

# The Point of Maximum Curvature as a Marker for Physiological Time Series

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## Abstract

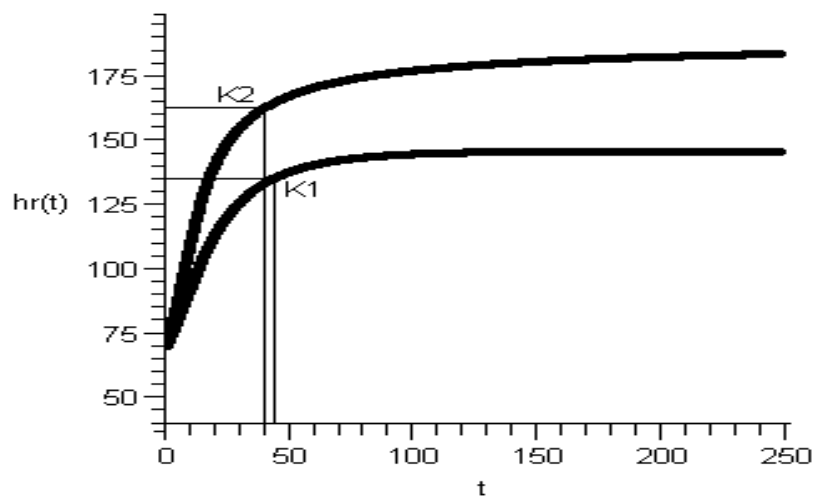
We present a geometric analysis of the model of Stirling et al. [14]. In particular we analyze the curvature of a heart rate time series in response to a step like increment in the exercise intensity. We present solutions for the point of maximum curvature which can be used as a marker of physiological interest. This marker defines the point after which the heart rate no longer continues to rapidly rise and instead follows either a steady state or slow rise. These methods are then applied to find analytic solutions for a mono exponential model which is commonly used in the literature to model the response to a moderate exercise intensity. Numerical solutions are then found for the full model and parameter values presented in Stirling et al. [14].

## 1 Introduction

In this paper we investigate geometric features of the model of heart rate kinetics in response to exercise developed by Stirling et al. [14] (see also Stirling et al. [17, 15], Zakyntinaki and Stirling [25] and Zakyntinaki et al. [24, 23]). We aim to find a feature of the curve corresponding to the heart rate time series in response to exercise which can be found using rigorous mathematical techniques and which can act as a marker. The term marker is used to mean a point on the curve which marks the transition from one response to another. Such concepts are standard in exercise physiology and medicine [19]. By tracking changes in the marker for different exercise loads or following changes in an individuals level of fitness, important physiological information can be obtained [1, 5, 12]. In this paper we use the point of maximum curvature as a marker for the heart rate kinetics in response to step function like increases in the exercise intensity. In particular we find analytic solutions for the point of maximum curvature for short term moderate exercise intensities where the heart rate reaches a plateau. We also find numerical solutions for short term slightly higher exercise intensities where the heart rate no longer plateaus but instead continues to rise slowly (i.e. in the case of the so called slow component).

The point of maximum curvature provides physiologists with a means of finding the time and heart rate for which we move from an steeply rising function to a plateau or slowly rising function (as in the slow component). Our method works with both the mono-exponential model used in the literature and the coupled ordinary differential equation model we introduced in Stirling et al. [14] (see also Zakyntinaki and Stirling [25], Zakyntinaki et al. [23] and Stirling et al. [17, 15]). It should be noted that in general for the model of Stirling et al. [14] (see also Zakyntinaki and Stirling [25], Zakyntinaki et al. [23] and Stirling et al. [17, 15]) there is no rate constant  $\tau$  as it is not an exponential model.

In section 2.3 we define the curvature,  $k$  and show how to calculate the point of maximum curvature in the  $t$  direction by solving for the derivative  $\frac{dk}{dt} = 0$ . Here however we introduce why the point of maximum curvature is of interest physiologically. The point of maximum curvature occurs when the rate of change, as one moves along the curve for the heart rate time series, of the tangential angle  $\phi$  to the  $hr(t)$  time series is a maximum. In a correctly scaled graph of the heart rate time series this would mark the point when there is a change from a rapidly increasing function of  $hr$  to a slowly increasing or steady state function, see figure 1. As a result knowledge of this point both in terms of heart rate and time give us fundamental physiological important information about the kinetics. In particular it will allow us to know how long it takes for the body to stabilize or at least slow its reaction to a specific demand. It will also allow us to calculate after what percentage of the demand the kinetics ceases to be a rapidly increasing function. It should be remembered that the rapidly increasing response and the slowly increasing or steady state response represent important differences at the physiological level and as such the point of maximum curvature allows us to differentiate between the two.



**Figure 1.** Showing the point of maximum curvature  $K1$  and  $K2$  for two heart rate time series, one which has a plateau and one which shows slow component behavior.

In the following section we first present the model and then go on to calculate the curvature and point of maximum curvature. This is followed by an analytic solution for the point of maximum curvature for a physiologically interesting case. We then present numerical solutions based on data presented in Stirling et al. [14] and Zakyntinaki and Stirling [25]. We finish with mathematical and physiological conclusions.

## 2 The model and how to find the point of maximum curvature

### 2.1 Model and the normalized version

We define  $HR(V, T)$  to be the function that describes the heart rate response to an exercise of intensity  $V$  for time  $T$ . In Stirling et al. [14] (see also Stirling et al. [17, 15] and Zakyntinaki and Stirling [25]) the following equations are used to model the heart rate kinetics for the case where the exercise intensity  $V$  is a constant. These equations are similar to those used in other applications by the same authors [21, 20, 18, 16].

$$\frac{d}{dT}HR(V, T) = \tilde{A} \left[ HR(V, T) - HR_{\min} \right]^B \left[ HR_{\max} - HR(V, T) \right]^C \left[ \tilde{D}(V) - HR(V, T) \right]^E \quad (2.1)$$

$$\frac{d}{dT}V = 0 \quad (2.2)$$

where the function  $\tilde{D}(V, T)$  denotes the heart rate demand and the parameters  $\tilde{A}, B, C, E$  control the shape of the curve (see [14, 17] for more details).

Parameter  $\tilde{A}$  has dimensions of  $(beats/min)^{1-B-C-E} min^{-1}$  whilst parameters  $B, C$  and  $E$  are dimensionless. The variables are written in upper case to denote their non normalized state. For this paper we make the usual approximation in exercise physiology that the heart rate demand  $\tilde{D}(V)$  is a constant for a particular constant exercise intensity  $V$  and hence is not a function of time for the short term and sufficiently low exercise intensities that we considered here. It should be noted that longer term, even moderate, exercise raises body temperature producing body fluid shifts and losses that lead to a gradual increase in the heart rate demand  $\tilde{D}(V)$  as a function of time.

In what follows  $hr(v, t)$  will refer to the normalized version of the heart rate such that  $0 \leq hr(v, t) \leq 1$ . The normalized variable  $hr(v, t)$  is derived from equation 2.1 as follows

$$hr(V, T) = \frac{HR(V, T) - HR_{\min}}{HR_{\max} - HR_{\min}} \quad (2.3)$$

The variable  $t$  will refer to the normalized time  $t = \frac{T}{t_p}$ , where we define  $t_p$  as the time to achieve a heart rate equal to  $HR(t_p) = HR_{\min} + 0.95(HR_{\max} - HR_{\min})$  for a demand  $D(V) = HR_{\max}$  and initial resting condition which we standardize in this paper to be such that  $HR(0) = 70$  beats/min. This value of  $t_p$  is obtained numerically from our model once the parameters have been fit, by solving for the time,  $t_p$  to achieve  $HR(t_p)$ . It should also be noted that all graphs are plotted from  $t = 0 \rightarrow t_p$  so not to add confusion due to the scale of the graph. The function  $D(v)$  corresponds to the normalized demand. Equation (2.1) hence takes the normalized form

$$\frac{d}{dt}hr(v, t) = t_p A \left[ hr(v, t) \right]^B \left[ 1 - hr(v, t) \right]^C \left[ D(v) - hr(v, t) \right]^E \quad (2.4)$$

which is the equation we will be working with what follows. The normalized parameter  $A$  is

$$A \equiv \tilde{A} (hr_{\max} - hr_{\min})^{B+C+E-1}, \quad (2.5)$$

$\tilde{A}, B, C$  and  $E$  are as in the non-normalized case.

## 2.2 The derivatives $\frac{dhr(v,t)}{dt}$ , $\frac{d^2hr(v,t)}{dt^2}$ and $\frac{d^3hr(v,t)}{dt^3}$

Equation 2.1 gives the first derivative of the heart rate with respect to time,  $\frac{dhr(t)}{dt}$ . The second derivative is

$$\frac{d^2hr(v,t)}{dt^2} = \left( \frac{dhr(v,t)}{dt} \right)^2 \left[ Bhr(v,t)^{-1} - C(1 - hr(v,t))^{-1} - E(D(v) - hr(v,t))^{-1} \right] \quad (2.6)$$

which we write as

$$\frac{d^2hr(v,t)}{dt^2} = \frac{\left( \frac{dhr(v,t)}{dt} \right)^2}{hr(v,t)(1 - hr(v,t))(D(v) - hr(v,t))} \left[ \gamma(v,t) \right] \quad (2.7)$$

where

$$\begin{aligned} \gamma(v,t) = & B(1 - hr(v,t)) \left( D(v) - hr(v,t) \right) - Chr(v,t) \left( D(v) - hr(v,t) \right) - \\ & - Ehr(v,t) \left( 1 - hr(v,t) \right). \end{aligned} \quad (2.8)$$

It should be remembered that as we assume that the demand is not a function of time then  $\frac{dD(v)}{dt} = 0$  and  $\frac{d^2D(v)}{dt^2} = 0$ . The third derivative is now found to be

$$\begin{aligned} \frac{d^3hr(v,t)}{dt^3} = & \left( \frac{dhr(v,t)}{dt} \right)^3 \left( 2 \left[ B(hr(v,t))^{-1} - C(1 - hr(v,t))^{-1} - E(D(v) - hr(v,t))^{-1} \right]^2 - \right. \\ & \left. - Bhr(v,t)^{-2} - C(1 - hr(v,t))^{-2} - E(D(v) - hr(v,t))^{-2} \right) \end{aligned} \quad (2.9)$$

which we write as

$$\frac{d^3hr(v,t)}{dt^3} = \frac{\left( \frac{dhr(v,t)}{dt} \right)^3}{hr(v,t)^2(1 - hr(v,t))^2(D(v) - hr(v,t))^2} \left[ 2\gamma(v,t)^2 + \theta(v,t) \right] \quad (2.10)$$

where

$$\begin{aligned} \theta(v,t) = & -B(1 - hr(v,t))^2 \left( D(v) - hr(v,t) \right)^2 - Chr(v,t)^2 \left( D(v) - hr(v,t) \right)^2 - \\ & - Ehr(v,t)^2 \left( 1 - hr(v,t) \right)^2. \end{aligned} \quad (2.11)$$

These derivatives can now be used to calculate the curvature,  $k$  and the point of maximum curvature.

### 2.3 Curvature and the point of maximum curvature

The curvature  $k$  of a curve is defined as  $k \equiv \left| \frac{d\phi}{ds} \right|$ , where  $\phi$  is the tangential angle and  $s$  is the arc length. The curvature  $k$  can be found as follows

$$k \equiv \left| \frac{d\phi}{ds} \right| = \left| \frac{\frac{d\phi}{dt}}{\frac{ds}{dt}} \right| \quad (2.12)$$

the arc length  $s$  of the heart rate time series in the normalized coordinate system now gives us

$$ds = \sqrt{dt^2 + dhr(v,t)^2} \quad (2.13)$$

therefore we have

$$\frac{ds}{dt} = \sqrt{1 + \left( \frac{dhr(v,t)}{dt} \right)^2}. \quad (2.14)$$

The tangential angle  $\phi$  now gives us

$$\tan \phi = \frac{dhr(v,t)}{dt} \Rightarrow \frac{d \tan \phi}{dt} = \frac{d^2 hr(v,t)}{dt^2} \quad (2.15)$$

hence

$$\frac{d \tan \phi}{dt} = (1 + \tan^2 \phi) \frac{d\phi}{dt} \quad (2.16)$$

using equations 2.15 and 2.16 we have

$$\frac{d\phi}{dt} = \frac{d^2 hr(v,t)}{dt^2} \frac{1}{1 + \tan^2 \phi} = \frac{\frac{d^2 hr(v,t)}{dt^2}}{1 + \left( \frac{dhr(v,t)}{dt} \right)^2} \quad (2.17)$$

Using 2.14 and 2.17 the curvature  $k$  is now

$$k = \left| \frac{\frac{d^2 hr(v,t)}{dt^2}}{\left[ 1 + \left( \frac{dhr(v,t)}{dt} \right)^2 \right]^{\frac{3}{2}}} \right|. \quad (2.18)$$

Using equations 2.1, 2.8 and 2.11 equations 2.18 can be expressed only in terms of  $hr(v,t)$ . Note only for the follow equation 2.19 we drop the part  $(v,t)$  to condense the formula.

$$k = \left| \frac{t_p^2 A^2 hr^{2B} (1 - hr)^{2C} (D - hr)^{2E} \left[ B(1 - hr)(D - hr) - Chr(D - hr) - Ehr(1 - hr) \right]}{hr(1 - hr)(D - hr) \left[ 1 + t_p^2 A^2 hr^{2B} (1 - hr)^{2C} (D - hr)^{2E} \right]^{\frac{3}{2}}} \right| \quad (2.19)$$

Maxima or minima of the curvature in the  $t$  direction can therefore be found via the derivative of equation 2.18 (or 2.19) with respect to  $t$ , when  $\frac{dk}{dt} = 0$ . For  $\frac{dk}{dt} = 0$  then assuming  $\frac{dhr(v,t)}{dt} \neq \infty$  we have

$$\frac{d^3 hr(v,t)}{dt^3} \left[ 1 + \left( \frac{dhr(v,t)}{dt} \right)^2 \right] - 3 \left( \frac{d^2 hr(v,t)}{dt^2} \right)^2 \frac{dhr(v,t)}{dt} = 0 \quad (2.20)$$

substituting equations 2.7 and 2.10 we now have  $\frac{dhr(v,t)}{dt} = 0$  or

$$\left( \frac{dhr(v,t)}{dt} \right)^2 (\theta(v,t) - \gamma(v,t)^2) + 2\gamma(v,t)^2 + \theta(v,t) = 0 \quad (2.21)$$

### 3 Special solutions for the maximum curvature: the case of $E = 1$ , $B = C = 0$ and $A \neq 0$

For these parameter values the model is in its most basic form with no ability to produce slow kinetics [22, 7, 11, 2, 3] either during exercise or recovery. This form of the equations however is of interest as it has been recognized since 1923 in a paper by Hill and Lupton [9] that such physiological signals rise approximately exponentially following the onset of an exercise of moderate intensity. More recently the mono-exponential given in equations 3.3 has been used to model heart rate [11, 8, 4, 6] and oxygen uptake kinetics in response to sufficiently low exercise intensities [22, 7, 11, 2, 13, 10]. An independent time delay is often used with these models to ensure the data is fit most optimally. The analytic solutions are valid for short term moderate intensities only.

The equation

$$\frac{dhr}{dt} = t_p A (D - hr(t)) \quad (3.1)$$

$$(3.2)$$

has the following general solution

$$hr = hr(0) + [D - hr(0)](1 - e^{-t_p A t}). \quad (3.3)$$

where  $hr(0)$  is the initial value of  $hr$  for  $t = 0$  and  $D$  is the constant demand. The second derivative is given by

$$\frac{d^2 hr}{dt^2} = -t_p^2 A^2 (D - hr(t)) \quad (3.4)$$

This gives

$$k = \left| \frac{-t_p^2 A^2 (D - hr(t))}{(1 + t_p^2 A^2 [D - hr(t)]^2)^{\frac{3}{2}}} \right| = \left| \frac{-t_p^2 A^2 (D - hr(0)) e^{-t_p A t}}{(1 + t_p^2 A^2 [D - hr(0)]^2 e^{-2t_p A t})^{\frac{3}{2}}} \right| \quad (3.5)$$

as  $k \geq 0$  then

$$k = \frac{t_p^2 A^2 (D - hr(t))}{(1 + t_p^2 A^2 [D - hr(t)]^2)^{\frac{3}{2}}} = \frac{t_p^2 A^2 (D - hr(0)) e^{-t_p A t}}{(1 + t_p^2 A^2 [D - hr(0)]^2 e^{-2t_p A t})^{\frac{3}{2}}} \quad (3.6)$$

hence

$$\frac{dk}{dt} = -t_p^2 A^2 \dot{hr} \left[ \frac{1 - 2t_p^2 A^2 (D - hr(t))^2}{(1 + t_p^2 A^2 (D - hr(t))^2)^{\frac{5}{2}}} \right], \quad (3.7)$$

which implies that for the point of maximum curvature we must have  $1 - 2t_p^2 A^2 (D - hr(t))^2 = 0$ , as we are not interested in the solution  $D - hr(t) = 0$ . The heart rate,  $hr_{k_{\max}}$  at which the maximum curvature occurs is given by

$$hr_{k_{\max}} = D \pm \frac{1}{t_p A \sqrt{2}} \quad (3.8)$$

and the time at which this occurs is given by

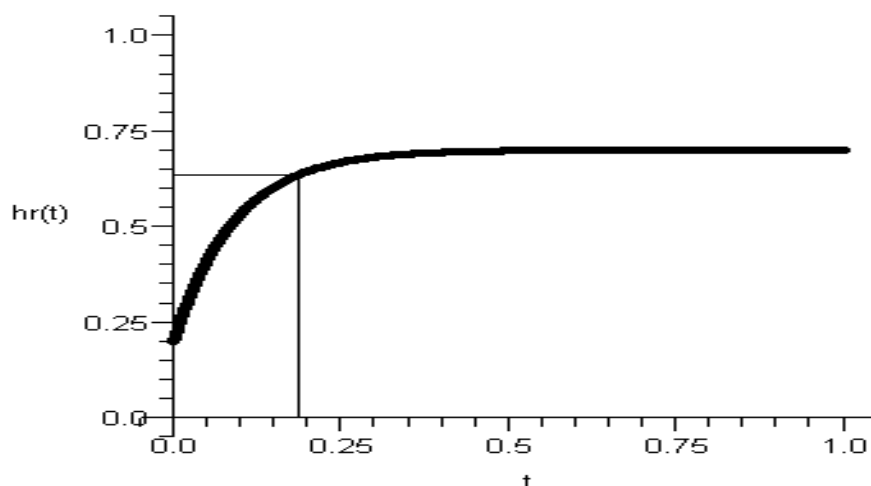
$$t_{k_{\max}} = -\frac{1}{t_p A} \ln \left( \frac{1}{t_p A (D - hr(0)) \sqrt{2}} \right) \quad (3.9)$$

Note that as expected by increasing  $A$  the point of maximum curvature occurs closer to the demand  $D$  and does so in less time. Equations 3.8 and 3.9 can be rewritten in the non normalized terms  $HR$  and  $T$  giving

$$\begin{aligned} HR_{k_{\max}} &= HR_{\min} + (HR_{\max} - HR_{\min}) \left( D \pm \frac{1}{t_p A \sqrt{2}} \right) \\ T_{k_{\max}} &= -\frac{1}{A} \ln \left( \frac{1}{t_p A (D - hr(0)) \sqrt{2}} \right) \end{aligned} \quad (3.10)$$

We choose, based on the data presented in Stirling et al [14] and Zakyntinaki and Stirling [25]  $A = 0.045$  and  $D = 0.7$  for a value of  $hr(0) = 0.2$  and  $t_p = 246s$ .

Using equations 3.8 and 3.9 we find  $hr_{k_{\max}} = 0.6361$ ,  $t_{k_{\max}} = 0.1859$  or in non normalized terms  $HR_{k_{\max}} = 132$  beats/min,  $T_{k_{\max}} = 46$  s,  $D = 142$  beats/min. The point of maximum curvature can be observed to equal to that seen in figure 1. It can also clearly be seen in figure 1 that the point of maximum curvature is a good marker of the transition from a rapidly rising response to a steady state.



**Figure 2.** The point of maximum curvature  $hr_{k_{\max}} = 0.6495, t_{k_{\max}} = 0.16375$  for the mono-exponential.

#### 4 Numerical solutions for the maximum curvature

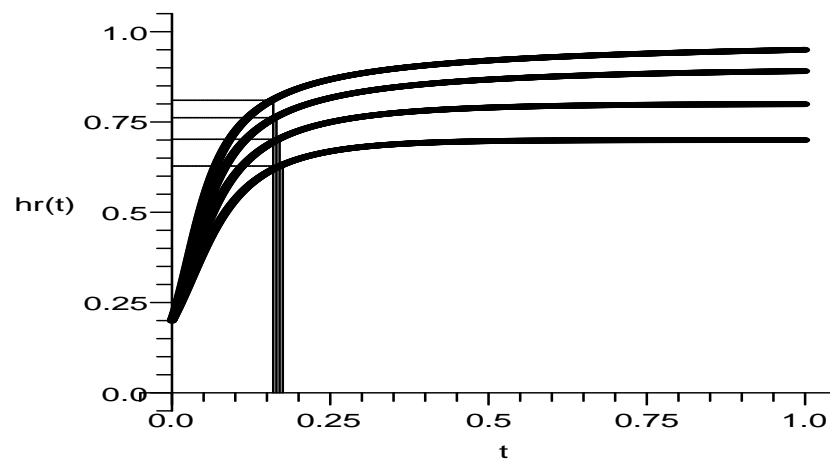
We now study the numerical solutions for the maximum curvature using parameters found by optimizing the fit of the model to a set of real heart rate data. We do so graphically as analytic solutions for the general cases of physiological interest (i.e.  $E = 1$  and  $A \neq B \neq C \neq 0$ ) cannot be found. The numerical analysis is valid for short term both moderate and slightly higher exercise intensities, inclusive of the so called slow component type behavior which as shown in Stirling et al. [14] (see also Zakynthinaki and Stirling [25], Zakynthinaki et al. [23] and Stirling et al. [17, 15]) can be modelled using a constant demand  $\tilde{D}(V)$ .

We use the optimal parameter values found in Stirling et al [14] and Zakynthinaki and Stirling [25], these values were found using stochastic optimization (Zakynthinaki and Stirling [25] and Zakynthinaki and Saridakis [26]). These values are  $A = 0.54, B = 1.63, C = 1.75$  and  $E = 1$ . The initial condition for the normalized heart rate is  $hr(0) = 0.2$ , this corresponds to a non-normalized heart rate of 70 beats/min for an individual with minimum and maximum heart rates equal to  $HR_{\min} = 40$  beats/min and  $HR_{\max} = 185$  beats/min respectively. The values  $HR_{\max}$  and  $HR_{\min}$  were obtained experimentally, with the  $HR_{\max}$  being the maximum heart rate observed in competition and  $HR_{\min}$  being the minimum heart rate observed during an extended period of deep relaxation. It should be noted that the value of  $HR_{\min} = 40$  is low however it is physiologically reasonable as the subject was a well trained marathon runner and such values are not uncommon amongst these athletes [12]. We estimate using the definition given in section 2.1 that  $t_p = 246$  seconds.

From figure 3 and table 1 we can see how the point of maximum curvature changes with  $D$ .

One of the interesting facts of physiological importance that can be observed in figure 3 and table 1 is that the decrease in  $t_{k_{\max}}$  with increasing demand is very small when compared to the increase in  $hr_{k_{\max}}$ . This is showing that there is very little difference in the time it takes to reach the point of maximum curvature for different demands given the same initial conditions, even though there are large differences in the heart rate  $hr_{k_{\max}}$ .





**Figure 3.** The point of maximum curvature for the 4 different demands shown in table 1.

**Table 1.** The point of maximum curvature, normalized and non normalized, for different demands.

$D(v)$	$hr_{kmax}$	$t_{kmax}$	$D(V)(beats/min)$	$HR_{kmax}(beats/min)$	$T_{kmax}(s)$
1	0.81	0.16	185	157	40
0.9	0.762	0.165	171	150	41
0.8	0.702	0.17	156	142	42
0.7	0.628	0.175	142	131	43

## 5 Conclusions

We show how to calculate the curvature and as a result the point of maximum curvature for the model of the heart rate time series presented in Stirling et al. [14]. In particular we analyze the curvature for the case of a heart rate response to a step like increment in the exercise intensity  $v$ . For the analysis we present we make the usual assumption generally used in exercise physiology that the demand  $D(v)$  is constant for a particular exercise intensity  $v$  of sufficiently short duration and low intensity.

The point of maximum curvature is as a marker which defines, for a correctly scaled graph, the point after which the heart rate changes from a rapidly increasing function to a steady state or slowly increasing function.

Analytic solutions for both the heart rate  $hr_{kmax}$  at which the curvature is maximum and the time  $t_{kmax}$  at which this occurs are presented for the case of a mono exponential model which is commonly used in the literature to model the response to moderate exercise intensities. The analytic solutions presented in section 3 are for exclusively short term moderate exercise.

Numerical solutions are also presented for  $hr_{kmax}$  and  $t_{kmax}$  for the model and optimal parameter values presented in Stirling et al. [14]. The numerical analysis in section 4 is not just for short term moderate exercise, but includes slightly higher non moderate short term exercise intensities

(where the heart rate is  $\leq 185$ ) for which we showed in the papers of Stirling et al. [14] (see also Zakyntinaki and Stirling [25], Zakyntinaki et al. [23] and Stirling et al. [17, 15]) we can still assume the demand to be constant. For higher exercise intensities where the demand is a function of time see Zakyntinaki et al. [23]. A physiologically interesting observation was found for these parameter values, which was that there was very little difference in the time  $t_{k_{\max}}$  after which we changed from a steeply rising function to a slowly rising or steady state function, even though the difference in the demand  $D(v)$  and also  $hr_{k_{\max}}$  was large.

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