constants, the $\dot{V}O_2$ response will be incomplete during exercise performed in the heavy intensity exercise domain.

Table. 1.1. Chronological review of the reported oxygen uptake response to a number of exercise modalities and intensities.

Research Group	Ex Int.	Ex Modality	Base	PC Mag.	PC TD	PC tau	SC Mag.	SC TD	SC tau	Other Info
Engelen *et al*, 1996	95% LT	Cycle ergometer	690	560	26.1	19.1	-	-	-	*8 healthy subjects, 7 males, 1 female, 29.5±6y, 78.1±9.1kg, #*
	50%Δ		650	1440	21.4	25.2	260	166.8	253.6	
Carter *et al* 2000	80% LT	Treadmill running	388	1570	25.5	15	-	-	-	7 recreationally active subjects, 3 men, 4 female, 27±5y, 69.3±9.3kg, 1.74±0.08m, *
	25% Δ		422	2347	22.6	19.4	73.5	120.1	207.6	
	50% Δ		411	2559	16.6	20.1	204.8	111.6	234.3	
	75% Δ		413	2736	17.9	15.9	301.5	105.2	256.9	
Carter *et al* 2000	80% LT	Cycle ergometer	439	858	23	18	-	-	-	7 recreationally active subjects, 3 men, 4 female, 27±5y, 69.3±9.3kg, 1.74±0.08m, *
	25% Δ		447	1522	22.3	21..6	102	131.3	232.5	
	50% Δ		442	1773	21.2	22.4	334	116.8	229.5	
	75% Δ		470	2110	21.8	22.6	430	119	254.7	
Hughson *et al*, 2000	57% Peak	Cycle ergometer	1016	940	18.1	29.4	-	-	-	8 healthy male subjects, 20.8±0.7y.
	96% Peak		1038	1631	14.1	22.1	1097	73.1	106.4	
	125%Peak		1046	1766	12.5	16.3	669	40.5	53.1	

Williams *et al*, 2000	80% LT 50% Δ	Cycle ergometer	418 454	2084 3193	26.8 16.5	14.7 19	- 288.5	- 115.9	- 254.3	8 males, 30±7.3y, 75±5.9kg, *
Bearden and Moffatt, 2001	30%D M. Ex 30%D Bi. Ex	Cycle ergometer	1510 1530	1350 1160	5.4 13.31	50.06 26.39	- 320	- 133	- 364	Mono and Bi exp ran for same data. 8 healthy males, 27±3y, 1.77±0.04m, 72±8kg, 10 minute test duration.
Bearden and Moffatt, 2001	90%GXT 30%Δ	Cycle ergometer	1530 1540	710 1140	22.9 18.7	21 19.5	- 290	- 118.6	- 211.6	8 healthy males. 27±3y, 1.77±0.04m, 72±8kg, 10 minute test duration.
Burnley, Doust, Carter and Jones. 2001	50%Δ	Cycle ergometer	800	2060	21.3	24.6	340	101.2	250.3	9 healthy subjects, 2 females, 7 males, 27±4y, 1.75±0.06m, 71.1±5.5kg, *
Scheuermann *et al*, 2001	90% LT 50% Δ	Cycle ergometer	338 634	1010 2334	27.5 20.8	20.4 27.2	- 230	- 132.4	- -	7 healthy males, 29±7y, 1.79±0.04m, 82±12kg, 46.2±9.6 ml·kg^{-1}min^{-1}, #
Burnley 2002, PhD thesis	50% Δ	Cycle ergometer	950	1840	20.2	23.9	570	106.4	269.2	10 healthy, active subjects, 8 males, 2 females, 29±5y, 1.75±0.07m,

										70.8±7kg, 3650±480 ml·min^{-1}, *
Burnley 2002, PhD thesis	50%Δ	Cycle ergometer	800	2060	21.3	24.6	640	101.2	250.3	9 healthy subjects, 7 males, 2 females, 27±4y, 1.75±0.06m, 71.1±5.5kg, *
Burnley 2002, PhD thesis	50%Δ	Cycle ergometer	900	1950	21	23.1	470	89.2	216.6	9 healthy males, 27±6y, 1.81±0.05m, 76.8±8.8kg, 51±7 ml·kg^{-1}min^{-1}, *
Carter *et al* 2002	80% LT	Treadmill	465	925	27.1	6.2	-	-	-	9 recreationally active subjects, 6 male, 3 female, 27±7y, 69.8±8kg, 4137±967 ml·min^{-1}, *
	100% LT	running	474	1018	21	5	-	-	-	
	20% Δ		496	995	19.2	5.8	139	131.5	221.7	
	40% Δ		513	1091	18.8	5.5	264	107.2	289.4	
	60% Δ		507	908	15.5	2.8	399	106	247.1	
	80% Δ		528	940	15.6	3.7	487	89.6	255.3	
	100% Δ		541	1048	13.7	4	317	81.3	224	
Pringle 2002, PhD thesis	80% LT	Cycle ergometer	761	610	26.6	20.8	-	-	-	14 healthy subjects, 4 female, 10 male, 25±4y, 72.6±3.9kg, 1.74±0.09m,
	50%Δ		747	1915	19	25.8	398	109.6	242.3	
	70% Δ		772	2179	17.4	21.8	545	110.2	269.4	

										3500±240 ml·min^{-1}, *
Pringle 2002, PhD thesis	MLSS	Cycle ergometer	493	2737	19.3	19.1	171	123.5	216.3	9 endurance trained and habituated subjects, 6 males, 3 females, 27±7y, 69.8±9kg, 1.76±0.03m, 59.1 ml·kg^{-1}min^{-1}, maximum of 30 minutes duration, data reported for first 6 minutes.
	CV		520	2980	17.8	19.4	234	99.9	278.7	
	>CV		539	3003	16.2	18.7	390	109.4	251.6	
Pringle 2002, PhD thesis	80% VT	Treadmill running	358	1945	24.7	16.7	-	-	-	9 healthy subjects, 7 males, 2 females, 29±7y, 1.77±0.07m, 73±7.5kg, *
	50%Δ		419	2940	17.2	19.6	283	118.8	260.2	
Pringle 2002, PhD thesis	50%Δ	Cycle ergometer	1290	1593	17	30.2	328	113.8	-	10 healthy subjects, 8 males, 2 females, 26±4y, 71.5±7.9kg, 1.76±0.05m, *
Wilkerson *et al* 2004	60% GXT	Cycle ergometer	789	540	16.9	23.2	-	-	-	7 healthy males, 24.7±3y, 76.6±8.8kg, *
	90% GXT		802	927	17	21.8	-	-	-	
	40%Δ		800	1862	13.4	26.4	186	133	-	

	80%Δ		798	2492	10.8	26.7	602	125	-	
	100%Δ		795	2634	8.6	26.2	349	96	-	
	110%Δ		788	2685	8.3	26	-	-	-	
	120%Δ		786	2740	7.4	28.1	-	-	-	
Burnley *et al*, 2005	80%Δ	Cycle ergometer	1010	2190	-	29	600	-	-	11 physically active, but not highly trained volunteers, 10 males, 1 female, 23±6y, 77.2±11kg, 1.77±0.04m, test performed until volitional exhaustion.
Deley *et al*, 2005	Heavy	Cycle ergometer	-	2510	6.1	34.2	750	150.6	269.6	9 healthy, trained males, 22.6±2.1y, 1.75±0.05m, 71.2±6.6kg, 10 minute test duration.
Sabapathy *et al*, 2005	50%Δ	Cycle ergometer	800	2125	-	31	561	132	-	8 recreationally active male subjects, 21.4±1y, 79.6±4.3kg, 1.79±0.02m, 7 minute test duration.

Wilkerson *et al*, 2005	90%T 70%∆	Cycle ergometer	810 770	1210 2320	15 12	28 32	- 600	- 134	- -	7 healthy male subjects, 26±4y, 83.5±4.9kg, *
Wilkerson *et al*, 2005	80% LT 70%∆	Cycle ergometer	830 830	1230 2520	13 10	27 29	- 660	- 129	- -	16 healthy subjects, 15 male, 1 female, 25±4y, 78±8.8kg, *
Berger *et al*, 2006	60%∆	Cycle ergometer	800	2340	12	29	590	120	-	7 healthy males, 26±5y, 1.83±0.06m, 81.7±7.1kg, *
Berger, Tolfrey and Jones. 2006	80%GXT 70%∆	Cycle ergometer	650 660	710 1320	14 15	30 25	- 660	- 100	- 256	7 active subjects, 3 males, 4 females, 24±5y, 1.71±0.1m, 74.2±11.2kg, 34.5±5.9 $ml \cdot kg^{-1} min^{-1}$, *
Burnley, Doust and Jones. 2006	70%∆	Cycle ergometer	1110	2420	-	25.9	440	-	-	9 healthy males, 29±9y, 1.79±0.06m, 77.7±11.3kg, *
Ingham *et al*, 2007	80%LT 50%∆	Rowing ergometer	613 677	3423 4547	23.8 17.5	13.9 18.7	- 541	- 90.6	- 242	8 elite male rowers, 25.8±2.3y, 96.3±5.2kg, 1.93±0.03m, *
Ingham *et al*, 2008	50%∆	Rowing ergometer	-	3330	17.3	21	510	103	248.6	9 experienced national standard male rowers,

										23.8±1.4y, 4.82±0.05m, 74.5+5.2kg, *
Malek *et al*, 2008	60%GXT 50%∆	Cycle ergometer	700 700	750 2040	31.2 37.4	21.2 30.2	- 720	- 121.1	- 283.7	13 healthy, untrained males, 7 minutes test duration.
Bailey *et al*, 2009	80% GXT 70%∆	Cycle ergometer	910 990	1520 2190	- -	26 33	- 740	- -	- -	8 healthy males, 26±7y, 1.8±0.03m, 82±6kg, *
Bailey *et al*, 2010	Low Int. High Int.	Knee extensor	389 391	870 1726	22 37	11 32	- 209	- -	- -	7 healthy, recreationally active males, 28±7y, 1.8±0.02m, 81±7kg, *
Bosquet *et al*, 2011	30% diff between CP and PPO	Cycle ergometer	1300	1805	23	28	589	96	232	30 moderate to well trained male endurance athletes, *
Breese 2011, PhD thesis	70%∆	Cycle ergometer	1350	2670	11	22	540	120	-	7 trained junior cyclists, 16.7±1y, 1.81++0.07m, 68.5±4kg, *

* denotes exercise of 6 minute duration, # denotes exercise of 8 minute duration, - denotes omission or non-reporting of value. Ex. Int., Exercise Intensity; Ex. Modality., Exercise Modality; Base., Baseline $\dot{V}O_2$ (ml·min^{-1}); PC Mag., Primary Component Magnitude (ml·min^{-1}); PC

TD., Primary Component Time Delay (s); PC tau., Primary Component Time Constant (s); SC Mag., Slow Component Magnitude (ml·min^{-1}); SC TD., Slow Component Time Delay (s); SC tau., Slow Component Time Constant (s). Other Info., Other information pertaining to the relevant study, including subject characteristics. %Δ (% difference in $\dot{V}O_2$ between that at GXT/LT/VT and $\dot{V}O_{2peak}$).

2.0 Methods

2.1 Participants

Eight recreationally active male volunteers agreed to take part in the present study. Each subject was familiar with a laboratory setting and exercise protocols. Subjects were instructed to arrive at the laboratory for testing rested, hydrated, having refrained from alcohol and caffeine intake 24 and 6 hours respectively prior to testing, a minimum of 3 hours post-prandial and to have avoided strenuous physical activity 48 hours preceding a test session. Tests were administered at the same time of day (± 2 hours), for each subject, to minimise the effect of diurnal variation on results (Valdez *et al*, 2010). After receiving information regarding the nature of the study, the procedures to be adhered to before and during testing, in addition to the related risks and benefits, the subjects provided their full written and informed consent (Appendix I). All subjects were required to complete a Health and Safety questionnaire (Appendix II) detailing their health status and medical history, prior to providing informed consent. All protocols were approved by the University of Gloucestershire Research Ethics Sub-Committee. Table 2.1 details the anthropometric and physiological attributes of the subjects.

Table. 2.1. Individual participant characteristics.

Participant	Age (y)	Stature (m)	Mass (kg)	$\dot{V}O_{2peak}$ ($L\cdot min^{-1}$)	$\dot{V}O_2$ at GXT ($L\cdot min^{-1}$)
1	22	1.75	74.8	3.22	2.08
2	22	1.83	81.1	4.76	3.15
3	44	1.95	94.6	4.26	1.92
4	20	1.65	62.6	3.58	1.89
5	21	1.73	68.3	3.17	1.69
6	22	1.86	84.2	4.84	2.64
7	19	1.77	70.2	4.23	2.06
8	20	1.75	77.4	3.09	1.87
Mean	24	1.78	76.7	3.89	2.16
SD	8	0.09	10.1	0.72	0.49

2.2 Experimental design

This research was conducted using an experimental design primarily utilising a within subject repeated measures design. The subjects were required to visit the laboratory on nine occasions for testing. The first visit involved determination of gas exchange threshold (GXT) and peak oxygen uptake ($\dot{V}O_{2peak}$) with a progressive ramp exercise test. The following tests involved multiple laboratory visits, with the subjects performing a square wave transition from rest to one of eight exercise intensities; -20%Δ (minus 20% of the difference in $\dot{V}O_2$ between that at GXT and VO_{2peak}), -10%Δ, GXT, 10%Δ, 20%Δ, 30%Δ, 40%Δ and 50%Δ. No more than two transitions were completed in 1 day, with at least one hour recovery between transitions. The square wave transitions were performed in a counterbalanced design using an 8x8 Latin square algorithm (Byers, 1991).

2.3 Procedures

All tests were performed on an electromagnetically braked cycle ergometer (Lode, Excalibur Sport, Groningen, The Netherlands). The horizontal and vertical adjustments of the handlebars and saddle were measured using a tape measure and recorded and reproduced for all subsequent tests. Subjects were instructed to cycle at a self-selected cadence and were encouraged to maintain this cadence throughout the entire test. If the self-selected cadence fell by more than 5 $rev{\cdot}min^{-1}$, verbal encouragement was given.

Throughout each test the participants breathed through a low dead-space (90 ml), low resistance (5.5 cm H_2O at 510 $L{\cdot}min^{-1}$) mouthpiece and turbine assembly, and the nose was occluded using a nose clip. Gases were drawn continuously from the mouthpiece through a 2 m sampling line (0.5mm internal diameter) to a mass spectrometer (Pulmolab EX671, Ferraris, Rainham, UK) where they were analysed for O_2, CO_2 and N_2. Expired volumes were determined using a turbine volume transducer (Interface Associates, Alifovieja, US). The mass spectrometer was calibrated before each test using gas mixtures (Linde Gas, London, UK) for which the concentrations of oxygen (O_2), carbon dioxide (CO_2) and nitrogen (N_2) were known. The turbine was calibrated before each test using a 3 L calibration syringe (Hans Rudolf, Kansas, US). Oxygen uptake was calculated and displayed on a breath-by-breath basis. The volume and concentration signals were integrated by computer, following analogue to-digital conversion, with account taken of the gas transit delay through the capillary and room temperature (which was maintained at 21°C).

Capillary blood samples (5 µL) were drawn from the fingertip and assayed for lactate concentration using a single use test strip and an automated analyser (Lactate Pro, Arkay Inc., Kyoto, Japan). When the blood sample drawn from the tip of the test strip reaches the reaction layer of the automated analyser, Lactate in the sample reacts with Lactate Oxidase. Simultaneously Potassium Ferrocyanide (oxidised form), contained in the reaction layer, produces Potassium Ferrocyanide (reduced form). Potassium Ferrocyanide is produced in proportion to the Lactate concentration of the sample. The accumulated Potassium Ferrocyanide is then oxidised to Potassium Ferricyanide and produces an electrical current which is converted to Lactate concentration. Body mass was determined using a calibrated set of digital scales (Seca, Birmingham, UK) while the subject was dressed for testing, without trainers. Stature was measured, without trainers, using a wall mounted stadiometer (Holtain Ltd., Crymych, UK). Subjects were required to stand erect, ensuring their heels were in contact with the floor and the back of the stadiometer. When the head was in the Frankfort plane, stature was recorded while the researcher applied minimal spinal traction during subject inspiration.

Subjects were required to remain seated for five minutes prior to test commencement to ensure true baseline values. Short-range radio-telemetry was used to derive heart rate from the R-R interval (FS3c, Polar Electro Oy, Kempele, Finland). Heart rate was recorded at 5 second intervals throughout all tests.

The subjects performed a progressive ramp exercise test to volitional exhaustion in order determine GXT and $\dot{V}O_{2peak}$. During the progressive ramp test the first two minutes were set at 0 W to allow respiratory data to stabilise. The ramp rate was set at 20 $W \cdot min^{-1}$, commencing at 60 W (altered dependent upon fitness level of individual to elicit exhaustion in approximately 12 min). Volitional exhaustion was determined when the subject could not maintain a self-selected cadence, after three verbal encouragements. At test cessation, a five minute recovery period at a power output of 50 W commenced.

Gas exchange threshold was identified using the V-slope method (Beaver, Wassermann and Whipp, 1986). This method consisted of plotting CO_2 production over O_2 utilization and identifying a breakpoint in the slope of the relationship between these two variables. The $\dot{V}O_2$ corresponding to this breakpoint is considered the GXT (Beaver, Wasserman and Whipp, 1986). In instances GXT could not be identified using the V-slope method, the ventilatory equivalent method was used; this identifies the oxygen uptake which causes the first rise in the ventilatory equivalent of oxygen ($\dot{V}_E/\dot{V}O_2$) without a simultaneous rise in the ventilatory equivalent of carbon dioxide ($\dot{V}_E/\dot{V}CO_2$) (Gaskill *et al*, 2001).

Extrapolation of the relationship between $\dot{V}O_2$ and power (W) from the progressive ramp exercise test was, after allowing for the delay effect, used to calculate the power requiring; -20%Δ (minus 20% of the difference in $\dot{V}O_2$ between that at GXT and $\dot{V}O_{2peak}$), -10%Δ, GXT, 10%Δ, 20%Δ, 30%Δ, 40%Δ and 50%Δ. Subsequently subjects performed a series of square wave transitions of eight minutes in duration at the eight exercise intensities on separate days. The exercise protocol began with subjects sitting on the cycle ergometer for five minutes, followed by two minutes unloaded (0 W) cycling for each exercise bout. Subjects cycled at a self-selected cadence and this was reproduced for all tests. Fingertip capillary blood samples were drawn and assayed immediately pre and one minute post the eight minute exercise period. The difference between the end exercise Lactate concentration [La^{-1}] and the resting [La^{-1}] was expressed as a delta value (Δ[La^{-1}]).

2.4 Data analysis

Following data collection from the ramp incremental exercise test, the breath-by-breath values for; $\dot{V}_E$, $\dot{V}O_2$, $\dot{V}CO_2$, Mixed expired O_2 (mexpO_2) and Mixed expired CO_2 (mexpCO2) were exported to a spread sheet (Microsoft Excel, 2010), where all subsequent data were analysed. Respiratory data were calculated and displayed on a breath-by-breath basis; the raw breath-by-breath data was then interpolated to second by second data. Graphical plots of the ventilatory equivalents ($\dot{V}_E$/ $\dot{V}O_2$ and $\dot{V}_E$/ $\dot{V}CO_2$) were plotted to allow identification, using a least squares approach, and removal of data past the respiratory compensation point (RCP) (Whipp *et al*, 1986). For step tests, breath by breath data had any values that were three or more Standard Error of the Estimate (SEE) removed (Lamarra *et al*, 1987).Oxygen uptake data were subsequently linearly interpolated to provide second by second values to aid noise reduction. Non-linear least squares regression techniques were used to fit the square wave data after the onset of exercise with an exponential function. An iterative process ensured the sum of squared error was minimised. The mathematical models used are detailed below (equation 2.1 (Whipp *et al*, 1982) and 2.2 (Barstow and Mole, 1991)).

$$\dot{V}O_2(t) = A_0 + A_1(1 - e^{-(t-\delta_1)/\tau_1})$$

Equation 2.1.

$$\dot{V}O_2(t) = A_0 + A_1(1 - e^{-(t-\delta_1)/\tau_1}) + A_2(1 - e^{-(t-\delta_2)/\tau_2})$$

Equation 2.2.

Where A_0 is the resting baseline value, A_1 and A_2 are the amplitudes for the two components, τ_1 and τ_2 are the time constants for the two components, and $t - \delta_1$ and $t - \delta_2$ are the time delays from the onset of exercise for the two components. Residual data for both model fits was also reported.

The Standard Error of the Estimate (SEE) for both mono and bi exponential models (Equation 2.3 and 2.4, respectively) was calculated using the following process;

$$SEEmono = \sqrt{(\frac{SSE}{NCASES - 3})}$$

Equation 2.3

$$SEEbi = \sqrt{(\frac{SSE}{NCASES - 6})}$$

Equation 2.4

Where SEEmono is the standard error of the estimate for the mono exponential model, SEEbi is the standard error of the estimate for the bi exponential model, SSE is the sum of squared errors and NCASES are the number of data sets.

2.5 Statistical analysis

All statistical tests were carried out using IBM Statistical Package for the Social Sciences (SPSS) for Windows (Version 20.0). A one sample *t*-test was utilised for slope analysis of the data for the final minute of each square wave exercise bout to assess difference from zero. Average blood Lactate responses for each exercise intensity and the SEE for each exercise intensity for both the mono and bi exponential mathematical models were reported and analysed using a paired samples *t*-test. Pearson's Product-moment correlation was carried out to assess the relationship between the mean modelled oxygen uptake variables for the mono exponential model ($\boldsymbol{A_1}$ Primary component amplitude, $\boldsymbol{t - \delta_1}$Primary component time delay, $\boldsymbol{\tau_1}$Primary component time constant) and the bi exponential model ($\boldsymbol{A_1}$ Primary component amplitude, $\boldsymbol{t - \delta_1}$Primary component time delay, $\boldsymbol{\tau_1}$Primary component time constant, $\boldsymbol{A_2}$ Slow component amplitude, $\boldsymbol{t - \delta_2}$ Slow component time delay and $\boldsymbol{\tau_2}$ Slow component time constant) across participants.

The group data are mean ± SD unless otherwise stated. The alpha level was set equal to 0.05 for all analyses before data collection. The outcome of this research was to comprehensively describe the relationship between exercise intensity and the slow component of $\dot{V}O_2$, sub- and supra-GXT, using a mono and bi exponential model. Secondly, to conduct a systematic investigation into whether a steady-state during constant work-rate exercise is achieved, measured using a one sample *t*-test for difference of the $\dot{V}O_2$ vs. Time slope (for the final minute of each square wave exercise bout) from zero.

3.0 Results

The data from one subject and mean subjects breath-by-breath oxygen uptake ($\dot{V}O_2$) response, mono and bi exponential model fits and residuals across exercise intensity domains are shown in Figure 3.2a. and Figure 3.2b., respectively, and the mean (SD) data are presented in Table 3.2 Subjects exercised at varying work rates dependent upon the exercise intensity imposed. The corresponding individual and mean (standard deviation (SD)) work rates based upon gas exchange threshold (GXT) and peak oxygen uptake ($\dot{V}O_{2peak}$) values are displayed in Table. 3.1 demonstrating the increase in work rate as exercise intensity increases.

Table. 3.1. Individual subject and group work rates (W).

Participant	-20%Δ	-10%Δ	GXT	+10%Δ	+20%Δ	+30%Δ	+40%Δ	+50%Δ
1	141	152	162	173	184	194	205	215
2	224	240	257	273	289	306	322	338
3	144	160	176	192	208	224	240	256
4	116	132	147	162	177	192	207	223
5	125	135	146	157	167	178	188	199
6	219	237	254	272	289	307	325	342
7	139	155	172	188	205	221	238	254
8	155	169	183	196	210	224	237	251
Mean	158	173	187	202	216	231	245	260
SD	41	43	44	46	48	50	51	54

An example of the biphasic response in the identification of the gas exchange threshold, to allow calculation of individual subject work rates is demonstrated below with Figure. 3.1. depicting an example $\dot{V}$-slope plot of $\dot{V}CO_2$ versus $\dot{V}O_2$.

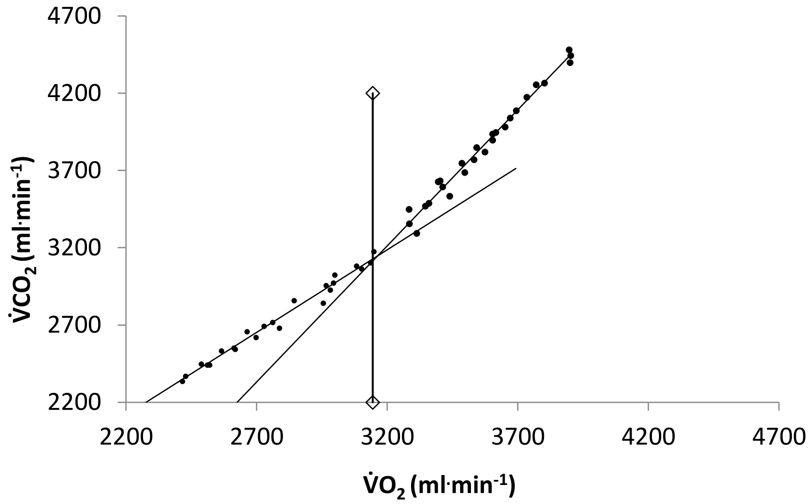


Figure. 3.1. An example $\dot{V}$-slope plot for GXT determination.

Parameters of the oxygen uptake response as a function of exercise intensity for the mono exponential model and bi exponential model (Table 3.2) demonstrates that for the mono exponential model all time constants would be complete within the 480 s exercise time frame. However, when applying the bi exponential model, the slow component time constants demonstrate that not one of the $\dot{V}O_2$ responses would be complete within the exercise duration. When applying the biexponential model the slow component of $\dot{V}O_2$ increased with exercise intensity. For both the mono and biexponential model, the primary amplitude increased with exercise intensity. Whereas the primary amplitude time delay decreased for both models. When applying the biexponential model, the slow component time delay tended to decrease and the slow component time constant tended to increase with exercise intensity. Visual inspection of the residual plots indicated a better fit for the biexponential model, although in some cases did not fit the non-steady state portion of the response.

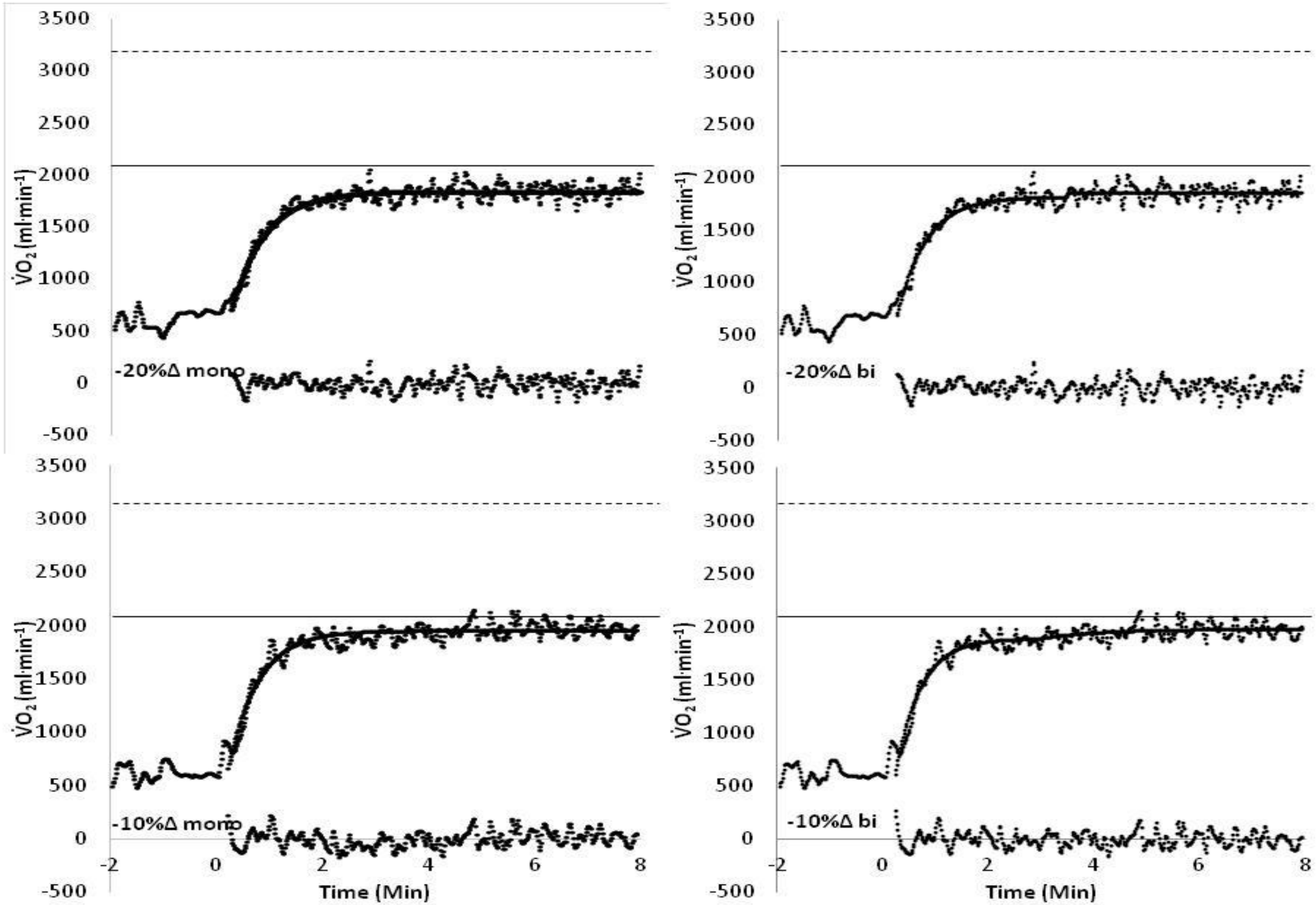
Table. 3.2. Parameters of the oxygen uptake ($\dot{V}O_2$) response as a function of exercise intensity for the mono exponential model and bi exponential model. Baseline, A_1 Primary amplitude, δ_1 Time delay for the primary amplitude, A_2 Slow component δ_2 Time delay for the slow component, τ_2 Time constant for the slow component. Values are presented as the mean (SD).

Mono exponential

Variable	-20%Δ	-10%Δ	GXT	+10%Δ	+20%Δ	+30%Δ	+40%Δ	+50%Δ
Baseline (ml·min^{-1})	737	630	680	620	617	737	800	758
	(247)	(200)	(335)	(302)	(334)	(219)	(353)	(236)
$\boldsymbol{A_1}$(ml·min^{-1})	1329	1568	1644	1803	2101	2139	2232	2592
	(387)	(476)	(474)	(569)	584	418	513	525
$\boldsymbol{\delta_1}$ (s)	12.3	8.3	9.1	8.3	8.1	9.1	9.7	13.9
	(8.1)	(4.9)	(5.4)	(5.4)	(3.7)	(7.4)	(7.1)	(12.9)
$\boldsymbol{\tau_1}$(s)	26.9	29.8	25.9	29.5	38.5	39.9	42	44.3
	(13.3)	(14.8)	(6.5)	(9.1)	(13.4)	(11.2)	(3.6)	(10.1)
Gain (ml·min·W^{-1})	8	9	9	9	9	9	9	10
	(1)	(2)	(1)	(2)	(2)	(2)	(2)	(1)

Bi exponential

Variable	-20%Δ	-10%Δ	GXT	+10%Δ	+20%Δ	+30%Δ	+40%Δ	+50%Δ
Baseline (ml·min^{-1})	737	630	680	620	617	737	800	758
	(247)	(200)	(335)	(302)	(334)	(219)	(353)	(236)
$\boldsymbol{A_1}$**(ml·min^{-1})**	1218	1410	1541	1659	1903	1876	2004	2092
	(334)	(369)	(410)	(556)	(554)	(478)	(505)	(499)
$\boldsymbol{\delta_1}$ **(s)**	15.7	14.4	12.5	12.7	11.5	12.6	12.1	10.5
	(9.91)	(7.39)	(7.08)	(5.43)	(2.02)	(4.17)	(3.4)	(4.05)
$\boldsymbol{\tau_1}$**(s)**	23.3	25.6	27.7	25.9	27.1	28.2	28.8	29.4
	(12.1)	(4.95)	(8.2)	(8.9)	(4.34)	(5.22)	(8.3)	(13.8)
$\boldsymbol{A_2}$**(ml·min^{-1})**	123	227	274	280	315	417	437	597
	(121)	(151)	(135)	(165)	(121)	(115)	(149)	(344)
$\boldsymbol{\delta_2}$**(s)**	110	165	166	161	148	148	131	137
	(67)	(81.3)	(111)	(56)	(29.9)	(52.8)	(47.5)	(53.9)
$\boldsymbol{\tau_2}$**(s)**	240	155	171	121	125	239	146	187
	(331)	(167)	(121)	(136)	(103)	(355)	(110)	(170)
Gain (ml·min·W^{-1})	9	10	10	10	11	11	11	12
	(1)	(2)	(2)	(1)	(2)	(2)	(2)	(2)



3500
3000
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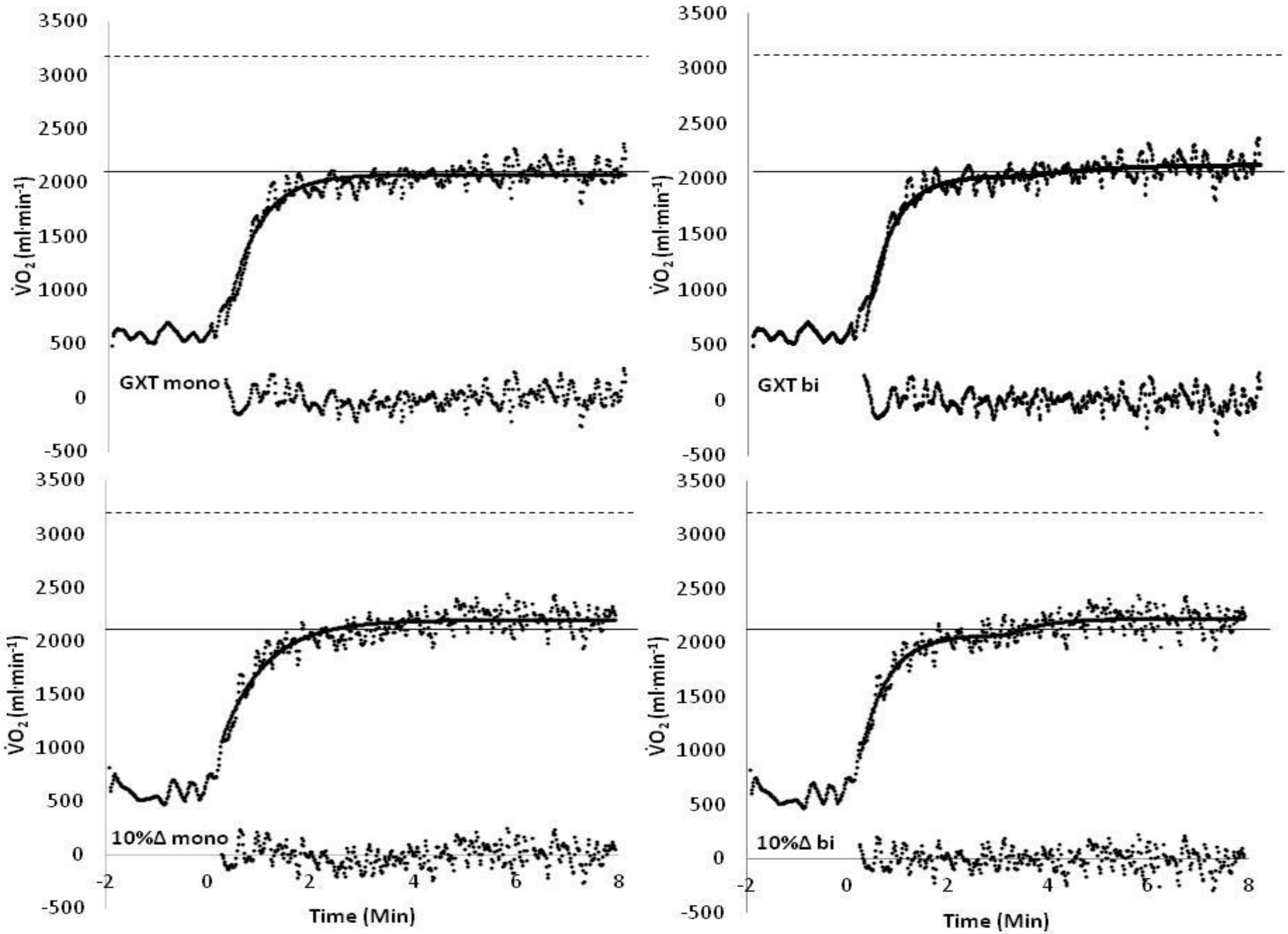
2000
1500
1000
500
0
-500
$\dot{V}O_2$ (ml·min^{-1})
-20%Δ mono
-20%Δ bi
-10%Δ mono
-10%Δ bi
-2
0
2
4
6
8
Time (Min)



3500
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V̇O2 (ml·min-1)
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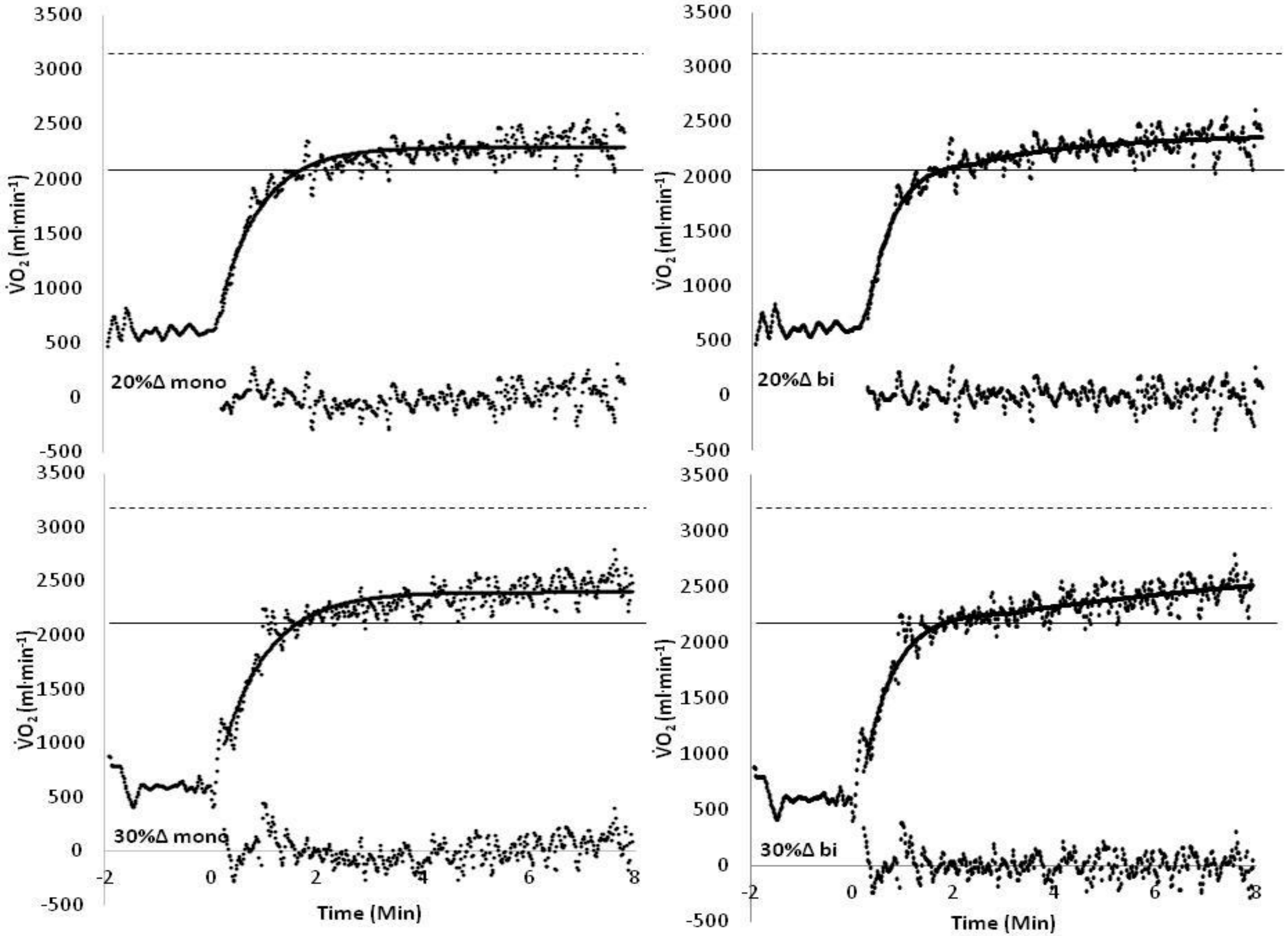
Time (Min)



20%Δ mono
20%Δ bi
30%Δ mono
30%Δ bi
$\dot{V}O_2$ (ml·min^{-1})
Time (Min)

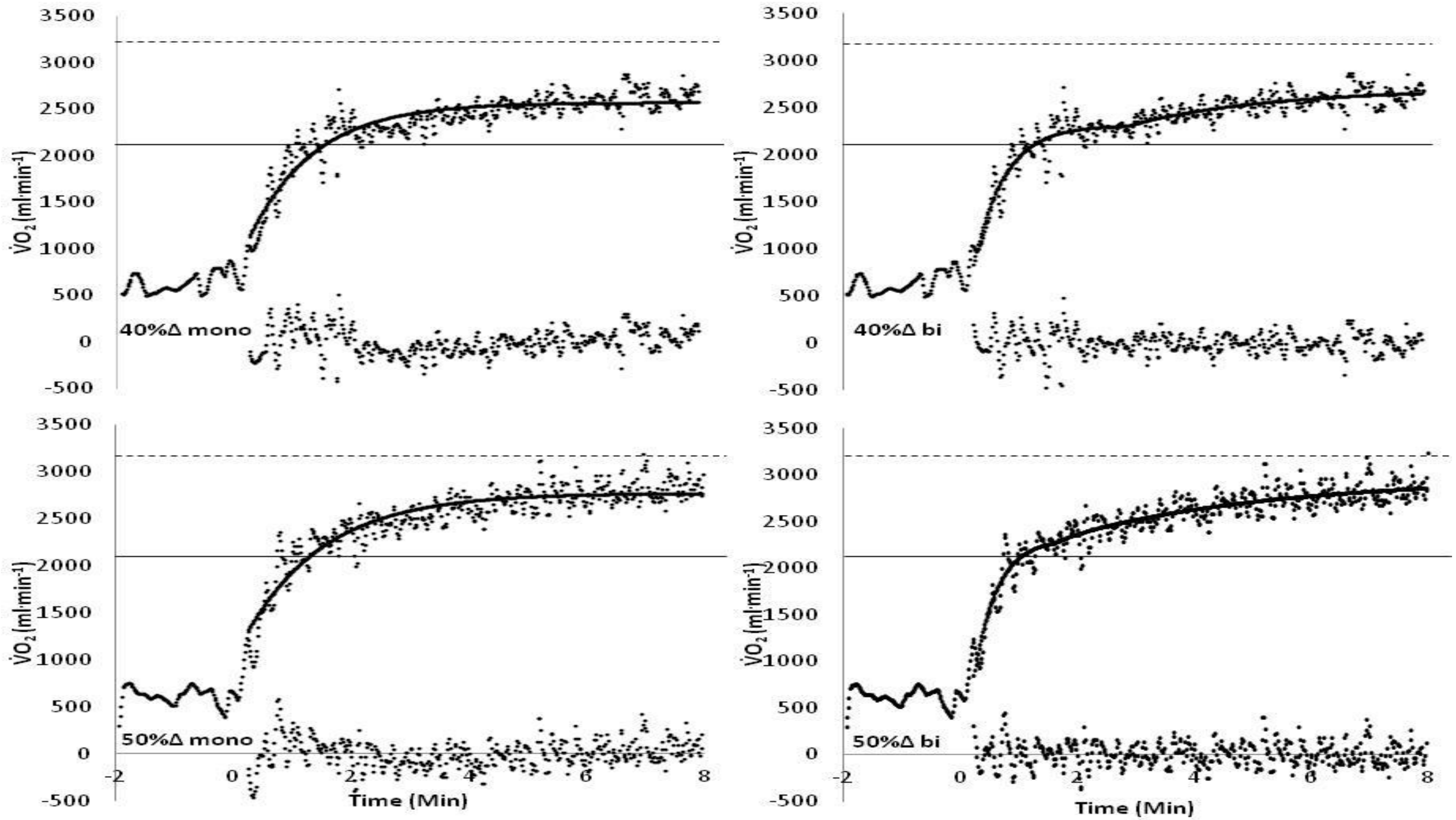
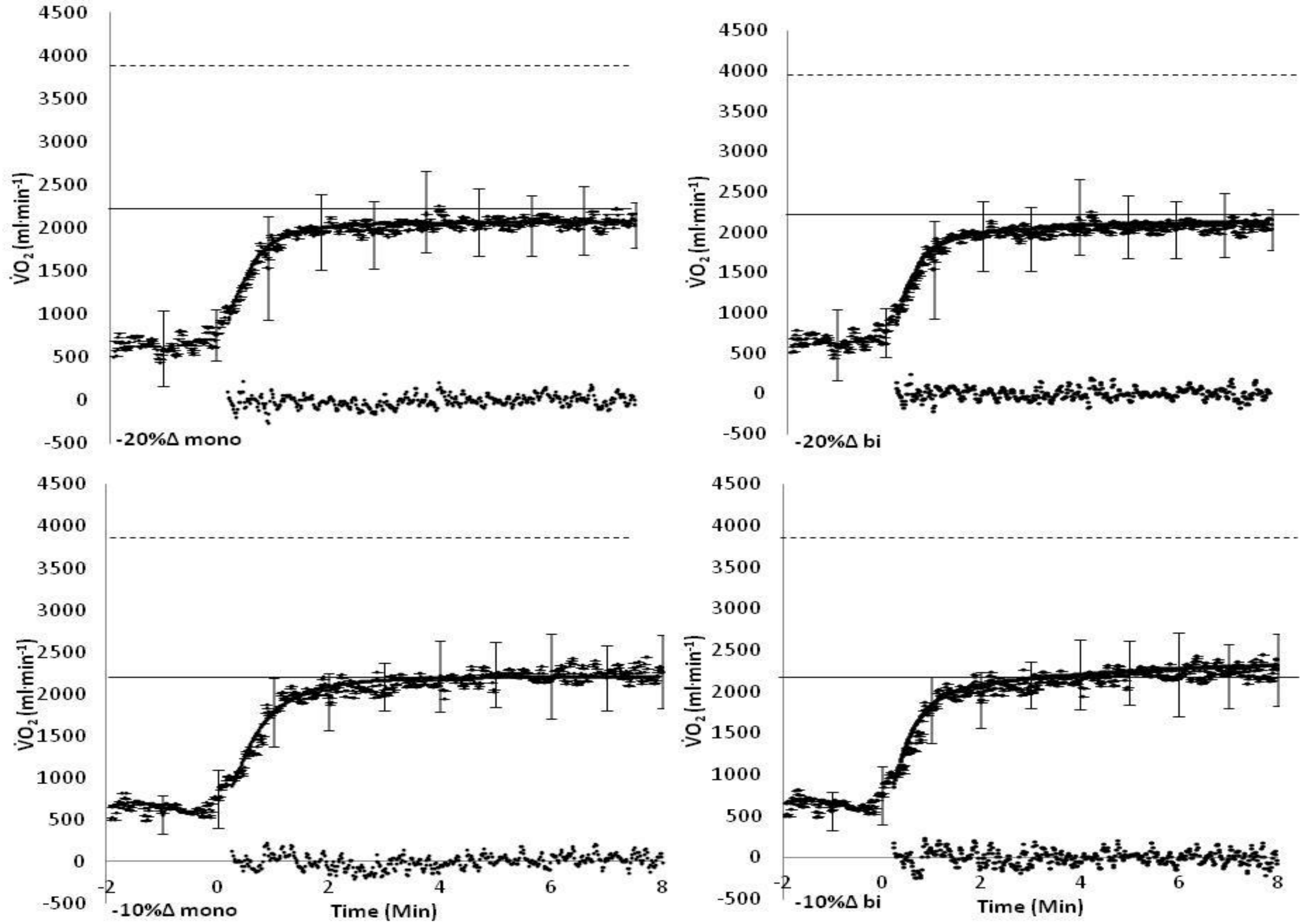


Figure. 3.2a. The breath-by-breath Oxygen uptake ($\dot{V}O_2$) response, mono and bi exponential model fits and residuals across exercise intensity domains in one subject. Data from the exercise performed at -20% of the difference of the $\dot{V}O_2$ at GXT and that at $\dot{V}O_{2peak}$ (-20%Δ), -10%Δ, GXT, +10%Δ, +20%Δ, +30%Δ, +40%Δ and +50%Δ. The $\dot{V}O_2$ at GXT (solid line) and $\dot{V}O_{2peak}$ (dashed line).



4500
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-500
$\dot{V}O_2$ (ml·min^{-1})
-20%Δ mono
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-10%Δ mono
-10%Δ bi
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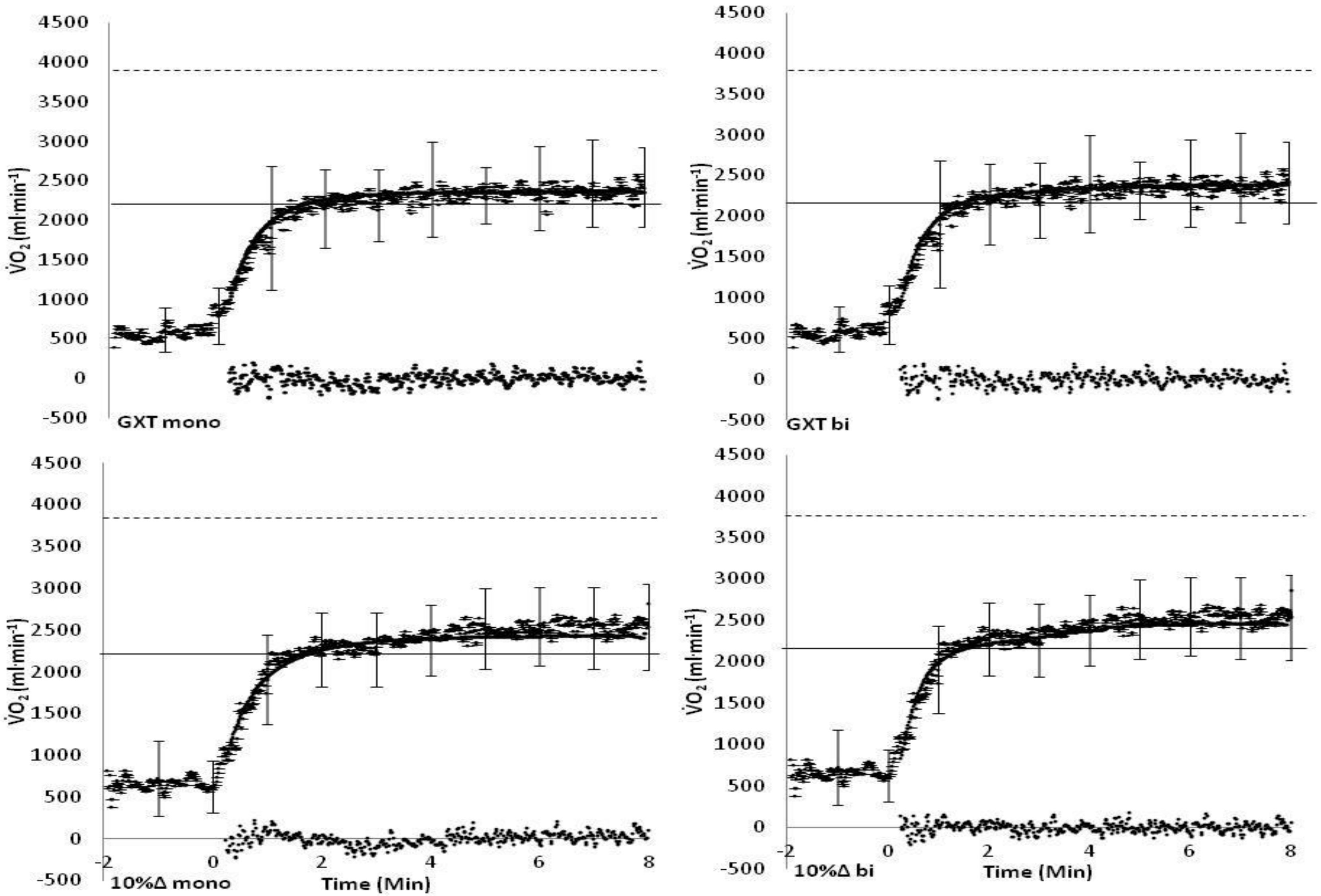
Time (Min)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$\dot{V}O_2$ (ml·min^{-1})
GXT mono
GXT bi
10%Δ mono
10%Δ bi
-2
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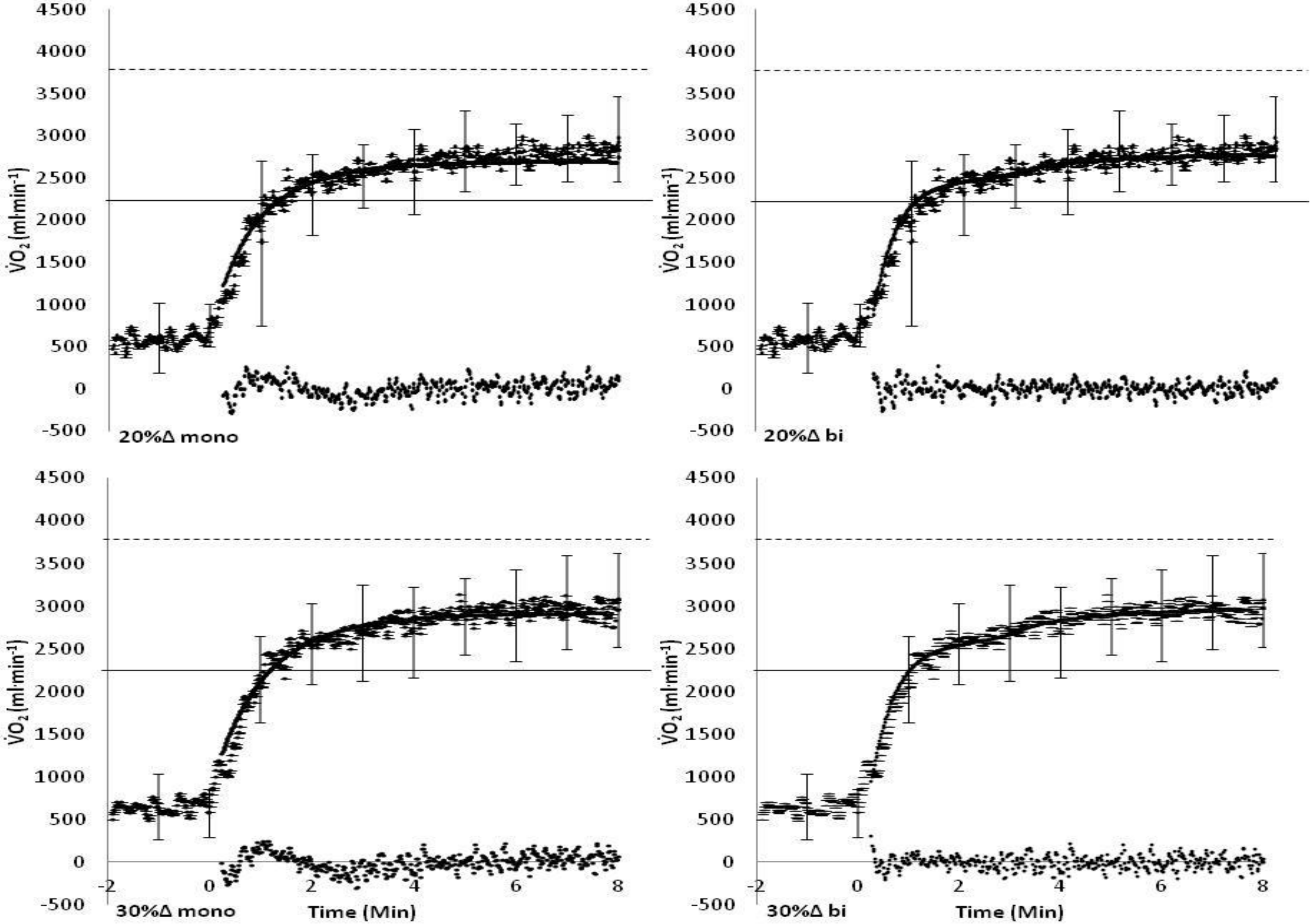
Time (Min)


4500
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-500
V̇O2 (ml·min-1)
20%Δ mono
20%Δ bi
30%Δ mono
30%Δ bi
-2
0
2
4
6
8
Time (Min)

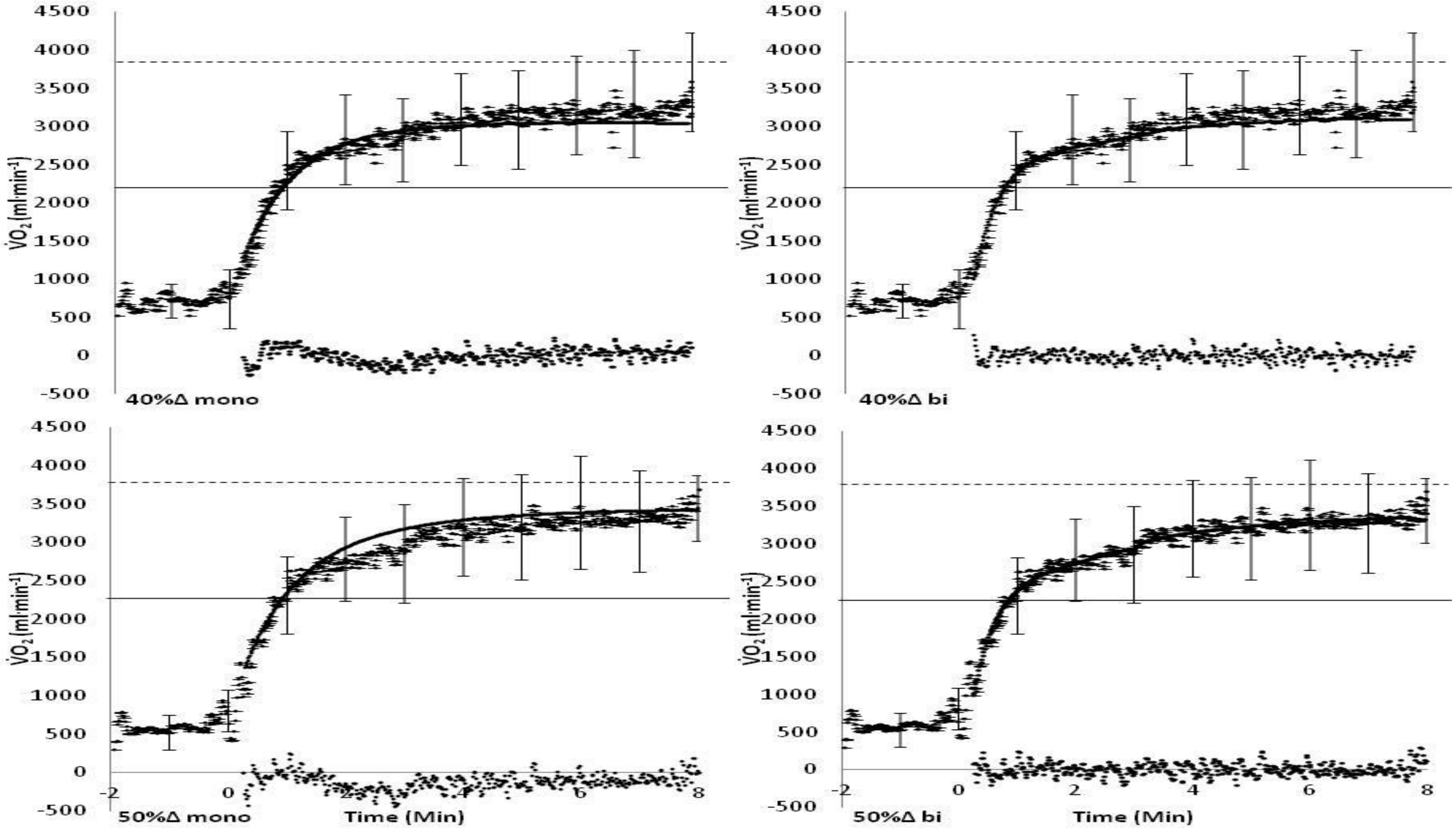

Figure. 3.2b. The mean breath-by-breath Oxygen uptake ($\dot{V}O_2$) response, mono and bi exponential model fits and residuals across exercise intensity domains in for all subjects. Data from the exercise performed at -20% of the difference of the $\dot{V}O_2$ at GXT and that at $\dot{V}O_{2peak}$ (-20%Δ), -10%Δ, GXT, +10%Δ, +20%Δ, +30%Δ, +40%Δ and +50%Δ. The $\dot{V}O_2$ at GXT (solid line) and $\dot{V}O_{2peak}$ (dashed line).

The mean slope (ml·min^{-1}·s^{-1}) of the final 60 s of exercise was calculated for each exercise intensity and indicated that there was no significant difference from zero in the mean slope of $\dot{V}O_2$ vs. Time for the final minute of exercise. The mean slope of $\dot{V}O_2$ vs. Time for the final minute of exercise is presented in Table. 3.3. Values presented as mean (SD) with statistical difference from zero.

Table. 3.3. Mean (SD) slopes presented with statistical difference from zero (*p* value) for the final minute of exercise.

Variable	-20%Δ	-10%Δ	GXT	+10%Δ	+20%Δ	+30%Δ	+40%Δ	+50%Δ
Mean slope (ml·min^{-1}·s^{-1})	0.398 (1.666)	-0.363 (1.289)	0.268 (1.551)	1.208 (1.937)	1.108 (0.993)	0.393 (1.329)	0.770 (1.669)	2.293 (4.465)
***p* Value**	0.521	0.453	0.641	0.121	0.160	0.431	0.233	0.189

* significant difference p<0.05

Fingertip capillary blood lactate samples indicated that there was no significant change in blood Lactate concentration sub-GXT from pre exercise values, with significant changes only being noted in supra-GXT exercise intensities. Average haematological responses, delta and *p* values for pre- and post-exercise are presented in Table. 3.4.

Table. 3.4. Average blood Lactate responses as a function of exercise intensity. Values are presented as the mean (SD).

Variable	-20%Δ	-10%Δ	GXT	+10%Δ	+20%Δ	+30%Δ	+40%Δ	+50%Δ
Pre Exercise [La$^-$] (mMol^{-1})	1.22 (0.15)	1.23 (0.25)	1.17 (0.18)	1.13 (0.17)	1.12 (0.14)	1.16 (0.17)	1.2 (0.16)	1.07 (0.16)
Post Exercise [La$^-$] (mMol^{-1})	1.23 (0.25)	1.26 (0.29)	1.6 (0.21)	2.42 (0.26)	2.98 (0.22)	3.97 (0.62)	4.55 (0.47)	5.93 (0.37)
Delta [La$^-$] (mMol^{-1})	0.01 (0.11)	0.03 (0.08)	0.43 (0.1)	1.29 (0.16)	1.86 (0.25)	2.81 (0.6)	3.35 (0.39)	4.86 (0.38)
***p* Value**	0.763	0.451	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

* significant difference p<0.05

Pearson's product-moment correlation demonstrated that whilst applying the mono exponential model there was a significant positive correlation found between the primary component amplitude and the primary component time constant. Pearson's product-moment correlation coefficients (*r*) and *p* values for the parameters of the mean oxygen uptake response to exercise, for mono exponential model are presented in Tables 3.5a.

Table. 3.5a. Pearson's product-moment correlation coefficients (*r*) of the mean oxygen uptake response to exercise (Mono exponential). $\boldsymbol{A_1}$ Primary amplitude, $\boldsymbol{\delta_1}$Primary amplitude time delay, $\boldsymbol{\tau_1}$Primary amplitude time constant. Values are presented as *r* (*p* value).

	$\boldsymbol{A_1}$	$\boldsymbol{\delta_1}$	$\boldsymbol{\tau_1}$
$\boldsymbol{A_1}$			
$\boldsymbol{\delta_1}$	0.262 (0.532)		
$\boldsymbol{\tau_1}$	0.941 (0.001)*	0.267 (0.522)	

* significant difference p<0.05

Pearson's product-moment correlation demonstrated that whilst applying bi exponential model, there were significant negative correlations found between; the primary component amplitude and the primary component time delay; the primary component amplitude and the primary component time constant; the primary component time delay and the primary component time constant; the primary component time delay and the slow component amplitude. There were significant positive correlations found between; the primary component amplitude and the slow component amplitude; the primary component time constant and the slow component amplitude. Pearson's product-moment correlation coefficients (*r*) and *p* values for the parameters of the mean oxygen uptake response to exercise, for mono exponential model are presented in Tables 3.5b.

Table. 3.5b. Pearson's product-moment correlation coefficients (*r*) of the mean oxygen uptake response to exercise (Bi exponential). A_1 Primary component amplitude, δ_1 Primary component time delay, τ_1 Primary component time constant, A_2 Slow component amplitude, δ_2 Slow component time delay, τ_2 Slow component time constant. Values are presented as *r* (*p* value).

	A_1	δ_1	τ_1	A_2	δ_2	τ_2
A_1						
δ_1	-0.922 (0.001)*					
τ_1	-0.898 (0.002)*	-0.895 (0.003)*				
A_2	0.873 (0.005)*	-0.803 (0.016)*	0.893 (0.003)*			
δ_2	0.022 (0.959)	-0.249 (0.569)	0.214 (0.611)	-0.025 (0.954)		
τ_2	-0.258 (0.535)	0.383 (0.349)	-0.175 (0.696)	0.114 (0.788)	-0.522 (0.185)	

* significant difference $p<0.05$

Whilst applying the mono and bi exponential models across all exercise intensities, the bi exponential model produced a significantly lower standard error of the estimates (SEE) for all exercise intensities, compared to the mono exponential model. The mean SEE's recorded for each exercise intensity and model comparisons are shown in Table 3.6. Values are presented as the mean (SD) with statistical difference between the two models.

Table 3.6. SEE values ($L \cdot min^{-1}$) of mono and bi exponential models. Values presented as mean (SD) with statistical difference between the two models.

Model	-20%Δ	-10%Δ	GXT	+10%Δ	+20%Δ	+30%Δ	+40%Δ	+50%Δ	Mean
Mono	0.179 (0.058)	0.199 (0.049)	0.206 (0.058)	0.214 (0.066)	0.243 (0.078)	0.254 (0.086)	0.271 (0.090)	0.287 (0.121)	0.232 (0.076)
Bi	0.173 (0.053)	0.186 (0.042)	0.194 (0.055)	0.201 (0.061)	0.226 (0.066)	0.238 (0.078)	0.259 (0.087)	0.271 (0.121)	0.219 (0.071)
***p* Value**	0.02*	0.01*	0.029*	0.003*	0.03*	0.02*	<0.001*	0.009*	<0.001*

* significant difference $p<0.05$.

4.0 Discussion

4.1 Main findings

The present study was able to detect a small value for the slow component of pulmonary oxygen uptake ($\dot{V}O_2$) sub and supra-gas exchange threshold (GXT), across all exercise intensities. The Standard Error of the Estimates were found to be significantly lower in the bi vs. mono exponential model for all exercise intensities. Slopes of $\dot{V}O_2$ vs Time were not different from 0 ($p<0.05$) for the final minute of any exercise intensity, indicating that a steady-state was achieved (Table 3.3). The modelled slow component time constants were typical of literature reported values (Table 3.2) but indicated that $\dot{V}O_2$ would not be achieved during the duration of the exercise (Table 3.2). Additionally, Pearson's product-moment correlation found that many model parameters were significantly related to each other ($p<0.05$). These findings are indicative of an issue with the model being able to adequately describe the $\dot{V}O_2$ response (to be discussed further).

4.2 Modelling the response

This present study utilised a mono and bi exponential modelling process for all exercise intensities, sub and supra-GXT, this approach has not been undertaken in previous research addressing the moderate intensity domain (Table 1.1). However, given that one of the aims of the study was to comprehensively describe the relationship between exercise intensity and the slow component of $\dot{V}O_2$, sub- and supra-GXT, this was deemed appropriate. Despite the convention that has emerged regarding the modelling of $\dot{V}O_2$ data, standard error of the estimates were measured in this study comparing the bi exponential to mono exponential models. As Table 4.6 shows, the bi exponential model produced standard error of the estimate (SEE) values that were significantly lower than the mono exponential model. The standard error of the estimate is a measure of the accuracy of predictions, so this may be an indication that the bi exponential model predictions were more accurate than the mono exponential model. This was evident across exercise intensities, below and above GXT. Furthermore, when modelling using the bi exponential model a small slow component was also evident below GXT (Table. 3.2).

Although SEE values indicated that the bi exponential model might fit the data better, it should be appreciated that by making a mathematical model more complex, i.e. by adding another parameter, a closer fit to the data will almost always obtained (Motulsky and Ransnas, 1987). Motulsky and Ransnas (1987) asserted that comparing two models with the same number of parameters is simple: the fit with the lower sum of squares is superior, for its curve lies closer to the points. However, when comparing two models with a different number of parameters it becomes more difficult. An increase in the number of parameters will allow more flexibility to the curve-fitting procedure, and almost always leads to a 'better' fitting model. However, when the number of parameters in a mathematical model are increased, the degrees of freedom are decreased (Motulsky and Ransnas, 1987). In either case, this presents an issue when deciding if one model is more suitable than another. Just because one model appears to fit the data better, this does not mean it should be assumed the correct model to use. The improved fit may be due to the larger number of parameters within the model. A further consideration is the residual plots of the data. Residuals should not be systematically related to the x values, and the residual plot will have a random arrangement of positive and negative residuals. However, when residual data appear to cluster, then the equation may be inappropriate or that the data points differ systematically (not just randomly) from the predictions of the curve (Motulsky and Ransnas, 1987). Rarely do studies display residual plots, however in the case of Barstow and Mole (1991), for example, these plots were displayed and trends in the residuals were discussed (further examples include; Gurd *et al*, 2005; Paterson *et al*, 2005). There are well established reports above GXT, but limited reports below GXT. Even when the kinetics below the GXT are explored, the relative exercise intensity tends to be well below the threshold (i.e. 80%GXT), and the occurrence of a slow component below GXT is not reported (Henson, Poole and Whipp, 1989; Whipp, 1994; Poole, 1994; Carter *et al*, 2000; Carter *et al*, 2002). No attempt has been made to fit the bi exponential model below threshold.

That being said, it is evident amongst the literature that research groups only tend to use relative exercise intensities either well below and/or well above GXT. Even in instances where studies do use an exercise intensity close to the threshold, it is universally assumed that the $\dot{V}O_2$ response should be modelled mono exponentially, with no attempt made to model the 2 component model below GXT (Berger, Tolfrey and Jones, 2006; Ingham *et al*, 2007; Ingham *et al*, 2008; Malek *et al*, 2008; Bailey *et al*, 2009). In support of the lack of clarity concerning which model to use Perrey (2009) noted that within a single exercise test, it is not clear that a mono exponential response pattern for moderate exercise intensity is the appropriate model choice. Given the evidence that blood flow adapts with two very distinct mechanisms, the muscle pump and regulatory feedback, it may not be surprising that availability of oxygen (O_2) as an important regulatory substrate could have clearly different impact on metabolism at different times in the adaptive process (Tschakovsky and Hughson, 1999).

At exercise intensities above GXT, there is generally an increased production and removal of lactate (Barstow, 1994; Poole, 1994) leading some to assume a causal relationship between slow component and arterial [BLa^-] (Xu and Rhodes, 1999). Given that although the two are in fact closely correlated (Whipp, 1987; Barstow, 1994), it has never been shown that they do actually coincide and a rise in blood lactate concentration has been shown not to mandate an additional $\dot{V}O_2$ requirement (Poole, 1994). Given the results from the present study, that SEE values were significantly lower whilst a bi exponential model, compared to a mono exponential model, was applied and the evident dissociation between lactate and the slow component, the use of such a threshold as the cut-off point may be questioned.

The correlations between model parameters found in the present study demonstrate that the parameters of the mathematical modelling process are related to one another and perhaps adds perhaps supports the concept of a high degree of interdependency in the parameters (Koga, Shiojiri and Kondo, 2005). Through conducting Correlations revealed significant relationships between a number of the measured parameters, for both mono and bi exponential models (Table 3.5a and 3.5b). To this authors' knowledge, these are relationships that have not previously been reported (Carter *et al*, 2000; Carter *et al*, 2002; Pringle, 2002). The implications of some of the relationships between model parameters are important. Firstly, the finding that the primary and slow component amplitudes increases together was to be expected. Virtually all previous literature that has studied across exercise intensities (moderate and heavy) have shown concurrent increases in both amplitudes (Carter *et al*, 2000; Carter *et al*, 2002; Pringle, 2002; Wilkerson *et al*, 2004). This is as a result of the increasing energy demand resulting in an increased oxygen uptake, with $\dot{V}O_2$ shown to be increasing linearly with work rate at ~10 $ml{\cdot}min^{-1}{\cdot}W^{-1}$ during moderate intensity exercise, whilst thought to increase to as much as ~13 $ml{\cdot}min^{-1}{\cdot}W^{-1}$ towards heavy intensity exercise (Whipp and Wasserman, 1972; Pearce and Milhorn, 1977; Whipp and Mahler, 1980; Barstow and Mole, 1991).

When modelling using the bi exponential equation the primary component was shown to be negatively correlated to the primary time constant and primary time delay, respectively. This demonstrates that as the primary component amplitude is increasing, the primary time delay and time constant are getting smaller. This would not be expected as the time delay and time constant length should not be dependent on the primary component amplitude. The finding that the slow component amplitude is also negatively correlated to the primary component time delay shows that as a result of the slow component amplitude increasing, the primary component time delay is being affected, and reduced, again something that would not be expected. Further to this, as the slow component amplitude is increasing, it is also having an effect on the primary component time constant, resulting in the two increasing synchronously. When modelling using the mono exponential equation, the only significant relationship found was that the primary component was positively correlated to the primary time constant. Although correlation between parameters was not studied, Bearden and Moffat (2001) found, whilst applying a mono and bi exponential model to the same set of data (30%Δ) that the primary time delay to be lower in the mono vs. bi exponential model (5.4±5.01 vs. 13.31±5.79 s) and that the primary time constant to be higher in the mono vs. bi exponential model (50.06±13.3 vs. 26.39±5.81 s).

The present study has shown that there may be an element of interdependency between parameters. Therefore the extent to which this interdependency may be affecting parameter estimates is of importance and should be addressed, as the confidence of the parameter estimates may be considered questionable (Engelen *et al*, 1996; Casaburi *et al*, 1998; Whipp and Rossiter, 2005). In nonlinear regression, the parameters are usually not entirely independent (Motulsky and Ransnas, 1987). Therefore, altering one parameter may make the fit worse, but this can be partially offset by adjusting the value of another parameter. Although correlation coefficients as large as 0.8 may be commonly seen (Motulsky and Ransnas, 1987), very high correlations can indicate that the equation includes redundant variables i.e. Nonlinear regression fails when one tries to fit an equation to data with too many parameters. In addition to the possible parameter interdependency altering the model fit to the same data can have a dramatic impact on the values attained. As Bell *et al* (2001) described, dependent upon the number of parameters and fitting period used to model data, the phase two time constant varied widely (from 19, 29.2, 30.7 or 31 s using different component models). One possible reason for the apparent interdependency is the idea that the existence of time-delayed phases is not supported by oxygen uptake kinetics data (Stirling and colleagues, 2004; 2007; 2008; 2009). It is argued that the physiological mechanism for such behaviour may be contended (Stirling and colleagues, 2004; 2007; 2008; 2009). Attempts have been made to improve the phase two fit by constraining the fitting window to start sometime after the onset of exercise (Whipp *et al*, 1982; Whipp and Rossiter, 2005). Furthermore, the fact a 20s muscle to mouth transit delay time was used in this study may have also contributed to the interdependency between parameters (Stirling and Zakynthinaki, 2009). Theoretically, the commencement of phase 2 (i.e., the first time delay) should be triggered by a fall in the respiratory exchange ratio (RER), however, this decrease may not be sufficiently clear for this purpose and it is reported that a value of at least 20s is typically utilised (Whipp and Rossiter, 2005). For the phase 1 and slow component, the best fit to the data can result in large values of the amplitude and/or time constant, i.e. time constants that mean the response would not be complete within the exercise bout (Koga, Shiojiri and Kondo, 2005).

There is evidence to suggest that through the ensemble averaging (performed by the vast majority of studies), a possible underlying physiological mechanism could be missed or misinterpreted (Stirling and Zakynthinaki, 2009). Respiratory and circulatory functions are thought to exhibit spontaneous fluctuations which will be superimposed as a ‘noise’ on the basic response pattern during the adaption to exercise, and become noticeable when breath-by-breath or beat-by-beat recordings are made (Linnarsson, 1974). Such fluctuations or fluctuations may be a result of noise attributable to the measuring device or may be physiological, such as abnormal breathing during exercise including shallow breathing or breath holding (Borrani *et al*, 2001). Borrani *et al*. (2001) states it is not possible to exclude the fact that the breath-by-breath variability may have biological significance, although Lamarra *et al*. (1987), suggest stochastic properties of the breath-by breath noise. There is also a potential biological significance of breath-by-breath interbreath fluctuations in exercise situations in which the breathing pattern is altered, as is the case in swimming (Rodriguez *et al*, 2003) due to the cyclic head immersion and the resulting breath holding phase. Nonlinear systems such as the physiological ones in question however can produce signals which look noisy (Kantz and Schreiber, 1999; Guckenheimer and Holmes, 1983). As a result, part of what is attributed to noise could contain an inherent feature of the system being studied and need not necessarily be completely random (Stirling, Zakynthinaki and Saltin, 2005).

A number of different algorithms (e.g. mono, bi and triple exponential models) with different assumptions have been employed to estimate the breath-by-breath $\dot{V}O_2$, resulting in notable differences observable throughout the whole on/off transient, most notably in the initial response (Koga, Shiojiri and Kondo, 2005). The mono exponential equation (Equation 2.1 (Whipp, 1982)), where the cardiodynamic component is not modelled as an exponential, and the subsequent response has one exponential component (A_1), with one time constant (τ_1) for the primary component and one time delay ($t - \delta_1$) from the onset of exercise. Above the GXT, however, the application of a bi exponential equation has been advocated to better model the slowly developing component of oxygen uptake (Carter *et al*, 2000; Pringle *et al*, 2002), whereby A_1 and A_2 are the amplitudes for the primary and slow components, τ_1 and τ_2 are the time constants for the two components, and $t - \delta_1$ and $t - \delta_2$ are the time delays from the onset of exercise for the two components. Further, a triple exponential function (Sheuermann *et al*, 2001; Carter *et al*, 2002) has also been widely used. Similar to equation 2.2, as described by Barstow and Mole (1991), the primary and slow components are each represented by an amplitude (A_1 and A_2), a time constant (τ_1 and τ_2) and a time delay ($t - \delta_1$ and $t - \delta_2$) from the onset of exercise for the two components. In addition to this, the cardiodynamic component is also modelled as an exponential function (equation 4.1 (Sheuermann *et al*, 2001)).

$$\dot{V}O_2(t) = VO_2(b) + A_0\,(1 - e^{-t/\tau_0})$$

Equation 4.1.

Where $VO_2(b)$ is the resting baseline value, A_0 is the magnitude of the cardiodynamic component and τ_0 is the time constant.

For this work, however, based upon the idea that first (cardiodynamic) response effectively represents a time delay of ~20 s which reflects the transit time that pooled deoxygenated blood takes to travel from the working muscles to the lungs, i.e. venous return (Casaburi, Daly, Hansen, and Effros, 1989; Hughson, O'Leary, Betik, and Hebestreit, 2000; Whipp, 1994) and not an exponential function, equation 2.1 and 2.2 were utilised.

As suggested above, breath-by-breath variability may be of biological significance (Borrani *et al*, 2001) as nonlinear systems such as those governing the respiratory and circulatory functions can produce signals that may appear as random noise but are actually not stochastic (Kantz and Kurths, 1998; Belair and Glass, 2003; Kantz and Schreiber, 2003; Ellner and Guckenheimer 2006; Shelhamer, 2007). Therefore, what is often attributed to noise, may contain vital information, as Borrani *et al* (2001) noted a scaling exponent over 0.5 (white noise) in constant and free-paced 10,000m runs. The reduction of what is considered noise is commonly accomplished through ensemble averaging the responses of repeated identical exercise bouts (Lamarra *et al*, 1987). This, however, as Whipp and Rossiter (2005) discuss, can only be justified when the noise is Gaussian and stochastic and the basic response pattern of each bout is identical, generally this is not the case (see literature review) (Bearden *et al*, 2004). Previous studies have reported disparities between white and non-white noise being produced by breath-by-breath algorithms (Lamarra *et al*, 1987; Potter *et al*, 1999; Rossiter *et al*, 2000; Capelli, Cautero and Di Prampero, 2001; Cauterro *et al*, 2002; Billat *et al*, 2006). Due to variation in parameter values, particularly in the time constants, between exercise bouts when ensemble averaged, it may be debatable whether ensemble averaging is the most appropriate approach (Bearden *et al*, 2004; Zakynthinaki *et al*, 2007). Furthermore, the indication of parameter interdependency may suggest the application of the bi exponential model could be questioned.

4.2.1 Steady state

The second aim of this study was to systematically investigate whether a steady-state during constant work-rate exercise (>GXT but) was achieved. Mean slope analysis of $\dot{V}O_2$ vs. Time for the final minute of exercise in the present study demonstrated that during exercise performed above GXT, $\dot{V}O_2$ did stabilise and reach a steady state (Table 3.3), meaning that there was no significant difference in the $\dot{V}O_2$ vs. Time slope from zero. Were any the exercise intensities above critical power (CP), $\dot{V}O_2$ would have risen inexorably to failure. The characteristics of the on-transient $\dot{V}O_2$ kinetic response to heavy exercise is said to take on a more complicated description than the simple mono exponential model (Whipp and Wasserman, 1970, Linnarsson, 1974, Barstow, 1994). A typical $\dot{V}O_2$ and metabolite response to heavy intensity exercise has been well established and previous research has recognised that during heavy exercise the $\dot{V}O_2$ response becomes appreciably more complex with both time and amplitude nonlinearities of response (Whipp, 1994). It was however clarified by Whipp (1994) that during exercise at heavy exercise intensities $\dot{V}O_2$ will reach a steady state. So, based on previous literature, it would be expected that all exercise intensities used in this study would result in a steady state if performed for sufficiently long. Generally 50%Δ is considered heavy intensity exercise; however there have been reports of the boundary between the heavy and severe exercise intensities being ~40%Δ (Carter *et al*, 2002), this was not found in the present study. Were a boundary at 40%Δ evident, both $\dot{V}O_2$ and arterial blood lactate concentration ($[BLa^-]$) would rise inexorably in the present study until fatigue ensues, at which point maximum values of $\dot{V}O_2$ would be attained (Wasserman and Whipp, 1975; Gaesser and Poole, 1996).

Although $\dot{V}O_2$ was found to reach steady state (Table 3.3), there were large standard deviations reported for most exercise intensities, particularly 50%Δ. However, through investigating the mean slopes of $\dot{V}O_2$ vs. time for the final part of a steady-state exercise bout and assessing the differences from zero, it would be clear if the exercise elicited a steady-state response, if the exercise elicits a steady-state response, there would be no significant difference from zero. The present study demonstrated for exercise intensities above GXT (up to 50%Δ), a delayed steady-state response was achieved. An issue with the modelling of the slow component is that, generally, the mathematical modelling process results in constraining the data to fit within a predetermined time frame i.e. the test duration ((typically 6 or 8 minutes) Table 1.1). Based on the resultant parameter values reported in the present study, and previous studies (Table 1.1), it is evident that the $\dot{V}O_2$ response is incomplete. After 1τ has elapsed the response will have attained 63% of its final value, and after 5 x τ the response will be complete (Jones and Poole, 2005). However, reported slow component values for steady-state heavy intensity exercise demonstrate an inconsistency with this rule. The shortest slow component time constant reported in this study was 121 s, meaning that the $\dot{V}O_2$ response would not be complete until 605 s, well beyond the 480 s test duration. There are many examples of this contradiction of the exponential modelling process in the literature; Carter *et al* (2002), using a 360 second test protocol, reported no slow component magnitude, time delay or time constant for exercise intensities; 80% LT and 100% LT, however for 20%Δ (20% of the difference in $\dot{V}O_2$ between that at GXT and $\dot{V}O_{2peak}$), 40%Δ, 60%Δ, 80%Δ and 100%Δ they reported time constants of 221.7, 289.4, 247.1, 255.3 and 224s, respectively. Based upon these reported time constants, the earliest the response would be complete is 1108.5s (for 20%Δ), well beyond the 360s test duration. Ingham *et al* (2007) and Ingham *et al* (2008) reported time constants of 242 and 258.6s, respectively, for 50%Δ, meaning it would take until 1210s had elapsed (at the earliest) for the $\dot{V}O_2$ to be complete. The reported time constants in these studies, and across the literature (Burnley, 2002; Pringle, 2002), clearly demonstrate that none of the $\dot{V}O_2$ responses would be complete within the test duration. Additionally, in all of these studies no attempt was made to fit a two component model below threshold.

It has previously been asserted that the use of a predetermined time frame for estimation of the slow component amplitude is not appropriate (Bearden and Moffat, 2001). Mathematical modelling whilst the $\dot{V}O_2$ response is incomplete, when the kinetics beyond end-exercise are assumed to follow the pattern of the recorded data, likewise, if a steady state has not been reached, any estimation procedures over a rigid period cannot accurately determine the slow component magnitude (Bearden and Moffat, 2001). Given the evidence surrounding an incomplete exponential process, in addition to the results of the present study, the ability of the current modelling process to accurately and adequately describe the delayed $\dot{V}O_2$ response should be questioned.

4.2.2 Oxygen uptake across exercise intensities

The present study demonstrated that with increasing exercise intensity, the amplitude of the primary component, for both models, also increased. This finding is evidently in agreement with many previous studies (Table 1.1). The reason for this is that with increasing exercise intensity, there is a concurrent increase in the primary component amplitude. This increase is to be expected, as with an increased exercise intensity comes an obligatory increase in O_2 uptake. Oxygen uptake is shown to increase linearly with work rate at ~10 $ml \cdot min^{-1} \cdot W^{-1}$, and once the new steady-state is attained, adenosine tri-phosphate (ATP) depletion within the myocytes and the rate of ATP synthesis from oxidative phosphorylation are in equilibrium. When an individual progresses into the heavy intensity exercise domain there is a greater oxidative cost and steady-state attainment is delayed due to the presence of the $\dot{V}O_2$ slow component and the O_2 cost of exercise is generally reported to increase to ~13 $ml \cdot min^{-1} \cdot W^{-1}$ (Whipp and Wasserman, 1972; Pearce and Milhorn, 1977; Whipp and Mahler, 1980; Barstow and Mole, 1991). Although the present study did not investigate the severe intensity exercise domain, if an individual continues into the severe intensity exercise domain it has been described that when exercise is performed within this domain both $\dot{V}O_2$ and arterial [BLa^-] will not reach a steady state. It has generally been shown that both $\dot{V}O_2$ and arterial [BLa^-] rise inexorably until fatigue ensues, at which point maximum values of $\dot{V}O_2$ are attained (Wasserman and Whipp, 1975; Gaesser and Poole, 1996).

As noted above, the present study found that the primary and slow component amplitudes are significantly positively correlated. The reasons for the primary component amplitude increasing are outlined above. However, the cause(s) of the slow component amplitude is more complicated. The physiological mechanisms for the slow component are not well understood. It has, however, been demonstrated that ~80% of the slow component may arise from within the contracting muscles (Poole *et al*, 1991; Rossiter *et al*, 2002). Glycogen depletion studies in cycling (Vollestad and Blom, 1985) and running (Costill *et al*, 1973) have demonstrated that type IIa and IIx motor units are recruited at the exercise intensities at which the slow component develops. Furthermore, although not universally noted (Scheuermann *et al*, 2001), electromyographic studies have indicated increased neuromuscular activation consistent with a progressive recruitment of type II fibres over the time course in which the slow component concurrently develops (Mateika and Duffin 1994; Pringle *et al*, 2000; Shinohara and Moritani, 1992). Consequently, the development of the slow component has been linked to the energetics of contraction of type II fibres (Barstow *et al*, 1996; Whipp, 1994). Barstow *et al* (1996) has previously demonstrated that the contribution made by the slow component to the total response during 8 min of heavy constant-load cycling was negatively correlated with the proportion of type I fibres. Crow and Kushmerick (1982) have demonstrated that the contraction of type II muscle fibres is less efficient than that of type I fibres (i.e. the phosphate:oxygen ratio is ~18% lower in the isolated mitochondria of type II fibres). The lack of efficiency may be due, in part, to a greater reliance on the α-glycerophosphate shuttle over the malate-aspartate shuttle compared to type I fibres (Crow and Kushmerick, 1982; Willis and Jackman, 1994). The lower efficiency of energy conversion by cross-bridges in type II fibres means that the utilisation of ATP is also less efficient, resulting in an increased ATP cost per unit force generated (Saugen and Vollestad, 1995).

4.3 Slow component in an applied setting

The slow component is appreciably important in an applied setting for the reasons outlined below. However, demonstrable and fundamental issues should be improved in order to aid in our understanding of determinants of exercise tolerance and limitations to, in particular, endurance sports performance. It has been shown that exercise priming may significantly change the metabolic and gas exchange responses to subsequent supra-threshold exercise. An initial performance of heavy intensity exercise, but not moderate intensity exercise, has been shown to speed overall $\dot{V}O_2$ kinetics during subsequent heavy intensity exercise (Gerbino *et al*, 1996; Burnley *et al*, 2000). Furthermore, longer term training studies have demonstrated diminution of the $\dot{V}O_2$ slow component with training (Womack *et al*, 1995; Burnley and Jones, 2007; Krustrup *et al*, 2010). It is evident that studying the slow component of $\dot{V}O_2$ further is important for its application to an applied setting. For higher exercise intensities (i.e. above CP), steady states in blood acid-base status and pulmonary gas exchange are not attainable and $\dot{V}O_2$ will increase with time until $\dot{V}O_{2max}$ is reached. It is the interaction of the $\dot{V}O_2$ slow component, $\dot{V}O_{2max}$, and the anaerobic capacity that is believed to determine the exercise tolerance (Burnley and Jones, 2007). It has been noted that an appreciation of the various exercise intensity domains and their characteristic effects on $\dot{V}O_2$ dynamics could be helpful in improving our understanding of the determinants of exercise tolerance and the limitations to endurance (and other) sports performance. This suggests that more needs to be known about its appearance and, furthermore, the most appropriate method of determination i.e. through modelling.

4.4 Limitation/delimitations

There are some limitations with number of thresholds used and interchanged in previous literature; this study referenced exercise intensity to GXT for clarity, avoiding confusion with Lactate threshold (LT), anaerobic threshold (AT) or any other similar threshold. This is, in part, due to the limitations with many thresholds i.e. problems with LT and AT. Problems that have been reported include; the lack of a precise criterion for the definition of LT, numerous sample sites and detection of blood Lactate accumulation. A large majority of studies have failed to consider possible differences in lactate levels among venous, mixed venous, arterial and capillary blood (Bosquet, Léger and Legros, 2002). All of these factors have been shown to cause variation up to 13% whilst identifying LT with the same data, clearly making comparative discussions between studies difficult (Bassett and Howley, 2000).

This study utilised only one exercise transition for each exercise intensity and this runs counter to established practice, which recognizes the need for a sufficiently high signal-to-noise ratio when kinetic analyses are being conducted. This is an acknowledged limitation, but for expediency this approach was deemed the appropriate choice. Although using SEE to analyse the fit of a model is a commonly used method (Motulsky and Ransnas, 1987), it is conceivable that the SEE, on its own, may not be sufficiently sensitive. However, in combination with residual plots, the fit of a model may be visually inspected (Motulsky and Ransnas, 1987).

Based upon the notion that notable differences are evident in both efficiency and $\dot{V}O_2$ requirement of a given work-rate, it is conceivable that cadence differences could influence the gas exchange responses (Gaesser and Brooks, 1975; Hagberg *et al*, 1981; Pringle, Doust, Carter, Tolfrey and Jones, 2003). Therefore, given that the body of research available on the effects of pedal cadence typically suggests that cadences within a range of around 60-100rpm will have little effect on overall $\dot{V}O_2$ kinetics (Hill *et al*, 2003); the present study allowed subjects to cycle at a self-selected cadence within this range. The final limitation was the participant population utilised in the study. This participant population ranged quite widely in age (24±8 years) and fitness level may be decreased with age (Wilmore, Costill and Kenney, 2008), this is however comparable to numerous previous studies (Table 1.1).

The present study used cycling as the exercise modality to comprehensively describe the relationship between exercise intensity and the slow component of $\dot{V}O_2$. Carter *et al*. (2000) demonstrated that the $\dot{V}O_2$ kinetics were similar for running and cycling, with the exception of the primary (higher in running) and slow component amplitudes (lower in running). Therefore, there is a need to evaluate the effect of the differences in the $\dot{V}O_2$ kinetic response of exercise modality, using a modality such as running. A consideration has to be given to the amount of previous literature that has conducted studies across exercise intensities. There are a limited number of studies that have done so and with this the exercise modalities comprehensively and systematically studied across exercise intensities are minimal. This produces a clear delimitation in the field; the conducting of a studies utilising different exercise modalities, enhancing the research that has already been conducted on different exercise modalities, such as; rowing, swimming, knee extensor exercise and arm crank exercise. This will allow the characterisation of $\dot{V}O_2$ kinetics and the slow component of $\dot{V}O_2$ to be studied further and the suitability of mathematical models already utilised within running and cycle exercise.

4.5 Conclusion

The present study was able to detect a small value for the slow component of $\dot{V}O_2$ sub and supra-GXT, across all exercise intensities. The Standard Error of the Estimates were found to be significantly lower in the bi vs. mono exponential model for all exercise intensities. Although SEE values indicated a better fit using the bi exponential model, consideration needs to be given to the idea that making a mathematical model more complex, i.e. by adding another parameter, a closer fit to the data is almost always obtained (Motulsky and Ransnas, 1987). In contrast however, when the number of parameters in a mathematical model are increased, the degrees of freedom are decreased, meaning that the number of independent observations in a sample of data that are available to estimate a parameter are lower (Motulsky and Ransnas, 1987). During the present study, exercise intensities covering the moderate and heavy intensity exercise domains were used. It is reported in the literature that $\dot{V}O_2$ should stabilise within these domains (Whipp, 1994; Vanhatalo, Doust and Burnley, 2007). The present study found that the slopes of $\dot{V}O_2$ vs Time were not different from 0 ($p<0.05$) for the final minute of any exercise intensity, indicating that a steady-state was achieved (Table 3.3). The modelled slow component time constants were typical of literature reported values (Table 3.2) but indicated that $\dot{V}O_2$ would not be achieved during the duration of the exercise (Table 3.2). Additionally, Pearson's product-moment correlation found that many model parameters were significantly related to each other ($p<0.05$), which may be indicative of an issue with the model being able to adequately describe the $\dot{V}O_2$ response.

Given the results of the present study, further investigations into current model fitting procedures, potential parameter interdependency and the suitability of current models to accurately describe the $\dot{V}O_2$ response are required.

5.0 References

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6.0 Appendices

6.1 Appendix I

UNIVERSITY OF
GLOUCESTERSHIRE

SPORT & EXERCISE LABORATORIES

Informed Consent Form

Description of study:

This study requests that the participants attend the laboratory for two stages of experimentation. The first stage involved determination of GXT and $\dot{V}O_{2peak}$ with a ramp incremental exercise test. The second stage involved multiple laboratory visits, with the subjects performing two repetitions of square wave transitions from rest to one of eight exercise intensities; -20%Δ (minus 20% of the difference in $\dot{V}O_2$ between that at GXT and VO_{2peak}), -10%Δ, GXT, 10%Δ, 20%Δ, 30%Δ, 40%Δ and 50%Δ. Respiratory data will be calculated and displayed on a breath-by-breath basis via mass spectrometry (Pulmolab EX671, Morgan Medical, Rainham, UK); the raw breath-by-breath data will then be time-aligned and interpolated to second-by-second data. Non-linear least squares regression techniques will be used to fit the data after the onset of exercise with an exponential function. With this data the aim is to comprehensively describe the relationship between exercise intensity and the slow component of $\dot{V}O_2$, sub- and supra-GXT, and to conduct a systematic investigation into whether a steady-state during constant work-rate exercise is achieved >GXT but <CP.

I have had full details of the tests I am about to complete explained to me. I understand the risks and benefits involved, and that I am free to withdraw from the tests at any point. I confirm that I have completed a health questionnaire, and I am in a fit condition to undertake the required exercise.

Name: ....

Signed: ……………………………………………………………	Date: ………………………………

Tester: …………………………………………………

Signed: ………………………………………………………………	Date: ……………………………

*to be completed only if the participant is under 18 years of age

6.2 Appendix II

UNIVERSITY OF
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SPORT & EXERCISE LABORATORIES

Health Questionnaire

About this questionnaire:

The purpose of this questionnaire is to gather information about your health and lifestyle. We will use this information to decide whether you are eligible to take part in the testing for which you have volunteered. It is important that you answer the questions truthfully. The information you give will be treated in confidence. Your completed form will be stored securely for 5 years and then destroyed.

Section 1, which has been completed by the tester, provides basic information about the testing for which you have volunteered. Sections 2 to 7 are for you to complete: please circle the appropriate response or write your answer in the space provided. Please also complete section 8. Sections 9 and 10 will be completed by the tester, after you have completed sections 2 to 8.

Section 1: The testing (completed by tester)

To complete the testing for which you have volunteered you will be required to undertake:

Moderate exercise (i.e., exercise that makes you breathe more heavily than you do at rest but not so heavily that you are unable to maintain a conversation)

☑

Vigorous exercise (i.e., exercise that makes you breath so heavily that you are unable to maintain a conversation)

☑

The testing involves:

Walking	☐	Generating or absorbing high forces through your arms	☐
Running	☐	Generating or absorbing high forces through your shoulders	☐
Cycling	☑	Generating or absorbing high forces through your trunk	☑
Rowing	☐	Generating or absorbing high forces through your hips	☑
Swimming	☐	Generating or absorbing high forces through your legs	☑
Jumping	☐		

Section 2: General information

Name: ………………………………………………… Sex: M F Age:

Height (approx.): ……………………………… Weight (approx.):

Section 3: Initial considerations

1. Do any of the following apply to you? No Yes

   a) I have HIV, Hepatitis A, Hepatitis B or Hepatitis C
   b) I am pregnant
   c) I have a muscle or joint problem that could be aggravated by the testing described in section 1
   d) I am feeling unwell today
   e) I have had a fever in the last 7 days

(If you have answered “Yes” to question 1, go straight to section 8)

Section 4: Habitual physical activity

2a. Do you typically perform moderate exercise (as defined in section 1) No
Yes
for 20 minutes or longer at least twice a week?

2b. Have you performed this type of exercise within the last 10 days? No
Yes

3a. Do you typically perform vigorous exercise (as defined in section 1) No
Yes
at least once a week?

3b. Have you performed this type of exercise within the last 10 days? No
Yes

Section 5: Known medical conditions

4. Do **any** of the following apply to you? No
Yes

a) I have had insulin-dependent diabetes for more than 15 years
b) I have insulin-dependent diabetes and am over 30 years old
c) I have non-insulin-dependent diabetes and am over 35 years old

5. Have you ever had a stroke? No Yes

6. Has your doctor ever said you have heart trouble? No
Yes

7. Do **both** of the following apply to you? No
   Yes

   a) I take asthma medication
   b) I have experienced shortness of breath or difficulty with breathing
   in the last 4 weeks?

8. Do you have any of the following: cancer, COPD, cystic fibrosis, No
   Yes
   other lung disease, liver disease, kidney disease, mental illness,
   osteoporosis, severe arthritis, a thyroid problem?

(If you have answered "Yes" to any questions in section 5, go straight to section 8.)

Section 6: Signs and symptoms

9. Do you often have pains in your heart, chest, or the surrounding areas? No
   Yes

10. Do you experience shortness of breath, either at rest or with mild No
    Yes
exertion?

11. Do you often feel faint or have spells of severe dizziness? No
    Yes

12. Have you, in the last 12 months, experienced difficulty with No
    Yes
Breathing when lying down or been awakened at night by shortness of breath?

13. Do you experience swelling or a build up of fluid in or around No
    Yes

your ankles?

14. Do you often get the feeling that your heart is racing or skipping beats, either at rest or during exercise? No Yes

15. Do you regularly get pains in your calves and lower legs during exercise that are not due to soreness or stiffness? No Yes

16. Has your doctor ever told you that you have a heart murmur? No Yes

17. Do you experience unusual fatigue or shortness of breath during everyday activities? No Yes

(If you have answered "Yes" to any questions in section 6, go straight to section 8.)

Section 7: Risk factors

18. Does **either** of the following apply to you? No Yes

    a) I smoke cigarettes on a daily basis
    b) I stopped smoking cigarettes on a daily basis less than 6 months ago

19. Has your doctor ever told you that you have high blood pressure? No Yes

20. Has your doctor ever told you that you have high cholesterol? No Yes

21. Has your father or any of your brothers had a heart attack, heart surgery, or a stroke before the age of 55? No Yes

22. Has your mother or any of your sisters had a heart attack, No
    Yes
    heart surgery, or a stroke before the age of 65?

23. Do **any** of the following apply to you? No
    Yes

    a) I have had insulin-dependent diabetes for less than 15 years
    b) I have insulin-dependent diabetes and am 30 or younger
    c) I have non-insulin-dependent diabetes and am 35 or younger

Section 8: Signatures

Participant: ……………………………………………Date: ....……….……........

Guardian*: ....……………………........Date: ....…………….........
(*Required only if the participant is under 18 years of age.)

Section 9: Additional risk factors (to be completed by the tester if relevant)

24. Is the participant's body mass index >30 kg/m^2? No Yes

25. Has the participant answered no to questions 2a **and** 3a? No
    Yes

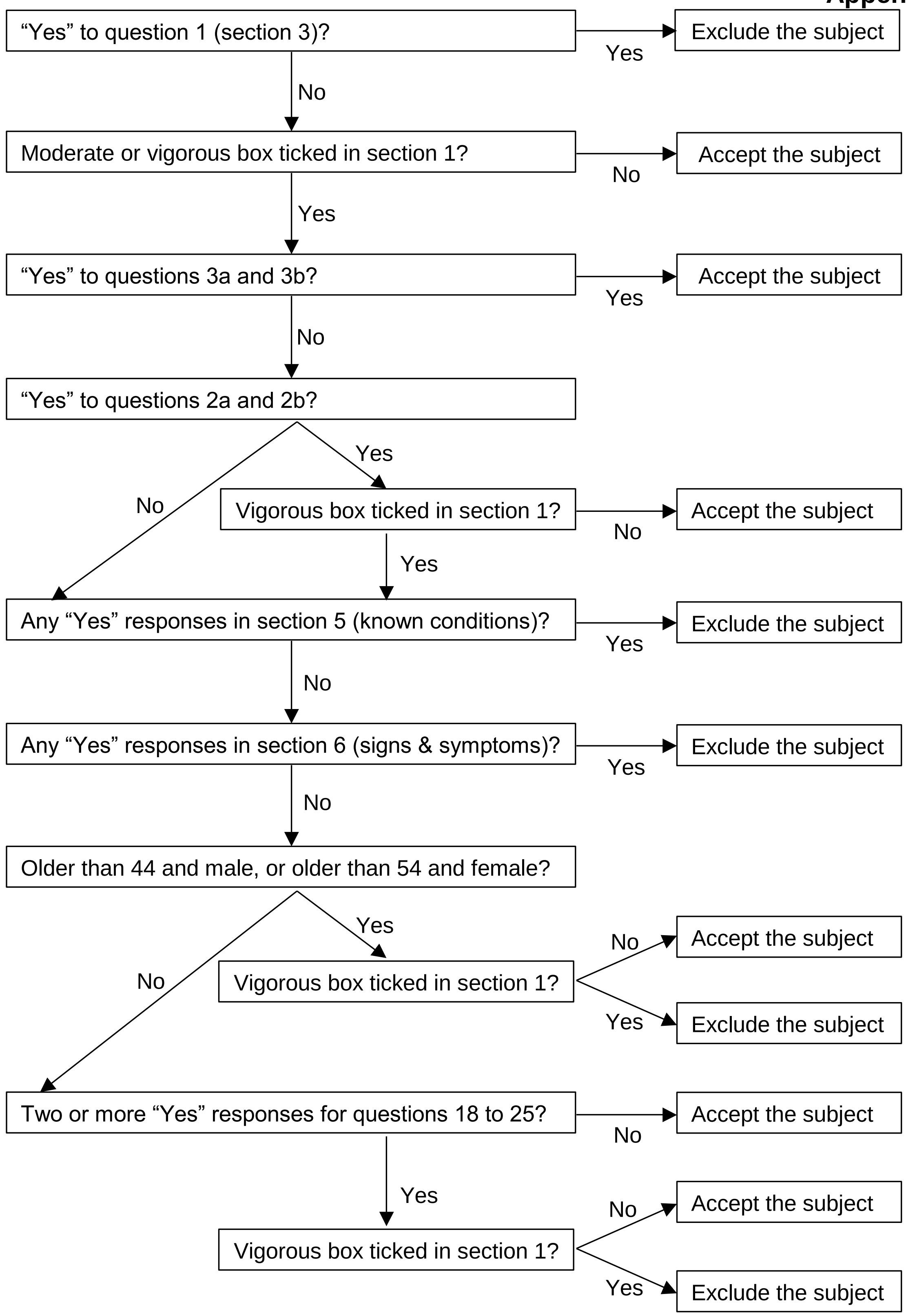
Section 10: Eligibility (to be completed by the tester)

26. Is the participant eligible for the testing? No
    Yes

Name (of tester): ....……….........……………………

Signature: …………………………………………………Date: ………....……….……...

Processing the completed questionnaire – a flow diagram



"Yes" to question 1 (section 3)?
Yes
Exclude the subject
No
Moderate or vigorous box ticked in section 1?
No
Accept the subject
Yes
"Yes" to questions 3a and 3b?
Yes
Accept the subject
No
"Yes" to questions 2a and 2b?
Yes
No
Vigorous box ticked in section 1?
No
Accept the subject
Yes
Any "Yes" responses in section 5 (known conditions)?
Yes
Exclude the subject
No
Any "Yes" responses in section 6 (signs & symptoms)?
Yes
Exclude the subject
No
Older than 44 and male, or older than 54 and female?
Yes
No
Vigorous box ticked in section 1?
No
Accept the subject
Yes
Exclude the subject
Two or more "Yes" responses for questions 18 to 25?
No
Accept the subject
Yes
Vigorous box ticked in section 1?
No
Accept the subject
Yes
Exclude the subject

Preparing and processing pre-test health questionnaires

Introduction

These notes should be read in conjunction with the standard Health Questionnaire of the sport & exercise laboratories. They are intended to assist staff and students with a) preparing a health questionnaire for distribution to a potential participant and b) processing the completed questionnaire. The questionnaire is designed to gather the information needed to decide whether an individual is or is not eligible for a particular set of testing. This information is highly confidential and should be handled accordingly. During the course of a project or sequence of testing, it is the tester's responsibility to ensure that all completed health questionnaires are kept under lock and key and that the information they contain remains confidential. On completion of the project or sequence of testing, these questionnaires should be submitted to a technician, who will store them for 5 years for insurance purposes.

Preparing the questionnaire

First you need to summarise the cardiorespiratory demands of the testing by indicating whether it involves moderate or vigorous exercise. You should tick the moderate box for sub-lactate threshold exercise and the vigorous box for supra-threshold exercise or when testing is likely to invoke a marked cardiorespiratory response. For example, it would be appropriate to tick the vigorous box if the testing involves cold-water immersion, sustained isometric muscle actions or sustained exercise in an unusually hot or humid environment. If cardiorespiratory demands of the testing are minimal, you should not tick either box. However, if you are unsure you should err on the side of caution. Similarly, if you are unsure whether the exercise involved in a particular set of testing will be sub- or supra-threshold, tick the vigorous box. Next you need to summarise the musculo-skeletal demands of the testing by naming the activity and giving an indication of the forces involved in the testing so that the participant can make a judgement about whether any physical problem they have is likely to be aggravated. If you are unsure, err on the side of caution.

Processing the completed questionnaire

The process all laboratory users are expected to follow to reach a decision about whether a particular participant is eligible for testing is outlined below. This process is closely aligned with Olds and Norton's (1999) interpretation of the American College of Sport Medicine's Guidelines for Exercise Testing and Prescription (ACSM, 1995, 2000). It is underpinned by two key principles: first that the risk of a cardiac or other potentially fatal event occurring in response to exercise is low in individuals who are accustomed to meeting the cardiorespiratory demands of the exercise; second that the risk of such an event occurring in an unaccustomed individual depends on their age, whether they have particular medical conditions or show signs or symptoms of cardiovascular or pulmonary disease, and how many risk factors for cardiovascular disease they have. The process itself comprises a series of sequential steps.

1) Automatic exclusions

Question 1 covers blood-borne diseases, pregnancy, muscle or joint problems, recent fever or feeling unwell on the day. If the participant answers ‘Yes’ to any of the criteria they are automatically excluded.

2) Cardiorespiratory demands

Section 4 of the standard questionnaire summarises how often they typically exercise and when they last performed moderate or vigorous exercise. An individual should be deemed to be accustomed to a particular intensity of exercise if they typically experience it at least twice a week for moderate or once a week for vigorous exercise and have done so within the last 10 days. Individuals who show themselves to be accustomed to moderate exercise need to be screened further if the testing involves vigorous exercise but accept them if it involves moderate exercise. All participants are eligible for testing where the cardiorespiratory demands are minimal (for which neither the moderate nor the vigorous box would be ticked in section 1).

3) Known medical conditions

If there are any “yes” responses in section 5 exclude the participant, otherwise go to step 4.

4) Signs and symptoms of cardiovascular or pulmonary disease

If there are any “yes” responses in section 6 exclude the participant, otherwise go to step 5.

5) Age and sex

If the participant is older than 44 and male, or older than 54 and female, and the testing involves moderate exercise only, accept the participant or if the exercise is vigorous exclude the participant.

If they are younger than 45 and male, or younger than 55 and female, proceed to step 6.

6) Risk factors for cardiovascular disease

The tester should have completed section 9. To calculate the individual's body mass index (BMI), divide their body mass in kg by their height in cm squared. A BMI of >30 kg/m^2 constitutes one risk factor. To classify the participant as sedentary or otherwise, use the information from section 4: a "no" response to question 2a **and** 3a constitutes one risk factor.

In section 7 and 9. if there is one or less "yes" response, accept the participant.

If there are two or more "yes" responses and the testing involves moderate exercise only, accept the participant or if it involves vigorous exercise, exclude the participant.

7) Signatures

Accepting or excluding a participant involves answering "yes" or "no" in section 10. Then print your name and sign and date the form. You then need to explain your decision to the participant.

It is sufficient for all participants (except those who report one or more signs or symptoms of cardiovascular or pulmonary disease), to provide a brief oral explanation of why they have been excluded. For those with two or more signs or symptoms, Appendix 8 contains a standard letter warning that the signs and symptoms listed on the questionnaire are not definitive indicators of disease and inviting the excluded participant to discuss with their GP the sensations or events they have reported.

Appendix 7 is a flow diagram showing how to process the completed questionnaire. The principle is that the processing stops when a decision to accept or exclude the participant can be made. Often this point will be reached after two or three steps. Performing all seven steps would only be necessary for testing involving moderate or severe exercise for which the potential participant is young and sedentary, with no known medical conditions or signs and symptoms.

Routine testing vs. specific projects involving special populations
Participants who would normally be excluded from a particular type of testing may be eligible provided the testing is conducted under medical supervision (e.g. in a cardiac rehabilitation programme). Projects involving high-risk populations, or vigorous exercise in moderate risk populations, involve medically qualified personnel and are most likely to be conducted in a hospital environment.

References
ACSM (1995). *Guidelines for Exercise Testing and Prescription* (5th ed.). London: Williams & Wilkins.

ACSM (2000). *Guidelines for Exercise Testing and Prescription* (6th ed.). London: Williams & Wilkins.

Olds, T.S. and Norton, K.I. (1999). *Pre-Exercise Health Screening Guide*. Leeds: Human Kinetics

6.3 Appendix III

Standard Error of the Estimate

MONO

	1	2	3	4	5	6	7	8	AVG	SD
-20	163.0768	103.3259	242.1921	104.4979	201.1983	266.4151	177.3905	178.844	**179.6176**	**58.13488**
-10	183.088	214.0271	246.6597	104.6564	203.2301	270.8827	191.3344	178.6683	**199.0684**	**49.72538**
GXT	199.6468	170.1395	265.46	139.0515	198.2153	289.683	252.4448	134.9832	**206.203**	**58.07327**
10	165.6939	228.7137	285.7816	141.4748	175.7459	319.351	252.2797	149.0263	**214.7584**	**66.76933**
20	207.2168	220.6501	343.064	133.4284	207.6721	367.287	270.6631	196.6305	**243.3265**	**78.74784**
30	205.8886	206.8927	377.409	179.1144	221.4627	401.632	253.2207	187.2405	**254.1075**	**86.75306**
40	204.4045	245.5858	382.2507	199.9982	213.0121	406.4737	341.0182	181.7215	**271.8081**	**90.30305**
50	198.3766	219.0276	426.129	161.3194	198.4262	500.2606	336.7882	263.389	**287.9646**	**121.8788**
									232.1068	**76.29821**

Standard Error of the Estimate

BI

	1	2	3	4	5	6	7	8	AVG	SD
-20	160.6631	101.7806	229.7581	107.7992	193.8362	253.9811	172.696	163.6287	**173.0179**	**53.15345**
-10	172.4861	204.1411	223.5727	110.6046	185.9632	247.7957	192.18	153.9524	**186.337**	**42.24241**
GXT	186.285	156.2504	239.7016	134.0316	180.3	263.9246	264.809	128.1455	**194.181**	**55.54534**
10	156.0367	214.6118	269.4002	123.7912	178.3586	290.0399	234.9338	139.2155	**200.7984**	**61.24426**
20	190.9897	209.6348	329.5703	131.3648	211.8884	310.66	251.6225	179.6993	**226.9287**	**66.90717**
30	184.5914	200.8437	367.9595	178.32	218.2844	353.7933	235.7723	171.3051	**238.8587**	**78.31103**
40	189.5747	233.5597	370.3614	197.9428	205.3581	392.1825	315.9847	170.5867	**259.4438**	**87.23862**
50	191.162	203.6926	389.4146	158.9326	163.699	499.9481	314.7936	244.0173	**270.7075**	**121.9259**
									218.7841	**70.82102**

-20 ttest
0.022592
-10ttest
0.016534
GXTttest
0.029446
+10ttest
0.003363
+20ttest
0.037426
+30ttest
0.023868
+40ttest
0.00108
+50ttest
0.009347
average model t test
9.25E-06

6.4 Appendix IV

Blood lactate responses

	-20			-10			GXT			+10		
	PRE	POST	DELTA	PRE	POST	DELTA	PRE	POST	DELTA	PRE	POST	DELTA
1	1.3	1.3	0	1.3	1.4	0.1	1.3	1.8	0.5	1.2	2.3	1.1
2	1	1	0	1	1	0	1.1	1.5	0.4	1.1	2.3	1.2
3	1.4	1.6	0.2	1.6	1.7	0.1	1.1	1.6	0.5	1.3	2.4	1.1
4	1.3	1.3	0	1.3	1.2	-0.1	1.3	1.9	0.6	1	2.3	1.3
5	1.2	1.3	0.1	1	1.1	0.1	1.2	1.5	0.3	1.3	2.7	1.4
6	1	0.8	-0.2	0.9	0.8	-0.1	0.8	1.2	0.4	0.8	2	1.2
7	1.2	1.2	0	1.3	1.4	0.1	1.2	1.6	0.4	1.1	2.6	1.5
8	1.4	1.4	0	1.5	1.5	0	1.4	1.7	0.3	1.3	2.8	1.5
AVG	1.225	1.2375	0.0125	1.2375	1.2625	0.025	1.175	1.6	0.425	1.1375	2.425	1.2875
ST. DEV	0.158114	0.244584	0.112599	0.250357	0.292465	0.088641	0.183225	0.213809	0.10351	0.176777	0.260494	0.164208
P Value	0.391002219			0.637618091			1.1722164447169E-03			0.00014825		

	+20			+30			+40			+50		
	PRE	POST	DELTA	PRE	POST	DELTA	PRE	POST	DELTA	PRE	POST	DELTA
1	1.1	2.9	1.8	1	4	3	1.3	4.7	3.4	1.2	6	4.8
2	1.2	2.8	1.6	0.9	3.5	2.6	1	4.4	3.4	1	5.7	4.7
3	1	3.2	2.2	1.4	4.5	3.1	1.2	5	3.8	0.9	6.6	5.7
4	1.2	3.1	1.9	1.2	4	2.8	1.2	4.3	3.1	1.1	5.8	4.7
5	1.3	3	1.7	1.1	4.1	3	1.2	5.1	3.9	1.3	5.9	4.6
6	0.9	2.6	1.7	1.1	3.2	2.1	1	3.8	2.8	0.8	5.3	4.5
7	1.3	3	1.7	1.2	5.1	3.9	1.2	4.1	2.9	1.1	6.2	5.1
8	1	3.3	2.3	1.4	3.4	2	1.5	5	3.5	1.2	6	4.8

	1.125	2.9875	1.8625	1.1625	3.975	2.8125	1.2	4.55	3.35	1.075	5.9375	4.8625
	0.148805	0.223207	0.255999	0.176777	0.622782	0.603413	0.160357	0.475094	0.396412	0.166905	0.377728	0.381491
P Value												
	0.000643119			0.000125792			0.000161561			0.000254213		

6.5 Appendix V

Average Breath by Breath responses

Time	min20	min10	0	10	20	30	40	50
-1.91667	516.6523	492.7408	395.2548	820.5693	432.2699	469.5362	529.5932	293.2828
-1.9	691.6904	528.9875	522.4157	600.3426	441.2699	493.1032	522.2559	396.634
-1.88333	582.9693	656.9995	577.8478	634.9598	471.2699	516.6702	651.0875	410.5657
-1.86667	521.8917	671.8778	626.4468	757.5474	510.3435	540.2372	648.2838	629.0234
-1.85	609.4015	677.4589	672.3995	478.4613	415.2284	563.8042	678.7122	664.4409
-1.83333	736.4354	502.808	655.2451	384.4611	580.6816	592.4305	684.1332	670.1396
-1.81667	784.3666	585.7271	577.4091	471.7189	603.4827	613.3421	720.5276	781.6991
-1.8	666.6752	651.1655	557.6217	573.4307	622.7541	651.6621	782.8331	792.9405
-1.78333	671.6711	691.2147	579.2852	626.7109	593.2895	709.1695	854.0083	735.9732
-1.76667	682.164	721.7715	620.007	638.004	604.3311	705.1328	952.8409	735.3561
-1.75	684.7094	688.2141	641.2024	692.7947	588.267	672.4628	865.3351	714.3703
-1.73333	667.9488	679.4199	617.8289	673.8534	582.3262	635.6052	814.2641	659.6341
-1.71667	630.0738	812.7596	578.4774	657.433	601.1321	660.5911	670.8924	604.0202
-1.7	595.3552	688.9813	554.3552	619.9303	584.7842	699.5816	644.3851	551.6252
-1.68333	587.3654	634.5789	528.1947	588.3274	533.1815	699.7587	625.0576	514.0379
-1.66667	611.3603	758.4687	531.0135	546.7605	531.5794	662.2028	625.2261	503.3471
-1.65	620.5065	816.8386	513.9344	617.504	452.9295	641.8002	611.5893	512.4509
-1.63333	633.8358	751.9371	541.2404	696.4511	378.0633	645.053	575.6625	511.5069
-1.61667	679.9188	705.504	556.4581	750.5759	415.2544	648.8075	564.1568	500.9079
-1.6	736.6697	658.7382	588.4043	819.4971	489.6943	653.0229	566.5346	506.6481
-1.58333	744.3529	628.7963	567.2057	818.6603	535.6583	635.4582	570.3708	500.7345
-1.56667	748.6507	608.6789	556.9106	782.3373	656.309	608.782	582.6221	526.2006
-1.55	745.3288	608.3765	519.3697	768.1009	688.7646	593.4645	583.6057	556.9881
-1.53333	734.8905	653.8813	503.2752	731.8271	714.7603	570.0563	579.2214	587.7779
-1.51667	728.4829	684.0971	494.052	699.9198	730.6419	601.4659	579.2622	581.9525

-1.5	737.7013	701.4877	512.553	681.3673	697.4086	637.6232	579.0296	570.1718
-1.48333	752.645	717.7314	513.136	650.7757	638.6696	619.1446	581.4742	559.3953
-1.46667	757.9089	713.6875	531.2706	611.2492	629.1921	635.2088	613.2712	546.152
-1.45	740.974	711.9166	542.0119	630.9552	585.4275	657.3476	675.1729	530.8905
-1.43333	692.5224	716.9892	592.8767	631.3831	544.0615	663.4369	734.462	527.8562
-1.41667	618.6073	714.366	625.3863	648.1769	538.7636	690.1355	754.5735	543.694
-1.4	622.0245	709.8866	627.9495	683.2829	522.1506	669.3077	722.5601	556.0884
-1.38333	640.5446	681.618	579.5301	687.919	481.0862	648.1956	699.0767	569.2989
-1.36667	658.5545	687.1848	536.0668	656.4362	506.6387	660.4998	707.3729	581.3059
-1.35	642.6299	704.0374	475.4073	658.1252	515.1257	669.0449	700.1841	577.4643
-1.33333	629.0578	712.8687	450.0938	636.5086	510.503	662.7404	702.8703	584.5049
-1.31667	631.7029	640.6041	440.09	616.4084	525.0092	651.8188	716.7923	591.5456
-1.3	638.5947	549.4091	467.5597	619.8544	525.1887	633.002	727.3198	592.9342
-1.28333	644.5544	485.5318	469.3805	612.9539	504.683	626.1712	664.7578	589.8393
-1.26667	655.3873	498.6514	483.4942	592.9241	535.286	642.1205	604.7597	582.5293
-1.25	669.8434	545.3794	467.1653	610.2812	525.8521	661.9138	596.6358	574.1301
-1.23333	688.6085	608.477	477.4432	593.225	522.7817	633.7014	591.1257	547.757
-1.21667	701.9578	656.6486	473.257	569.8315	567.422	601.26	604.4146	528.0004
-1.2	722.3812	687.9535	492.1256	575.2571	590.379	563.177	603.2342	510.2239
-1.18333	696.483	680.7765	492.6127	575.9149	581.1415	523.5939	589.0758	516.6123
-1.16667	665.94	687.2445	512.7991	585.6754	622.1421	514.3603	644.5705	525.4139
-1.15	635.9704	693.3828	492.1545	632.7704	630.8458	488.1098	745.8473	534.3087
-1.13333	628.8139	681.6941	492.0314	686.6549	583.5016	551.4972	810.3278	545.5258
-1.11667	624.804	666.9282	468.9749	709.8936	569.6388	647.0547	830.8903	554.2258
-1.1	594.9796	652.9033	473.0823	702.74	571.3004	728.8518	833.7699	558.2115
-1.08333	542.6257	667.6425	483.2444	670.0288	557.2015	769.2091	840.7481	562.1972
-1.06667	491.2235	678.6897	514.565	642.4262	589.0078	747.6224	843.977	553.6717

-1.05	446.0922	666.2955	536.5426	672.2385	565.54	738.9552	852.1649	540.3364
-1.03333	481.9669	641.4592	583.0469	682.532	541.2778	707.184	823.0571	521.8607
-1.01667	530.6582	606.0667	593.4869	688.7806	583.0575	698.4677	803.6743	516.3461
-1	593.9516	575.0135	608.0703	716.9706	610.0962	692.2825	742.6438	527.2518
-0.98333	608.0938	557.8738	618.2371	722.5004	599.3626	650.5823	717.4999	525.6583
-0.96667	601.6023	577.7622	673.0194	690.3247	624.1887	636.978	707.3545	530.1793
-0.95	585.7262	634.0749	704.594	692.31	615.0153	613.9562	722.9047	571.1684
-0.93333	571.7026	686.7195	740.9784	645.3333	594.7277	587.0204	735.3562	606.7925
-0.91667	575.6637	691.9324	716.5304	599.9007	595.5034	591.8752	722.9855	583.2354
-0.9	584.4985	677.185	656.7285	557.3127	550.5615	579.1444	717.6021	573.0308
-0.88333	580.9431	655.1757	586.2283	519.608	496.0191	563.2131	721.8323	573.3292
-0.86667	601.3189	645.9532	561.5282	493.8657	495.03	581.4288	750.6076	603.3991
-0.85	631.9096	624.1841	567.6116	565.5883	464.3388	596.7749	766.305	624.2559
-0.83333	660.1995	634.0511	585.8584	599.9885	461.153	596.8116	736.5599	622.0813
-0.81667	664.28	655.8912	583.5205	638.7668	553.2971	604.2721	716.7409	610.5715
-0.8	638.2668	669.2477	597.6856	678.454	627.1122	617.5106	723.8259	604.8167
-0.78333	611.7903	672.6103	596.1995	692.8043	668.679	606.9847	741.2735	599.7866
-0.76667	577.9867	683.0289	605.5191	679.401	714.7546	619.0998	753.3826	603.0625
-0.75	524.9126	686.915	618.1623	701.2994	677.2982	618.0113	743.9612	607.2865
-0.73333	515.3102	675.0338	622.5553	707.0807	632.1564	578.0784	719.6539	623.9733
-0.71667	549.3221	640.5652	610.9607	704.1754	611.7571	572.2921	691.1886	633.1604
-0.7	642.4474	631.6942	591.1291	695.2178	582.3377	554.1514	670.2211	629.7016
-0.68333	716.5368	629.5939	544.0732	667.0477	528.0156	548.945	662.2366	604.6266
-0.66667	794.6557	641.0037	534.9531	636.9631	521.5184	567.3384	595.0619	575.0038
-0.65	817.3173	628.3202	516.365	671.491	474.8708	571.5642	525.2138	539.2519
-0.63333	800.2858	608.1393	535.5503	669.4108	450.2758	569.5594	598.2275	567.485
-0.61667	760.8131	600.4921	555.0397	666.1294	480.5772	602.971	675.5451	587.5347

-0.6	691.7378	594.4915	531.2069	695.9335	501.1996	663.6309	714.2516	605.1849
-0.58333	652.513	588.0549	502.612	698.4676	495.8863	728.4978	718.2504	587.9202
-0.56667	646.2052	593.8496	523.3288	662.0153	538.5269	780.8044	718.8362	586.833
-0.55	643.8539	586.025	581.5608	657.4635	531.4318	807.6289	720.6147	587.9222
-0.53333	645.6139	583.1462	635.4022	644.3237	522.8149	753.2149	702.1361	582.8387
-0.51667	667.638	589.6367	662.8678	639.0487	538.8704	719.7276	696.6492	572.2463
-0.5	691.0345	596.8027	661.2416	642.9682	565.0274	731.6618	664.9509	561.654
-0.48333	683.9863	592.138	663.2446	641.9946	565.7282	720.0103	645.6471	561.7513
-0.46667	655.0213	567.1273	662.8491	646.2894	591.0061	735.5196	666.9905	558.0645
-0.45	610.1095	562.6756	670.5913	701.8114	577.9793	708.9772	678.4211	555.7084
-0.43333	579.9598	569.7796	680.4427	724.5524	582.4596	669.3231	680.8597	531.1088
-0.41667	552.718	591.6988	683.7894	731.9639	616.2052	635.8128	701.9978	523.0871
-0.4	535.4343	613.3209	674.9372	762.9925	631.8568	586.1658	688.3553	545.8363
-0.38333	588.8349	613.2596	665.0003	796.913	639.0227	547.1419	685.1218	592.5876
-0.36667	640.7391	633.161	629.4914	787.9445	708.3808	519.786	706.5778	643.8076
-0.35	679.8808	635.2719	592.8776	777.0063	743.854	513.3815	724.3062	563.8281
-0.33333	693.4729	630.6912	574.7535	747.7357	752.3773	552.1697	735.5241	519.1854
-0.31667	705.7103	625.0059	562.8522	728.9296	744.5889	588.8449	745.3769	563.3625
-0.3	714.5253	609.2375	552.3066	726.6876	719.8216	658.7465	746.4351	619.3973
-0.28333	712.0736	587.6643	565.1704	692.715	663.0559	694.6832	761.4978	728.1079
-0.26667	690.0573	551.64	579.1759	641.1366	665.324	721.6362	804.9204	768.7745
-0.25	680.2741	519.6201	612.9392	650.6464	643.2909	740.097	852.1252	750.7896
-0.23333	678.7925	538.2498	642.1597	638.687	619.1471	719.9841	877.0149	729.7138
-0.21667	668.1031	593.3617	687.4514	618.9525	622.1394	737.0166	865.4914	685.7226
-0.2	662.9565	668.8926	678.455	632.6624	619.6105	731.0555	804.6656	667.8896
-0.18333	709.9519	701.3516	622.084	655.242	583.1818	710.404	739.3832	650.0479
-0.16667	789.3548	681.1145	549.5629	655.6521	621.7773	708.2887	719.2162	642.8201

-0.15	866.7691	620.8931	560.771	662.5968	610.3491	685.4342	703.8856	666.8868
-0.13333	854.1945	549.7905	585.3715	632.613	592.801	666.0793	700.3708	704.2679
-0.11667	841.1518	526.5543	638.7299	602.4596	595.7553	676.6185	758.5862	764.2258
-0.1	797.4933	593.6124	701.8775	595.7228	571.8153	719.7511	835.4593	851.374
-0.08333	715.8222	689.669	806.275	571.137	515.0545	765.7526	909.9797	938.5221
-0.06667	642.9343	753.8465	894.349	563.4769	548.3939	792.4458	945.6426	913.0704
-0.05	615.3198	754.2514	919.0061	606.9318	564.359	809.5217	960.3286	858.1445
-0.03333	615.8434	773.3332	939.9952	609.4915	622.6311	742.8799	894.5324	797.1242
-0.01667	631.1024	767.4895	901.2569	589.9129	668.1408	698.4416	823.3471	765.6148
0	704.7098	765.2083	842.3771	612.3237	720.6588	657.5349	772.5473	797.0179
0.016667	760.7707	746.5799	796.0608	627.3524	755.2533	578.3696	746.9879	807.0108
0.033333	771.1388	736.4073	799.2095	618.0868	825.8414	590.8694	774.2154	635.3551
0.05	785.1855	781.3038	802.368	640.3673	843.0827	654.8364	818.2401	454.0362
0.066667	785.6235	852.3024	824.1046	640.9606	812.8798	705.1361	830.5483	425.8368
0.083333	853.9848	887.8915	833.712	683.1192	790.1667	790.7615	826.0254	412.3044
0.1	914.7523	905.3297	858.4257	734.956	785.314	839.0104	871.0942	424.3326
0.116667	932.0154	913.7876	879.3108	786.7141	741.4506	868.4766	910.284	540.1871
0.133333	914.0562	913.1512	900.9027	837.2717	765.1311	925.2121	915.1825	672.7733
0.15	888.0499	924.6994	943.2813	901.3072	785.1676	998.7777	942.7437	795.5821
0.166667	914.2879	965.1371	989.0574	915.1372	852.4739	1074.196	1012.462	977.565
0.183333	963.0629	1009.059	954.5821	908.5624	951.8638	1134.164	1030.285	1140.783
0.2	1034.469	1025.999	885.7258	985.6803	1035.665	1179.262	1087.677	1218.479
0.216667	1087.99	1025.489	970.3658	1074.22	1036.973	1185.117	1148.144	1402.006
0.233333	1101.233	999.3886	1128.532	1092.926	1062.342	1156.771	1137.034	1429.982
0.25	1065.04	978.0577	1160.022	1082.271	1044.781	1133.16	1069.192	1247.048
0.266667	1044.674	982.4554	1123.348	1026.062	1021.834	1079.641	1086.032	1090.44
0.283333	1039.265	969.1719	1153.931	943.6239	1048.004	1060.682	1228.929	987.6665

0.3	1022.556	970.6833	1227.651	933.5481	1071.313	1032.196	1340.75	1079.596
0.316667	1018.572	975.4397	1236.526	952.5808	1111.528	1025.064	1297.263	1161.094
0.333333	1035.06	999.0188	1211.869	1021.075	1162.208	1037.493	1252.207	1086.31
0.35	1048.499	1014.633	1190.702	1126.556	1159.17	1024.745	1193.05	1032.177
0.366667	1065.171	1031.602	1187.538	1155.042	1141.351	1022.462	1170.787	1184.134
0.383333	1108.373	1064.753	1230.373	1121.821	1148.589	995.2993	1193.615	1367.453
0.4	1157.422	1076.117	1252.487	1079.029	1132.484	1006.208	1256.188	1379.853
0.416667	1174.496	1088.037	1256.212	1082.12	1080.47	1047.637	1346.695	1412.657
0.433333	1169.358	1099.633	1245.016	1072.554	1085.617	1078.496	1407.186	1618.674
0.45	1163.801	1058.589	1273.641	1099.738	1128.687	1187.312	1438.753	1730.573
0.466667	1177.713	1023.488	1337.532	1206.81	1169.034	1256.32	1418.465	1702.556
0.483333	1210.139	1121.518	1387.626	1345.468	1224.211	1356.548	1406.417	1671.073
0.5	1269.43	1236.508	1413.762	1528.977	1344.035	1396.662	1441.499	1692.329
0.516667	1312.014	1319.693	1414.203	1621.212	1478.345	1362.967	1475.929	1718.38
0.533333	1340.074	1294.022	1371.641	1510.43	1572.82	1330.539	1544.964	1716.604
0.55	1344.927	1263.404	1379.538	1325.178	1489.239	1346.274	1631.781	1706.174
0.566667	1340.812	1255.437	1405.76	1434.26	1458.37	1378.786	1707.813	1702.991
0.583333	1319.197	1329.878	1469.855	1558.85	1502.675	1455.688	1792.255	1692.53
0.6	1308.11	1375.667	1533.089	1542.89	1552.868	1506.289	1889.064	1642.727
0.616667	1358.945	1305.674	1601.6	1519.125	1565.587	1525.954	1966.103	1730.714
0.633333	1413.468	1300.645	1644.856	1519.141	1576.121	1588.845	2022.609	1844.881
0.65	1436.69	1297.477	1658.774	1564.413	1522.313	1673.473	2021.218	1884.43
0.666667	1462.902	1291.28	1660.318	1595.303	1465.812	1765.238	2024.074	1886.887
0.683333	1487.165	1284.002	1732.908	1582.806	1507.56	1861.822	2054.914	1908.251
0.7	1512.056	1282.007	1743.241	1576.812	1610.44	1906.355	2010.223	1917.531
0.716667	1471.774	1374.748	1721.874	1558.306	1766.991	1908.731	1878.591	1951.759
0.733333	1471.86	1459.286	1687.763	1605.699	1900.179	1945.116	1859.43	1986.209

0.75	1518.858	1516.772	1739.711	1664.553	1981.548	1932.099	1972.765	1973.756
0.766667	1593.283	1509.893	1753.448	1622.725	2005.229	1817.037	2064.986	2042.497
0.783333	1626.443	1464.362	1768.793	1690.514	2038.139	1784.624	2128.673	2224.301
0.8	1618.87	1423.923	1791.22	1759.313	2016.407	1827.213	2149.729	2291.457
0.816667	1605.985	1399.786	1818.354	1786.839	1941.846	1867.386	2231.247	2246.351
0.833333	1613.388	1500.286	1792.875	1767.001	1964.262	1928.296	2276.846	2182.56
0.85	1739.679	1642.916	1733.906	1768.231	1972.024	1940.097	2223.211	2171.507
0.866667	1829.05	1774.317	1691.044	1737.502	1991.936	1975.179	2159.167	2159.919
0.883333	1796.202	1869.915	1644.147	1778.397	1985.881	2012.657	2170.513	2200.84
0.9	1705.085	1825.08	1724.265	1852.113	1988.307	1982.555	2222.588	2233.853
0.916667	1693.087	1783.482	1797.137	1915.187	2030.771	1870.908	2283.979	2277.666
0.933333	1718.838	1741.441	1733.563	1961.95	2066.877	1947.777	2286.121	2278.889
0.95	1739.76	1723.639	1636.321	2005.756	2045.076	2036.593	2262.443	2248.071
0.966667	1777.866	1742.223	1582.414	1975.871	1969.624	2093.451	2265.768	2240.076
0.983333	1665.404	1775.208	1668.608	1832.102	1924.261	2134.598	2284.196	2260.277
1	1546.912	1770.26	1782.888	1743.291	1871.123	2185.649	2312.629	2239.539
1.016667	1534.66	1781.063	1904.465	1906.117	1732.188	2146.283	2428.343	2311.887
1.033333	1637.734	1784.584	1985.269	2034.723	1751.947	2105.635	2494.581	2415.644
1.05	1762.05	1807.831	1983.185	2105.648	1992.135	2057.245	2450.4	2540.527
1.066667	1893.948	1830.568	1967.156	2081.218	2201.578	2044.037	2388.314	2627.959
1.083333	1925.033	1829.127	1975.184	2122.25	2284.757	2101.6	2366.8	2633.177
1.1	1872.301	1808.446	2050.421	2217.555	2254.519	2225.242	2449.692	2501.624
1.116667	1829.168	1802.113	2096.096	2237.992	2189.022	2316.741	2479.157	2435.404
1.133333	1794.629	1863.773	2127.012	2223.242	2174.928	2428.43	2475.636	2460.707
1.15	1769.012	1984.717	2138.799	2206.952	2174.432	2444.895	2410.194	2478.084
1.166667	1758.438	2016.586	2153.23	2146.092	2144.954	2433.479	2470.567	2423.504
1.183333	1745.158	2029.662	2136.484	2087.021	2110.182	2435.047	2514.032	2391.36

1.2	1785.886	1953.588	2119.601	2142.04	2078.768	2451.397	2516.748	2367.04
1.216667	1781.309	1929.697	2012.103	2168.442	2076.668	2422.055	2559.572	2452.7
1.233333	1771.004	1936.083	1886.252	2123.226	2175.067	2440.295	2663.253	2578.967
1.25	1812.517	1950.475	1882.732	2081.835	2283.915	2388.619	2674.967	2656.384
1.266667	1895.196	1931.687	1878.182	2055.236	2340.704	2329.055	2630.542	2646.453
1.283333	1918.465	1935.6	2042.308	2120.355	2268.868	2325.79	2588.907	2568.347
1.3	1935.086	1987.486	2019.956	2166.24	2200.151	2334.111	2525.938	2497.049
1.316667	1899.577	2058.958	2041.322	2123.355	2192.397	2365.395	2489.749	2468.139
1.333333	1927.587	2097.247	2099.883	2145.494	2222.414	2432.812	2513.825	2463.154
1.35	1933.347	2092.453	2148.217	2234.509	2234.519	2383.817	2579.343	2495.377
1.366667	1927.977	2022.585	2182.898	2202.425	2232.094	2297.841	2618.434	2533.827
1.383333	1977.434	1994.53	2255.825	2213.676	2254.157	2275.528	2608.72	2595.106
1.4	1975.911	2021.171	2164.537	2245.559	2268.565	2322.395	2569.66	2598.727
1.416667	1966.197	2016.141	2105.281	2244.002	2217.226	2382.89	2558.567	2593.01
1.433333	1944.515	1964.81	2062.513	2196.695	2177.093	2459.284	2580.771	2615.676
1.45	1937.461	1909.48	2038.824	2162.323	2120.415	2478.911	2563.817	2649.016
1.466667	1948.928	1916.657	2011	2149.57	2106.439	2454.715	2548.086	2619.24
1.483333	1943.077	1936.449	2039.509	2187.557	2190.068	2432.25	2544.811	2590.446
1.5	1943.496	1916.149	2094.031	2203.213	2362.244	2264.782	2600.638	2532.476
1.516667	1930.797	1905.292	2118.439	2201.529	2477.291	2148.32	2626.626	2613.101
1.533333	1930.032	1883.075	2142.803	2183.336	2598.825	2294.123	2593.577	2675.011
1.55	1920.194	1897.94	2145.362	2195.907	2513.071	2449.772	2587.303	2700.31
1.566667	1873.912	1935.748	2114.761	2173.245	2380.882	2455.954	2582.479	2746.73
1.583333	1886.83	2001.968	2118.292	2185.676	2315.788	2538.572	2633.969	2788.206
1.6	1972.028	2072.212	2130.074	2263.318	2284.096	2614.373	2669.82	2753.684
1.616667	2021.619	2069.308	2148.489	2289.77	2223.805	2625.191	2647.03	2689.516
1.633333	1979.219	2040.779	2159.779	2219.483	2290.883	2577.439	2576.443	2661.293

1.65	1965.103	2007.195	2224.034	2221.526	2342.624	2533.072	2617.453	2734.087
1.666667	2001.355	1954.955	2277.868	2210.227	2359.258	2490.828	2632.416	2626.974
1.683333	2008.72	1952.528	2304.04	2224.851	2348.989	2459.377	2652.198	2529.563
1.7	1968.058	1947.307	2243.611	2247.108	2370.779	2421.82	2662.41	2507.056
1.716667	1942.962	1956.117	2213.928	2246.563	2397.827	2409.017	2656.357	2578.459
1.733333	1965.557	1968.384	2173.176	2235.381	2455.898	2449.732	2692.911	2644.404
1.75	1983.273	2007.202	2170.96	2232.08	2454.336	2531.46	2721.23	2739.911
1.766667	1979.388	2026.269	2120.126	2206.305	2434.489	2568.563	2651.902	2773.44
1.783333	1996.079	2003.176	2085.285	2244.593	2455.941	2551.266	2643.681	2793.536
1.8	1992.689	1987.168	2158.411	2295.513	2485.811	2504.899	2677.134	2799.911
1.816667	2017.718	1997.558	2268.744	2281.275	2479.001	2530.807	2727.809	2711.7
1.833333	2031.193	2049.432	2217.688	2258.103	2487.248	2641.962	2700.481	2653.107
1.85	2016.521	2078.067	2229.747	2275.688	2451.291	2717.735	2719.791	2627.237
1.866667	1965.255	2101.905	2241.882	2291.649	2430.692	2681.115	2736.914	2663.973
1.883333	1916.732	2179.212	2307.612	2371.047	2447.418	2674.182	2741.959	2719.594
1.9	1928.533	2209.508	2301.417	2414.27	2498.922	2624.977	2707.543	2740.454
1.916667	1958.774	2179.542	2307.72	2395.407	2479.17	2565.446	2666.208	2736.553
1.933333	1953.865	2122.855	2261.113	2302.593	2461.169	2547.038	2616.883	2726.157
1.95	1964.627	2044.33	2202.434	2261.014	2376.209	2554.117	2580.494	2647.006
1.966667	1975.707	2000.269	2161.163	2226.717	2334.388	2582.894	2587.144	2675.266
1.983333	1971.999	1983.881	2208.255	2188.455	2342.945	2616.803	2662.381	2744.029
2	1967.148	1949.768	2184.405	2202.905	2343.435	2594.349	2782.807	2774.659
2.016667	1955.403	1900.414	2152.264	2271.733	2304.478	2555.277	2832.846	2788.601
2.033333	1947.72	1869.317	2178.202	2303.306	2443.662	2538.011	2840.788	2751.863
2.05	1942.573	1896.76	2221.488	2324.897	2515.628	2509.102	2835.29	2726.174
2.066667	1946.093	1950.492	2228.887	2322.19	2552.946	2541.171	2779.404	2749.926
2.083333	1950.675	2048.445	2226.987	2344.303	2558.618	2622.135	2688.845	2768.377

2.1	1964.646	2081.734	2195.211	2375.196	2543.378	2636.854	2628.636	2667.709
2.116667	1972.893	2066.856	2196.821	2360.026	2536.469	2588.689	2681.253	2681.674
2.133333	2008.91	2018.815	2247.178	2309.998	2516.536	2547.723	2773.983	2770.381
2.15	2021.759	2018.09	2320.625	2312.029	2526.342	2505.032	2790.732	2838.101
2.166667	2018.993	2025.16	2347.556	2337.935	2564.654	2556.556	2755.495	2835.611
2.183333	2073.143	2079.722	2317.003	2383.287	2567.706	2654.756	2758.2	2841.29
2.2	2136.273	2134.516	2207.483	2374.563	2556.077	2687.123	2779.669	2756.996
2.216667	2115.035	2201.11	2167.952	2316.924	2542.456	2630.44	2771.267	2712.689
2.233333	2066.391	2235.194	2236.621	2289.612	2545.026	2593.568	2749.947	2665.924
2.25	2029.391	2183.962	2339.979	2343.35	2486.881	2604.748	2695.388	2664.77
2.266667	2029.262	2132.501	2318.929	2356.035	2453.369	2603.888	2666.464	2739.106
2.283333	2012.619	2041.403	2317.429	2314.29	2426.109	2617.828	2647.774	2796.43
2.3	2004.842	1962.992	2293.848	2248.302	2405.118	2642.224	2665.064	2742.056
2.316667	2021.993	1969.154	2254.729	2207.745	2356.033	2605.817	2712.047	2722.32
2.333333	2011.829	2042.317	2148.049	2157.226	2333.723	2595.19	2713.855	2725.571
2.35	1967.131	2105.044	2120.244	2237.165	2353.094	2608.741	2753.632	2795.511
2.366667	1940.009	2114.546	2189.045	2308.265	2373.782	2585.062	2819.378	2844.619
2.383333	1962.052	2160.115	2250.439	2348.075	2416.864	2593.597	2863.217	2850.47
2.4	2000.615	2122.448	2235.949	2375.094	2459.643	2649.533	2836.869	2833.399
2.416667	2018.459	2096.034	2266.42	2360.157	2440.731	2681.07	2832.616	2829.134
2.433333	2027.218	2036.644	2287.858	2330.597	2506.948	2647.486	2814.241	2857.563
2.45	2034.861	1961.43	2317.97	2356.406	2540.527	2609.917	2775.315	2877.216
2.466667	2058.408	1957.535	2259.919	2299.198	2517.124	2545.515	2760.258	2874.594
2.483333	2044.481	2014.513	2200.154	2237.835	2502.696	2505.89	2789.29	2830.776
2.5	2028.107	2080.391	2128.861	2222.267	2557.818	2528.338	2771.979	2702.21
2.516667	2051.427	2137.375	2162.49	2259.011	2555.945	2606.27	2733.471	2666.844
2.533333	2048.224	2129.584	2244.656	2307.238	2555.353	2669.458	2640.065	2761.584

2.55	2001.336	2093.881	2330.617	2349.505	2471.502	2650.05	2526.498	2827.223
2.566667	1965.49	2043.105	2293.983	2313.752	2387.462	2606.855	2519.562	2861.894
2.583333	1977.313	2069.147	2280.282	2231.975	2379.722	2578.296	2737.641	2882.119
2.6	2004.324	2077.28	2314.299	2214.043	2455.356	2556.854	2875.991	2967.64
2.616667	2028.027	2064.383	2353.762	2201.031	2478.337	2578.883	2942.525	2969.393
2.633333	2066.365	2037.993	2298.5	2175.904	2533.022	2658.64	2976.779	2918.851
2.65	2091.552	2033.866	2251.094	2235.643	2577.429	2713.017	2935.665	2926.503
2.666667	2089.962	2025.234	2231.28	2276.442	2608.238	2725.431	2870.318	2919.346
2.683333	2060.426	2046.962	2237.97	2321.862	2618.16	2746.587	2833.614	2898.677
2.7	1989.882	2059.762	2222.708	2326.713	2609.294	2744.35	2878.268	2881.541
2.716667	1927.415	2058.312	2235.375	2304.29	2504.689	2651.367	2902.185	2850.607
2.733333	1930.981	2033.255	2230.107	2297.232	2460.575	2582.678	2873.08	2874.179
2.75	1960.503	2021.856	2233.16	2334.528	2431.761	2564.641	2836.281	2948.566
2.766667	1976.131	2023.555	2223.301	2300.972	2512.783	2572.003	2755.739	2897.107
2.783333	1925.413	2042.599	2235.306	2253.122	2534.937	2566.711	2737.704	2870.361
2.8	1873.315	2094.217	2239.852	2263.038	2483.755	2489.868	2754.854	2830.423
2.816667	1896.551	2020.461	2310.281	2301.572	2479.62	2564.49	2757.615	2791.636
2.833333	2016.86	1955.717	2379.699	2284.469	2490.632	2752.351	2757.542	2751.143
2.85	2101.311	1996.346	2403.33	2351.146	2429.324	2776.553	2777.315	2750.353
2.866667	2078.332	2170.672	2303.733	2387.998	2419.62	2758.14	2745.843	2702.724
2.883333	2108.739	2259.663	2223.532	2401.042	2522.096	2753.59	2693.688	2718.42
2.9	2089.717	2167.314	2166.274	2351.742	2677.005	2709.535	2749.289	2754.38
2.916667	2024.336	2107.579	2169.854	2283.986	2723.626	2620.429	2789.969	2855.149
2.933333	1994.578	2108.684	2215.719	2237.573	2705.81	2629.432	2818.371	2934.226
2.95	1986.06	1967.568	2263.652	2246.499	2613.599	2690.814	2858.333	2929.616
2.966667	2007.844	1989.118	2232.538	2224.202	2529.062	2707.588	2918.602	2902.02
2.983333	1976.109	2024.574	2181.618	2210.428	2516.562	2710.934	2907.95	2904.86

3	1944.561	2056.663	2138.648	2235.889	2534.902	2661.458	2839.266	2887.999
3.016667	1921.123	2080.492	2195.542	2262.736	2523.58	2686.821	2821.78	2854.959
3.033333	1963.52	2009.891	2267.074	2301.677	2561.705	2735.698	2874.345	2877.76
3.05	1968.974	1993.771	2321.641	2380.041	2605.187	2768.899	2914.23	2905.767
3.066667	1950.765	1981.465	2294.081	2392.505	2608.431	2720.835	2973.331	2969.206
3.083333	1957.272	2065.813	2266.414	2382.288	2567.645	2673.716	3046.947	3041.629
3.1	1983.391	2158.283	2286.635	2383.112	2574.807	2663.89	3020.318	3020.011
3.116667	2004.569	2211.619	2347.925	2360.767	2568.604	2696.13	3001.431	3012.159
3.133333	2007.603	2162.209	2376.547	2343.673	2602.246	2735.971	2960.568	3035.387
3.15	1999.202	2081.064	2380.646	2420.226	2665.747	2801.895	2902.599	3047.43
3.166667	1975.445	2020.137	2378.062	2419.29	2682.59	2762.681	2908.346	3024.04
3.183333	1936.724	2047.299	2360.043	2429.889	2607.343	2690.301	2981.956	2944.909
3.2	1975.648	2113.16	2293.843	2411.891	2546.22	2660.674	2950.682	2965.729
3.216667	2078.217	2119.352	2315.984	2401.514	2532.82	2660.233	2845.109	3098.94
3.233333	2066.49	2108.623	2325.058	2370.503	2579.967	2647.12	2822.506	3183.807
3.25	2057.189	2156.417	2283.68	2383.134	2586.415	2695.735	2926.853	3187.709
3.266667	2017.313	2235.515	2225.254	2386.159	2560.904	2773.769	3027.989	3178.631
3.283333	1929.817	2238.654	2258.732	2397.753	2555.557	2819.205	3063.876	3133.963
3.3	1904.959	2237.878	2303.529	2398.336	2598.696	2740.417	2983.059	3053.327
3.316667	1981.588	2234.7	2339.189	2377.453	2592.36	2753.771	2894.368	3014.081
3.333333	2049.425	2187.996	2267.21	2337.039	2614.216	2792.249	2886.786	3087.744
3.35	2055.108	2164.374	2235.383	2303.185	2604.131	2763.729	2962.741	3154.729
3.366667	2038.377	2179.218	2274.237	2324.623	2630.407	2756.51	3012.923	3152.256
3.383333	2023.188	2197.286	2354.033	2374.676	2584.819	2786.222	3034.484	3122.774
3.4	2018.085	2129.265	2360.089	2371.679	2614.205	2831.757	3018.744	3104.783
3.416667	1965.94	2082.792	2338.623	2353.26	2610.11	2849.924	2969.715	3105.313
3.433333	1932.211	2098.507	2268.977	2335.223	2615.543	2866.596	2928.456	3059.031

3.45	1948.936	2112.914	2301.487	2329.157	2549.415	2865.896	2947.456	3039.617
3.466667	1975.359	2143.583	2341.555	2297.11	2476.897	2857.212	2981.866	3073.28
3.483333	2016.796	2168.393	2398.625	2313.084	2463.471	2765.739	3054.378	3145.659
3.5	2088.655	2178.083	2407.283	2355.874	2562.554	2657.422	3038.293	3201.267
3.516667	2103.866	2165.255	2424.82	2405.2	2673.256	2627.803	2934.807	3175.076
3.533333	2060.224	2127.151	2409.897	2446.629	2653.089	2701.027	2859.918	3126.134
3.55	2036.416	2120.49	2400.763	2484.22	2661.237	2811.646	2837.685	3174.201
3.566667	2054.114	2099.234	2356.648	2427.468	2761.948	2858.762	2866.488	3152.79
3.583333	2078.568	2073.397	2296.61	2377.17	2785.619	2891.144	3034.22	3069.854
3.6	2086.686	2094.05	2210.819	2366.517	2692.398	2886.516	3180.184	3064.607
3.616667	2070.244	2163.995	2129.777	2371.949	2601.152	2852.406	3150.669	3072.951
3.633333	2077.048	2244.44	2096.04	2385.768	2632.242	2825.538	3102.956	3068.136
3.65	2096.188	2251.49	2176.542	2374.639	2672.276	2813.371	3088.146	3050.4
3.666667	2043.65	2200.081	2245.822	2387.189	2690.824	2798.626	3088.238	3037.66
3.683333	1974.252	2149.126	2344.407	2423.083	2702.257	2872.267	3042.978	2982.689
3.7	1989.556	2113.153	2434.138	2433.456	2717.209	2940.474	2993.384	2959.18
3.716667	2054.361	2107.64	2488.108	2393.423	2682.166	2930.681	2972.122	2976.103
3.733333	2078.688	2116.352	2456.352	2354.896	2666.471	2912.51	2984.458	3047.059
3.75	2065.463	2158.087	2424.537	2360.493	2636.1	2945.645	2985.068	3202.076
3.766667	2058.551	2187.839	2371.848	2384.892	2619.126	2926.826	2945.189	3217.189
3.783333	2052.954	2171.781	2339.576	2416.393	2624.15	2849.178	2949.761	3186.577
3.8	2082.244	2166.838	2297.772	2402.121	2597.127	2819.605	3045.288	3187.206
3.816667	2091.894	2186.199	2273.64	2405.004	2581.963	2803.387	3122.16	3178.87
3.833333	2097.944	2200.004	2217.338	2388.779	2631.276	2787.793	3101.381	3124.644
3.85	2076.797	2159.802	2170.145	2414.128	2661.765	2749.783	3096.102	2968.976
3.866667	2048.585	2097.919	2200.996	2460.411	2635.939	2656.075	3084.175	2959.053
3.883333	2022.54	2077.064	2302.605	2502.803	2661.451	2670.357	3053.867	3103.57

3.9	2007.305	2086.959	2359.562	2495.262	2684.357	2821.628	2994.384	3180.359
3.916667	1986.151	2125.405	2333.108	2477.85	2713.934	2934.878	2955.273	3222.134
3.933333	1974.153	2123.096	2287.595	2474.493	2681.44	2962.949	2978.649	3245.903
3.95	2009.958	2107.425	2320.502	2479.784	2642.792	2932.03	2991.817	3244.429
3.966667	2049.658	2093.275	2342.548	2485.884	2648.499	2815.731	2988.752	3197.961
3.983333	2065.29	2131.715	2341.664	2449.719	2721.477	2717.248	2998.592	3210.361
4	2089.357	2186.435	2360.507	2399.711	2715.599	2691.923	3057.661	3220.02
4.016667	2190.595	2211.855	2393.777	2382.295	2575.658	2698.053	3098.203	3204.029
4.033333	2161.694	2204.43	2391.687	2419.394	2478.657	2743.86	3097.951	3184.699
4.05	2035.366	2159.21	2389.28	2476.39	2494.102	2821.997	3101.149	3156.077
4.066667	2010.302	2048.892	2345.539	2493.826	2576.435	2874.136	3104.578	3089.351
4.083333	2057.01	1941.455	2346.809	2517.759	2642.892	2859.063	3055.567	3036.05
4.1	2106.78	2036.4	2341.218	2471.184	2720.693	2853.677	3004.378	3057.429
4.116667	2056.096	2166.182	2358.199	2417.219	2790.661	2850.539	3117.581	3101.514
4.133333	1994.38	2181.217	2257.264	2382.224	2852.193	2804.26	3241.961	3086.76
4.15	1966.022	2167.952	2206.812	2395.598	2882.809	2743.755	3231.844	3071.291
4.166667	1993.394	2202.748	2347.249	2389.68	2843.131	2679.602	3195.706	3138.214
4.183333	2037.603	2217.771	2494.72	2374.804	2821.597	2772.378	3134.591	3243.261
4.2	2047.354	2218.723	2445.442	2375.467	2734.293	2942.397	3125.782	3315.95
4.216667	2001.595	2236.553	2435.845	2382.592	2633.138	2979.921	3154.017	3304.624
4.233333	2031.456	2229.8	2402.727	2386.976	2704.661	2914.803	3137.432	3228.013
4.25	2203.403	2198.825	2313.766	2387.182	2743.879	2908.82	3094.015	3112.743
4.266667	2258.93	2164.437	2280.917	2398.362	2645.296	2904.923	3095.366	3125.757
4.283333	2211.986	2140.969	2335.167	2436.317	2718.95	2833.699	3114.262	3177.833
4.3	2192.847	2163.249	2367.45	2438.592	2734.013	2796.256	3085.164	3163.97
4.316667	2159.988	2167.351	2379.409	2431.518	2708.137	2826.988	3037.426	3064.001
4.333333	2144.727	2176.682	2336.82	2408.164	2706.01	2849.191	3005.484	3008.487

4.35	2144.817	2197.631	2281.745	2480.048	2657.723	2822.921	3003.689	3035.769
4.366667	2146.24	2190.118	2257.344	2516.112	2602.87	2785.617	3048.894	3108.451
4.383333	2102.551	2165.004	2225.306	2504.004	2651.36	2807.805	3065.813	3265.427
4.4	2061.128	2138.492	2246.165	2508.647	2728.645	2852.305	3075.477	3299.863
4.416667	2033.476	2113.441	2346.87	2568.878	2719.95	2913.94	3051.216	3317.549
4.433333	2046.918	2089.575	2401.385	2568.479	2746.092	2934.746	3044.996	3229.473
4.45	2083.883	2067.428	2409.387	2551.084	2784.137	2937.228	3024.134	3119.271
4.466667	2082.74	2127.209	2377.759	2501.111	2775.603	2895.941	3060.541	3175.241
4.483333	2087.799	2205.32	2379.828	2517.444	2727.165	2860.287	3177.056	3276.78
4.5	2086.354	2222.334	2365.475	2524.453	2683.451	2879.732	3250.094	3309.107
4.516667	2073.236	2179.329	2317.881	2542.964	2756.214	2912.509	3190.282	3247.594
4.533333	2019.348	2168.594	2279.256	2540.169	2815.041	2886.783	3149.293	3135.617
4.55	1995.305	2233.076	2278.511	2504.11	2803.785	2853.07	3166.398	3140.647
4.566667	1997.319	2285.732	2271.1	2461.146	2782.245	2839.931	3189.17	3188.006
4.583333	2028.901	2323.326	2279.195	2424.106	2765.611	2896.542	3134.624	3232.801
4.6	2056.914	2291.426	2230.947	2390.981	2692.758	2951.482	3074.143	3242.913
4.616667	2078.031	2200.148	2219.244	2368.216	2625.356	2912.019	3005.656	3226.447
4.633333	2058.007	2128.896	2262.126	2414.003	2636.415	2899.853	2998.664	3167.19
4.65	2017.375	2119.784	2368.178	2635.261	2700.078	2914.195	3035.525	3150.27
4.666667	1970.586	2121.056	2433.331	2658.014	2753.865	2900.504	3102.475	3173.311
4.683333	2001.681	2118.758	2399.848	2397.728	2767.021	2916.918	3112.123	3224.276
4.7	2101.705	2072.141	2331.738	2307.568	2803.52	2917.496	3085.554	3206.809
4.716667	2135.064	2086.767	2308.977	2468.92	2748.635	2909.059	3149.436	3227.704
4.733333	2137.305	2138.105	2332.284	2541.325	2666.257	2948.236	3218.453	3297.607
4.75	2120.096	2199.612	2402.833	2482.051	2615.853	2977.873	3197.727	3221.833
4.766667	2071.83	2229.425	2388.698	2479.251	2565.376	2911.753	3174.954	3078.409
4.783333	2097.29	2282.927	2396.864	2565.858	2626.946	2847.397	3178.784	3009.03

4.8	2090.865	2327.612	2373.841	2571.279	2774.93	2888.986	3185.05	3158.419
4.816667	2066.975	2312.647	2355.407	2585.953	2867.807	2892.355	3145.466	3305.02
4.833333	2053.64	2269.649	2308.771	2501.48	2811.868	2839.965	3104.223	3349.646
4.85	2088.866	2229.546	2299.965	2352.967	2750.378	2796.403	3051.932	3352.99
4.866667	2076.051	2214.591	2300.828	2325.774	2717.401	2847.277	3065.237	3358.99
4.883333	2072.831	2211.113	2360.016	2563.437	2696.172	2864.744	3198.027	3336.307
4.9	2102.186	2198.333	2408.689	2644.13	2673.965	2796.63	3274.43	3270.031
4.916667	2088.284	2215.48	2414.703	2462.365	2658.18	2973.067	3247.646	3201.71
4.933333	2047.434	2240.14	2367.539	2414.55	2633.52	3142.558	3191.932	3156.993
4.95	1987.707	2139.702	2382.806	2507.244	2635.058	3063.132	3127.18	3177.759
4.966667	1992.717	2020.388	2431.546	2580.364	2643.569	2990.161	3104.334	3151.181
4.983333	2012.851	2052.376	2464.882	2571.557	2703.169	2950.012	3036.87	3175.67
5	2047.189	2185.822	2380.121	2554.608	2775.341	2911.17	3021.852	3212.456
5.016667	2069.997	2229.041	2317.366	2513.199	2822.4	2880.818	3089.1	3201.257
5.033333	2032.797	2231.676	2278.533	2528.872	2855.735	2914.79	3199.155	3180.259
5.05	2003.322	2258.482	2308.611	2470.123	2866.283	2890.353	3237.94	3184.489
5.066667	2035.204	2252.446	2353.846	2428.672	2854.574	2846.506	3214.459	3239.783
5.083333	2069.695	2249.116	2422.978	2499.117	2822.186	2897.263	3086.388	3240.286
5.1	2080.369	2244.926	2386.277	2542.61	2777.894	2992.664	3015.977	3162.177
5.116667	2061.863	2227.001	2366.81	2508.458	2758.977	2995.151	3005.975	3109.87
5.133333	2030.869	2209.522	2355.992	2455.467	2773.003	2955.431	3040.214	3121.27
5.15	1998.265	2230.402	2392.551	2471.309	2750.173	2936.358	3117.6	3126.074
5.166667	2081.426	2247.669	2371.884	2481.695	2667.713	2960.381	3190.536	3159.723
5.183333	2137.628	2227.466	2425.348	2502.623	2636.939	2934.964	3235.742	3321.74
5.2	2141.866	2209.566	2475.862	2488.673	2668.502	2791.262	3177.478	3425.381
5.216667	2109.204	2217.104	2433.381	2482.587	2686.826	2737.763	3071.393	3481.68
5.233333	2088.654	2282.867	2302.277	2464.879	2776.18	2849.494	3049.635	3474.6

5.25	2079.472	2306.521	2260.848	2471.468	2858.389	2957.518	3058.805	3398.667
5.266667	2068.806	2286.308	2353.219	2477.06	2891.028	3001.457	3084.369	3311.346
5.283333	2081.056	2250.253	2435.235	2440.858	2812.688	2946.343	3210.567	3256.097
5.3	2069.585	2258.403	2449.183	2467.479	2749.967	2945.73	3254.092	3217.166
5.316667	2038.212	2244.883	2448.271	2516.13	2736.444	2975.518	3220.141	3233.951
5.333333	2051.21	2224.826	2420.017	2523.133	2720.588	2985.106	3181.635	3293.366
5.35	2111.38	2221.326	2378.297	2477.84	2737.64	2994.285	3188.869	3262.957
5.366667	2129.523	2199.913	2339.709	2445.179	2707.651	3036.297	3220.301	3207.72
5.383333	2132.472	2209.103	2319.421	2462.483	2640.147	3030.876	3226.877	3216.951
5.4	2145.412	2192.065	2259.319	2461.831	2642.964	2933.065	3198.807	3250.766
5.416667	2133.522	2213.281	2239.079	2458.545	2714.399	2888.076	3154.145	3302.296
5.433333	2100.611	2232.839	2253.552	2468.816	2733.36	2949.102	3179.778	3286.956
5.45	2056.59	2186.027	2297.063	2485.711	2749.704	2981.732	3237.966	3291.566
5.466667	2026.957	2183.972	2298.865	2499.178	2770.81	2946.692	3125.503	3271.24
5.483333	1988.572	2261.567	2300.077	2530.585	2754.179	2906.199	2964.894	3236.606
5.5	1975.661	2302.623	2341.765	2524.817	2769.72	2866.853	2961.227	3216.803
5.516667	1996.892	2289.422	2354.524	2500.342	2779.346	2806.746	3078.823	3203.447
5.533333	2042.459	2264.346	2355.982	2466.064	2785.295	2810.636	3146.164	3194.02
5.55	2085.069	2249.835	2383.212	2465.62	2740.867	2927.51	3161.662	3165.544
5.566667	2104.521	2249.338	2378.661	2447.84	2687.633	3024.04	3169.255	3170.413
5.583333	2110.097	2257.879	2387.119	2430.532	2717.102	2997.177	3115.167	3255.317
5.6	2075.195	2242.438	2350.3	2393.282	2745.437	2927.96	3039.915	3292.313
5.616667	2024.607	2208.465	2381.216	2427.495	2739.656	2856	3048.926	3335.67
5.633333	1985.186	2196.885	2418.587	2482.205	2784.006	2951.216	3184.594	3386.039
5.65	1963.251	2190.478	2455.473	2601.352	2834.524	2990.406	3290.64	3308.656
5.666667	1981.98	2191.575	2486.957	2623.657	2791.405	2954.057	3247.704	3155.267
5.683333	2040.588	2164.193	2510.674	2585.623	2738.715	2987.301	3180.73	3216.747

5.7	2125.373	2170.98	2487.495	2567.538	2670.979	3024.401	3199.768	3329.541
5.716667	2122.046	2185.725	2449.897	2540.426	2591.269	3002.773	3194.729	3225.41
5.733333	2075.757	2168.387	2399.392	2510.273	2594.736	2945.278	3191.028	3247.064
5.75	2033.914	2145.901	2362.947	2473.512	2719.946	2887.508	3235.124	3300.293
5.766667	2044.931	2135.881	2328.373	2479.004	2792.569	2987.802	3222.278	3270.21
5.783333	2033.444	2193.793	2365.416	2564.397	2795.102	3050.511	3176.549	3317.876
5.8	2011.534	2245.443	2346.608	2608.608	2802.451	3061.56	3150.076	3300.623
5.816667	2042.494	2285.267	2358.031	2611.609	2793.543	3045.402	3138.721	3260.219
5.833333	2073.325	2329.391	2395.057	2538.565	2805.261	2949.627	3100.576	3283.729
5.85	2082.762	2328.537	2413.973	2451.53	2849.645	2887.066	3089.044	3322.621
5.866667	2135.138	2252.765	2380.771	2430.613	2815.167	2855.462	3223.114	3280.171
5.883333	2160.008	2170.866	2364.174	2473.11	2731.611	2837.682	3305.095	3244.101
5.9	2118.525	2141.194	2343.022	2499.961	2736.843	2801.486	3176.828	3261.611
5.916667	2087.159	2149.638	2374.127	2517.851	2731.667	2772.536	3028.873	3282.734
5.933333	2063.453	2161.27	2326.857	2508.351	2692.351	2900.392	3041.996	3183.591
5.95	2071.035	2150.505	2264.869	2490.874	2676.709	3028.898	3229.248	3159.999
5.966667	2095.094	2159.18	2268.691	2455.19	2680.935	2985.982	3292.262	3329.469
5.983333	2102.656	2173.356	2368.688	2510.868	2679.512	2934.304	3298.184	3447.881
6	2066.234	2190.217	2393.233	2568.356	2686.768	2925.772	3343.914	3472.286
6.016667	2030.004	2210.57	2402.002	2546.663	2780.239	2894.441	3282.482	3386.186
6.033333	2034.607	2195.584	2335.86	2498.088	2867.892	2865.473	3157.584	3326.509
6.05	2052.525	2191.737	2281.114	2437.977	2801.344	2899.201	3084.607	3343.083
6.066667	2090.731	2205.387	2295.873	2473.736	2719.422	2946.178	3080.14	3263.897
6.083333	2106.333	2275.184	2384.631	2560.111	2737.317	2936.401	3089.177	3257.684
6.1	2106.697	2280.867	2449.55	2587.848	2807.059	2902.834	3150.977	3276.969
6.116667	2110.096	2228.189	2485.185	2535.563	2897.533	2874.353	3186.565	3265.227
6.133333	2155.742	2223.913	2372.254	2474.268	2991.608	2903.121	3161.798	3266.564

6.15	2119.464	2246.49	2113.731	2467.498	2954.492	3010.967	3198.545	3236.123
6.166667	2095.526	2297.56	2083.46	2477.012	2817.469	3070.899	3204.909	3230.863
6.183333	2058.757	2338.176	2247.981	2492.059	2738.529	3030.002	3170.974	3204.94
6.2	2078.397	2321.339	2352.688	2492.269	2697.156	3000.377	3171.851	3276.183
6.216667	2125.972	2280.195	2364.717	2468.441	2692.502	2979.044	3128.566	3367.249
6.233333	2163.471	2224.507	2405.007	2402.404	2677.117	2950.873	3103.666	3351.551
6.25	2173.232	2157.163	2475.046	2370.659	2635.791	2937.483	3188.846	3279.774
6.266667	2146.771	2127.5	2500.696	2499.964	2608.907	2908.596	3232.531	3228.591
6.283333	2142.049	2122.781	2493.833	2610.054	2595.771	2888.083	3160.871	3244.189
6.3	2169.7	2151.897	2414.414	2616.261	2648.684	2880.703	3118.607	3399.956
6.316667	2160.657	2251.862	2350.036	2625.321	2766.853	2835.471	3166.51	3306.857
6.333333	2133.669	2332.952	2343.52	2648.294	2936.822	2911.378	3210.956	3237.703
6.35	2079.68	2364.513	2402.677	2688.421	2956.21	3059.12	3202.534	3246.951
6.366667	2045.703	2371.88	2437.091	2648.643	2889.834	3084.661	3189.048	3237.659
6.383333	2066.032	2398.024	2436.311	2570.667	2836.419	3101.901	3162.333	3280.969
6.4	2097.928	2429.15	2406.087	2476.284	2851.428	3018.066	3171.452	3347.171
6.416667	2119.528	2357.439	2328.164	2431.819	2819.429	2978.573	3163.081	3420.954
6.433333	2127.713	2252.617	2249.747	2432.771	2756.654	2973.296	3107.67	3372.181
6.45	2124.571	2168.333	2232.338	2464.268	2704.294	2933.792	3068.032	3201.294
6.466667	2113.437	2138.227	2248.449	2554.778	2724.658	2959.802	3080.202	3273.277
6.483333	2091.704	2102.175	2300.922	2659.847	2789.972	2940.531	3212.173	3320.454
6.5	2098.203	2116.11	2340.799	2656.881	2852.494	2922.867	3275.92	3263.886
6.516667	2142.029	2131.38	2430.43	2574.841	2887.148	2997.868	3252.748	3234.339
6.533333	2133.454	2151.271	2500.767	2561.141	2818.123	3035.084	3204.072	3291.313
6.55	2078.439	2247.451	2500.462	2557.084	2782.906	3012.676	3073.423	3327.997
6.566667	2015.62	2322.017	2406.23	2586.907	2867.299	3015.916	3097.345	3281.906
6.583333	1978.783	2349.014	2346.835	2647.73	2886.641	3072.171	3305.225	3299.44

6.6	1973.966	2308.539	2315.742	2655.919	2853.231	3106.391	3300.242	3394.739
6.616667	2031.133	2234.375	2330.223	2614.471	2813.346	3061.485	3219.387	3326.573
6.633333	2080.594	2199.178	2344.829	2568.218	2774.092	3004.148	3112.868	3263.187
6.65	2103.165	2156.857	2358.106	2486.141	2762.146	2917.542	2921.316	3217.777
6.666667	2091.3	2153.436	2348.446	2415.229	2740.408	2863.657	2728.915	3275.184
6.683333	2101.89	2202.536	2369.401	2420.199	2753.526	2937.993	3108.831	3298.626
6.7	2087.295	2217.701	2372.39	2447.38	2774.903	3053.896	3473.462	3276.366
6.716667	2026.31	2222.486	2393.729	2487.639	2779.097	3043.511	3472.206	3261.321
6.733333	2001.365	2226.984	2408.66	2564.246	2787.059	2948.828	3380.203	3239.061
6.75	2035.264	2211.942	2439.653	2606.745	2770.612	2966.751	3289.289	3240.814
6.766667	2038.124	2327.222	2426.602	2597.863	2731.364	3050.205	3249.766	3298.096
6.783333	2034.22	2355.468	2423.188	2558.536	2737.3	3038.181	3235.3	3263.006
6.8	2027.231	2396.213	2401.826	2531.957	2797.979	3005.699	3165.22	3212.404
6.816667	2059.558	2357.883	2369.383	2537.245	2846.506	3028.913	3128.927	3259.544
6.833333	2081.604	2295.341	2356.945	2531.42	2773.813	3033.559	3165.265	3253.153
6.85	2119.358	2258.579	2365.875	2543.054	2695.021	2971.377	3158.868	3270.433
6.866667	2124.329	2266.041	2347.282	2549.694	2669.046	2932.068	3160.334	3322.206
6.883333	2091.89	2251.438	2369.269	2563.218	2664.436	2976.004	3177.563	3370.011
6.9	2005.012	2254.905	2400.006	2564.584	2735.036	3002.397	3185.484	3310.797
6.916667	1986.258	2212.442	2393.293	2558.08	2796.409	2925.966	3210.092	3260.353
6.933333	1984.067	2215.911	2318.269	2562.971	2829.975	2862.171	3196.115	3306.324
6.95	2039.774	2200.194	2294.327	2612.23	2857.812	2846.083	3137.089	3294.88
6.966667	2097.222	2224.132	2336.384	2642.04	2852.594	2874.073	3116.015	3276.684
6.983333	2107.142	2242.108	2389.83	2632.158	2802.888	3001.849	3132.992	3278.11
7	2100.499	2218.011	2398.807	2582.963	2788.549	3123.283	3229.212	3282.233
7.016667	2091.726	2191.009	2472.791	2523.188	2854.345	3042.718	3298.844	3275.297
7.033333	2112.972	2208.005	2483.942	2448.947	2895.844	2959.616	3265.158	3281.724

7.05	2108.923	2256.971	2441.946	2404.418	2788.505	2987.078	3248.333	3344.723
7.066667	2068.422	2281.178	2329.459	2458.38	2698.433	3023.469	3227.594	3386.593
7.083333	2062.515	2286.087	2254.5	2566.651	2721.41	3008.864	3206.315	3395.62
7.1	2106.807	2273.546	2299.065	2596.929	2788.839	3043.369	3220.378	3340.146
7.116667	2092.376	2251.413	2388.682	2580.015	2868.417	3038.289	3250.796	3278.697
7.133333	2076.46	2242.765	2376.616	2555.119	2863.673	2980.235	3225.237	3267.924
7.15	2128.131	2219.676	2343.94	2563.142	2764.946	2965.322	3165.007	3301.479
7.166667	2194.75	2243.681	2351.295	2572.827	2717.86	3005.999	3157.985	3288.213
7.183333	2191.974	2297.65	2387.857	2566.425	2730.335	2984.141	3131.207	3383.406
7.2	2199.699	2341.467	2365.417	2523.717	2723.779	2916.278	3066.169	3370.88
7.216667	2161.88	2357.569	2334.508	2487.534	2730.33	2895.141	3059.314	3313.083
7.233333	2086.912	2308.766	2298.723	2445.354	2821.89	2975.324	3135.275	3365.494
7.25	2018.183	2272.713	2278.064	2366.118	2906.826	3024.884	3178.102	3351.927
7.266667	1996.317	2241.083	2271.364	2393.608	2868.312	2949.865	3161.906	3310.353
7.283333	1974.292	2190.594	2272.929	2456.968	2713.073	2891.294	3102.001	3333.641
7.3	1972.393	2179.749	2329.154	2417.138	2683.264	2874.688	3113.958	3304.624
7.316667	1964.085	2187.687	2428.094	2490.845	2741.184	2910.566	3163.303	3287.771
7.333333	1940.077	2238.047	2370.31	2605.203	2741.617	2976.93	3157.521	3266.059
7.35	1936.526	2278.871	2328.925	2628.386	2725.487	2907.452	3171.198	3326.076
7.366667	1936.04	2254.144	2303.415	2568.904	2737.255	2835.157	3204.261	3348.767
7.383333	1957.537	2180.35	2365.628	2574.934	2786.959	2866.329	3182.575	3434.61
7.4	2000.429	2101.455	2393.546	2648.184	2885.938	2869.888	3178.168	3445.014
7.416667	2040.131	2095.23	2401.133	2682.685	2973.558	2819.895	3143.353	3357.099
7.433333	2063.441	2150.901	2389.164	2609.966	3001.75	2829.813	3075.093	3297.584
7.45	2115.44	2194.169	2408.488	2507.118	2975.095	2939.519	3086.761	3294.333
7.466667	2159.215	2249.676	2340.962	2401.372	2928.245	2986.286	3246.565	3334.557
7.483333	2103.829	2308.781	2218.987	2434.922	2847.428	2975.931	3329.717	3334.259

7.5	2112.936	2366.542	2337.851	2498.131	2841.887	2966.053	3266.392	3248.084
7.516667	2097.94	2285.936	2524.295	2509.43	2885.161	2963.763	3191.32	3253.897
7.533333	2082.307	2195.377	2544.798	2481.682	2899.996	2931.196	3086.036	3264.821
7.55	2064.68	2247.51	2488.386	2465.97	2843.705	2852.58	3090.394	3245.731
7.566667	2077.125	2330.179	2444.868	2440.77	2783.165	2818.144	3177.141	3406.081
7.583333	2043.669	2385.058	2427.773	2486.266	2776.264	2799.901	3243.519	3467.607
7.6	2006.437	2323.201	2390.012	2510.234	2790.152	2971.971	3277.175	3367.504
7.616667	2098.107	2266.866	2381.379	2523.885	2817.521	3090.744	3321.207	3334.237
7.633333	2231.863	2165.325	2401.766	2561.911	2821.542	3106.064	3333.618	3350.163
7.65	2219.263	2121.521	2367.89	2536.564	2818.993	3056.164	3257.685	3351.89
7.666667	2163.03	2151.696	2364.259	2541.574	2836.831	3053.045	3182.653	3272.79
7.683333	2098.252	2264.36	2410.647	2518.163	2775.426	3094.921	3154.971	3207.906
7.7	2071.724	2360.897	2409.483	2438.228	2697.096	3073.911	3138.393	3247.354
7.716667	2086.398	2443.875	2405.491	2454.04	2733.698	3038.986	3167.411	3191.286
7.733333	2088.62	2441.027	2386.502	2517.975	2857.958	2975.174	3230.849	3353.945
7.75	2071.616	2299.94	2311.434	2590.33	2925.749	2909.421	3233.36	3569.8
7.766667	2086.961	2197.415	2268.888	2580.544	2908.835	2808.458	3251.499	3515.785
7.783333	2098.888	2159.524	2278.315	2538.573	2905.227	2759.771	3276.861	3311.752
7.8	2067.542	2178.771	2202.347	2566.284	2861.843	2853.845	3255.704	3259.885
7.816667	2042.64	2173.367	2177.069	2623.176	2811.673	2933.12	3220.469	3347.49
7.833333	2033.751	2178.768	2330.65	2651.837	2768.917	2996.961	3262.29	3449.097
7.85	2032.237	2158.298	2520.088	2642.805	2751.206	3069.988	3329.336	3501.057
7.866667	2023.748	2118.554	2584.144	2629.047	2804.611	2993.35	3308.036	3522.35
7.883333	2027.123	2136.801	2560.004	2639.537	2860.343	2870.053	3282.82	3421.937
7.9	2057.032	2167.246	2501.155	2628.375	2863.783	2911.888	3340.425	3298.547
7.916667	2093.825	2220.931	2415.382	2608.613	2878.256	3038.724	3412.34	3413.315
7.933333	2158.062	2265.015	2423.405	2591.891	2865.471	3074.005	3350.162	3612.65

7.95	2173.002	2284.956	2458.546	2569.308	2841.653	3052.97	3271.208	3604.937
7.966667	2165.51	2334.185	2425.957	2559.023	2828.71	2976.22	3253.591	3509.958
7.983333	2097.576	2316.175	2417.915	2528.855	2849.885	3051.99	3314.793	3403.798
8	2034.511	2286.427	2458.546	2578.332	2886.252	3071.348	3450.794	3409.613

Appendix VI

Slop analysis

-20			-10			0			+10		
	Zero	X		Zero	X		Zero	X		Zero	X
SD	0	0.16	SD	0	-1.49	SD	0	-1.61	SD	0	4.96
RP	0	-0.32	RP	0	-1.27	RP	0	-0.49	RP	0	0.59
NY	0	-0.97	NY	0	-0.07	NY	0	-1.15	NY	0	0.75
MP	0	-0.15	MP	0	-1.44	MP	0	-0.03	MP	0	3.16
JS	0	0.39	JS	0	0.15	JS	0	0.39	JS	0	0.39
DC	0	-0.74	DC	0	2.18	DC	0	0.21	DC	0	-0.21
PH	0	4.32	PH	0	0.4	PH	0	1.56	PH	0	-1.05
CC	0	0.5	CC	0	-1.36	CC	0	3.26	CC	0	1.08
AVG	0	0.39875	AVG	0	-0.3625	AVG	0	0.2675	AVG	0	1.20875
SD	0	1.666111	SD	0	1.289781	SD	0	1.551062	SD	0	1.937387324
	ttest	0.520188		ttest	0.452752		ttest	0.6406		ttest	0.120973447

+20			+30			+40			+50		
	Zero	X		Zero	X		Zero	X		Zero	X
SD	0	0.58	SD	0	1.18	SD	0	-0.86	SD	0	1.84
RP	0	0.4	RP	0	2.01	RP	0	0.37	RP	0	-0.48
NY	0	2.63	NY	0	-2.2	NY	0	-1.35	NY	0	13.01
MP	0	0.25	MP	0	0.06	MP	0	2.45	MP	0	-0.96
JS	0	2.41	JS	0	0.3	JS	0	-0.73	JS	0	1.55
DC	0	1.67	DC	0	-0.14	DC	0	3.16	DC	0	1.4
PH	0	0.12	PH	0	1.79	PH	0	1.28	PH	0	0.12
CC	0	0.81	CC	0	0.14	CC	0	1.84	CC	0	1.86
AVG	0	1.10875	AVG	0	0.3925	AVG	0	0.77	AVG	0	2.2925
SD	0	0.993456	SD	0	1.329713	SD	0	1.66908	SD	0	4.46557867
	ttest	0.016002		ttest	0.43135		ttest	0.233202		ttest	0.189793936