MATHEMATICAL MODELLING OF HEART RATE DURING CYCLING EXERCISE

by

Stian Roti Svendby

Thesis
for the degree of

Master of Science
in Computational Physics

Faculty of Mathematics and Natural Sciences
University of Oslo
June 2016
Abstract

The aim of this thesis was to develop a mathematical model able to simulate heart rate during cycling exercise with power as input. From an optimization of free model parameters to fit the model to heart rate recordings, we wanted to extract information that possibly could indicate the health of subjects. Our model is based on physiological principles, and three physiologically interpreted parameters are being optimized. The parameters $\tau_L$ and $\nu_{\text{min}}$ are assumed to predict the relative condition of a subject, while the last parameter $\bar{p}_T$ is assumed to predict the absolute performance of a subject. Maximal heart rate is the only subject dependent parameter that has to be known a priori as input to the model. Results in this thesis indicate that the model predicts parameters consistent within subjects, and parameter variations are observed between subjects. However, a further validation of the model is needed to decide if all parameters change as expected according to health of subjects, such that it can be used as a tool in training analysis.
Acknowledgements

I started studying physics at UiO in 2010, which I combined with being an active cross country skier. Already in the first semester, to my consternation, programming turned out to be a fundamental part of modern natural science. I was skeptical in the beginning, and I didn’t master programming until I participated in the course “Computational Physics” held by professor Morten Hjorth-Jensen. Morten made the class a nice place to be, and in his course we worked on interesting and larger projects that gave great insight into how real problems in physics could be solved with a computer. This opened my eyes for programming, and it was an easy choice to start at the master program “Computational Physics” after I had completed my bachelor degree in four years.

When I started my master degrees, I was unsure what I wanted to write about in my thesis. I didn’t find the most theoretical parts of physics that interesting, and I also wanted to do something different. After speaking to the very helpful study advisor about courses in my masters study plan, she suggested to make contact with professor Dag Kristian Dysthe. He had been a supervisor for another cross country skier during his master thesis in computational physics, ph.d. candidate Øyvind Nøstdahl Gløersen. After making contact with Dag Kristian Dysthe, he immediately came up with the idea of modelling heart rate when I mentioned my background from sports. This was a great opportunity for me to combine physics and programming with my interest in sports and physiology.

Working on my master thesis proved to be both interesting and educational, but also quite challenging in some parts. However, many long and productive (and less productive) discussions with Øyvind Nøstdahl Gløersen made it manageable. I really appreciated our good cooperation, and I think it would be impossible to do this thesis without it. He was also responsible for buying all the new equipment we needed to do experiments, participated in parts of the mathematical model and contributed a lot in the collection of experimental data. I also have to thank my other supervisors, professor Dag Kristian Dysthe and professor Anders Malthé-Sørenssen, for their enthusiasm in my untraditional thesis in physics. Thanks to all the people who participated in the study and really pushed themselves through some strenuous workouts. There wouldn’t be much of a thesis without them. In addition, I must commend the dedicated and hardworking
people at the computational physics group, and especially Jostein Blyverket and Gøran Brekke Svaland whom I collaborated with through my bachelors degree and shared an office with during the first year of my masters degree. I must give a special thanks to my sister Heidi and her cohabitant Alexander for proofreading my master thesis, and of course my mother and father for always supporting me and showing interest in what I do.

Oslo, June 15, 2016
Stian Roti Svendby

Personal motivation

A challenge in the field of physiological data analysis and modelling is the required interdisciplinary skills. You should know physiology, master some mathematics and mathematical tools and be able to write programs on a computer to test and develop a model. In addition you should know how to collect and process experimental data, and have a basic understanding of training to design relevant exercises to obtain valuable and fruitful results. A physiologist knows a lot of physiology and is likely to have a good background within various physical activities. On the other hand, a physicist with coding experience has some of the required skills, but could lack knowledge about physiology and training. As a physicist I have learned a lot of mathematics and programming and how to perform experiments. I also have a great interest in physiology, and have participated in a lot of organized activities my whole life. Therefore I saw the possibility of combining physics with physiology to develop mathematical models through theory from physiology and physical experiments, followed by numerical analysis and modelling.

Collaboration details

During this project I have regularly discussed issues and possibilities with my three supervisors. One of my supervisors, ph.d. candidate Øyvind Nøstdahl Gløersen, has also contributed much in the collecting experimental data, and has been involved in some parts of the model development. Since much of my work has been discussed with my supervisors, I will usually refer to what “we” did and “our” model, but will use “I” if it’s obviously something that I did.
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Definitions

- HR data - sampled heart rate from experiments.
- cardiovascular fitness - the ability to produce high power (cycling) for a long time \textit{compared to other subjects}, relative to body weight.
- physical condition - the ability to produce high power (cycling) for a long time \textit{relative to the subject}. Better physical condition is recognized as lower resting heart rate and faster dynamics of HR during exercise.
- health - collective term of cardiovascular fitness and physical condition.
- workload - the absolute power applied in [watt] to the pedals during cycling experiments, but can also be related to speed in other sports.
- intensity - the relative effort of a subject at a given workload. “Intensity” ranges from total rest to maximal effort.
Symbols and abbreviations

- **HR** - *Heart Rate*, the frequency the heart beats with, unit [bpm] (beats per minute)
- **HRR** - *Heart Rate Reserve*, difference between minimum and maximum heart rate, unit [bpm]
- **HRR** - normalized *Heart Rate Reserve*, dimensionless
- **hrr** - *heart rate recovery*, time constant of heart rate decay, unit [s]
- **CO** - *Cardiac Output*, amount of blood in liters pumped by the heart per time (in minutes), unit [l/min]
- **HR_{min}** - minimum heart rate, unit [bpm]
- **HR_{max}** - maximal heart rate, unit [bpm]
- **p** - power, unit [watt]
- **p_T** - threshold power, unit [watt]
- **MAP** - *Maximal Aerobic Power*, unit [watt]
- **\bar{p}** - normalized power, dimensionless
- **\bar{p}_T** - normalized threshold power, dimensionless
- **\kappa** - defined to *always* be 0.8, connected to normalized threshold power, dimensionless
- **La_0** - basal lactate concentration in blood, unit [mmol/l]
- **La_T** - lactate threshold, unit [mmol/l]
- **\nu** - modelled heart rate, unit [bpm]
- **\nu_{min}** - minimum modelled heart rate, unit [bpm]/dimensionless
- **\nu_{max}** - maximum modelled heart rate, unit [bpm]/dimensionless
- $\nu_T$ - modelled threshold heart rate, unit [bpm]/dimensionless
- $\nu_R$ - modelled heart rate reserve ($\nu_{max} - \nu_{min}$), unit [bpm]/dimensionless
- $G$ - “global”, a function with nonlinear behaviour connected to accumulation of lactate, dimensionless
- $M$ - “metabolism”, a linear function that contributes to nonlinear behaviour, dimensionless
- $\nu_L$ - modelled heart rate for local component, unit [bpm]/dimensionless
- $\nu_G$ - modelled heart rate for global component, unit [bpm]/dimensionless
- $\nu_M$ - modelled heart rate for metabolism component, unit [bpm]/dimensionless
- $\tau_L$ - time constant for local component, unit [s]
- $\tau_G$ - time constant for global component, the inherent time constant of the $G$-model and not specified
- $\tau_M$ - time constant for metabolism component, unit [s]
- $\alpha_L$ - determines the shape of $\nu_L$, dimensionless
- $\alpha_G$ - determines the shape of $\nu_G$, dimensionless
- $\alpha_M$ - determines the shape of $\nu_M$, dimensionless
- $HbO_2\%$ - fraction of hemoglobin bound to oxygen, unit [%]
- ATP - adenosine triphosphate, energy produced in glycolysis used by body cells
- rpm - rounds per minute, cadence unit
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Chapter 1

Introduction

In recent years there have been enormous developments of portable devices that are able to continuously record data connected to health and physiology. The most common physiological data to collect has been heart rate (HR), but also oxygen saturation of blood in the fingertip and skin temperature has been measured. Some devices even collect all those measurements into small armbands, and combine it with an accelerometer and GPS to track the activity simultaneously. In this way, we can investigate how different physiological parameters change during activity or at rest. Some large companies like Garmin, Polar, Suunto and Strava among others, have tried to bring the analysis further to extract information from physiological data through mathematical models. This further analysis often tries to extract numbers that tells something about our health, to evaluate how large the training load has been during or after an exercise.

1.1 Motivation

HR is probably the most easily available physiological parameter to continuously measure. For several years it has been common to wear a chest strap during activity to keep track of HR during exercise, and the technology is precise and inexpensive. In recent years a lot of watches with built in measurements of HR have entered the mass marked. The technology varies in its precision and has some limitations for different activities. Anyway, the absence of an annoying chest strap makes people more motivated to track their own health both during activity and rest, due to the growing interest in healthy lifestyles. However, since measurements of HR have entered the mass marked, many users have little knowledge of how to interpret measurements of HR, and graphs of various data give little information to the users.

As already mentioned, some companies have developed algorithms in an attempt to deliver simple numbers from advanced analysis of HR data. However,
most of the algorithms are based on theory on HR beat-to-beat analysis\textsuperscript{1}. To my knowledge, there are no companies that actually model HR directly for extracting numbers connected to health, and a lot of useful information might be overlooked. The reason is probably the need of a workload input which might be inaccurate in some activities, together with the complexity of HR.

Some researchers have tried to develop models for modelling HR directly, but their results have weaknesses. Due to the interdisciplinary skills needed to model HR, a few researchers with strong mathematical background have successfully modelled HR with good accuracy, but their models were not based on physiological principles, and the parameters they obtained were difficult to interpret from a physiological viewpoint. Hence, there is a need for a mathematical model that models HR based on physiological principles, with the possibility of obtaining more information about health from HR, in a different way than the large companies do it.

1.2 Overview of this thesis

I am going to combine physiology with my background as computational physicist to develop a model with the aim of modelling HR during bicycle exercise, to obtain parameters that may indicate something about health. The reason for choosing cycling is the possibility of accurately measuring the workload/power a subject exposes its body to, independently of terrain and weather conditions\textsuperscript{2}.

First I am going to present some properties of HR. I will then introduce physiology which will give us a sufficient theoretical basis on the processes in the body which are the origin of the properties of HR. I will also present earlier models that have tried to model HR dynamics. After that I will present mathematical and numerical tools necessary for the analysis of experimental data, together with numerical strategies for extracting parameters from HR data. Thereafter I am going to present equipment and sensors used in experiments, before I go through experimental procedures and look at experimental results. From the theoretical basis, earlier work by other scientists and our own experimental data, I will in detail go through the new mathematical model for simulating HR presented in this thesis. The new model will be tested on synthetic workload input, an experiment in the laboratory and real life outdoor tests. The reproducibility and sensitivity of the parameters extracted from HR data will be investigated. I will also show how the model is able to predict the cardiovascular fitness of a subject without knowing anything about the subject but maximal HR. I will then summarize and discuss my most important findings and evaluate the validity of the model presented in this thesis.

\textsuperscript{1}A widely used method for analyzing HR data is Heart Rate Variability analysis (HRV), which will be briefly explained in section 2.6.

\textsuperscript{2}Such as wind, rain, etc.
1.3 Superior goal

The superior goal in this thesis is to investigate if it’s possible to model HR and extract physiologically interpreted parameters that might discover differences in HR properties in different datasets. I will not validate if the parameters are correct or how they change over time in subjects.
Chapter 2

Properties of heart rate

The heart beats all the time, with a frequency that may vary a lot through the day. At rest, lying on the couch, the heart beats slowly. If you stand up, HR might do a jump and obtain a new frequency. All the time, the heart adjusts its frequency to deliver vital oxygen to the body. Dynamics and properties of HR have been studied for a long time to survey the connection between HR and health.

2.1 Resting heart rate

Heart rate at rest ($HR_{\text{min}}$) is known to change with cardiovascular fitness\(^1\), since a trained (bigger) heart can deliver more oxygen per beat [51]. However, we have no scientific basis to compare $HR_{\text{min}}$ among subjects to conclude which subject has best cardiovascular fitness, although $HR_{\text{min}}$ in many cases might be lowest in the subject with best cardiovascular fitness. On the other hand, changes in $HR_{\text{min}}$ for a specific subject are known indicate the physical condition\(^2\)/fatigue of this subject [36] [40]. If a subject does regular aerobic exercise for a period, together with sufficient rest afterwards, the subject might obtain a lower $HR_{\text{min}}$.

2.2 Maximal heart rate

The maximal HR ($HR_{\text{max}}$) may vary a lot from person to person. $HR_{\text{max}}$ is not dependent of cardiovascular fitness or physical condition, but reduced with age due to properties of the heart [16]. $HR_{\text{max}}$ is therefore threatened as a constant in this thesis.

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\(^1\)cardiovascular fitness - the ability to produce a high power (cycling) for a long time compared to other subjects, relative to body weight

\(^2\)physical condition - the ability to produce a high power (cycling) for a long time relative to the subject.
2.3 Heart rate and linearity

In 1973, Fujihara et al. [24] investigated how the heart responded to 5- and 10-second impulses from low to high workload, and to a step from low to medium workload during bicycle exercise. All tests were well below strenuous intensities\(^3\). They found that the delay in HR response after increased workload was less than 2 seconds, and the response was almost linear\(^4\). They argued that they had chosen intensities where they assumed HR to behave most linear. They suggested that the linear response was a result of neural control of the heart, but were aware of the high possibility of nonlinearities at high intensities. From their results shown in Figure 2.1, we can see how HR fell almost exponentially after the impulses.

As with most biological systems, the HR response is nonlinear. Nonlinear behaviour can be seen in experimental results by Cheng et al. [15] (2008) in Figure 2.2. Nonlinearities appears as a slow upward drift\(^5\) at constant workload, together with slower dynamics\(^6\) at high intensities. A study by Su et al. [64]

\(^3\)intensity - the relative effort of a subject (person) at a given workload. “Intensity” ranges from total rest to maximal intensity.

\(^4\)The properties of a linear system, and how we can investigate linear properties, are explained in section 5.1.

\(^5\)The slow upward drift in HR during exercise at high intensities, is often referred to as the slow component in the literature.

\(^6\)It’s hard to observe slower HR dynamics from the results in Figure 2.2.
Section 2.4 Heart rate dynamics

Figure 2.2: HR response to tree different treadmill speeds (workloads), where we observe nonlinear behaviour for the highest speed at 7 km/h, Cheng et al. [15] (2008).

(2010) showed how both steady-state gain of HR and the time constant of the HR response to step exercise, changed when the intensity increased.

2.4 Heart rate dynamics

Another aspect of HR that has been studied is how fast HR decays during and after exercise, often referred to as heart rate recovery (hrr). Dimkpa [19] (2009) accentuated how hrr should be added to the list of possible indicators of cardiovascular fitness, while Børresen and Lambert [12] (2008) also suggested hrr as an index of physical condition/fatigue. hrr can be obtained from looking at a HR decay after a short impulse or after a step at high intensity. A rapid decrease in HR is assumed to reflect a rapid change in neural stimulation of the heart. Dimkpa referred to studies where hrr was shown to be faster in athletes than in non-athletes, while subjects with cardiovascular disease had much slower hrr. A reduction in HR less than 12 bpm\(^7\) the first minute after medium to strenuous intensity, was defined to represent a high relative risk of cardiovascular mortality. Since the decay of HR almost looks like an exponential (as shown in the results by Fujihara et al. [24] (1973), ref. Figure 2.1), a time constant can possibly be obtained from HR data. However, the exponential decay is disputed and is probably only valid on medium to low intensities as it was in the studies by Fujihara et al. [24] (1973).

It turns out that it’s not only the decaying hrr that may reflect cardiovascular fitness or physical condition. Børresen and Lambert [12] (2008) referred to studies where the overall response to exercise was faster in trained subjects. We cannot predict cardiovascular fitness of a subject by only looking at how fast the response is compared to others, but changes for one subject might indicate changes in the physical condition [12]. If the HR dynamics are slower than usual for a subject,

\(^7\)Beats per Minute
the subject is probably over trained or ill, and therefore needs rest. If the HR
dynamics are faster than usual for a subject, the subject is probably in good
physical condition and has a lot of excess energy.

![Figure 2.3](image)

**Figure 2.3:** The figure shows how HR slowly tends towards the pre-exercise
value of $HR_{\text{min}}$ after exercise. The upper part is before exercise and the period
of exercise, while the lower part is after exercise, Javorka et al. [35] (2002).

### 2.5 Elevated resting heart rate

After exercise, resting heart rate ($HR_{\text{min}}$) is usually elevated compared to before
the exercise, before it slowly tends towards the value before exercise. Javorka et
al. [35] (2002) showed this by recording HR of 17 subjects, where the subjects first
rested for 25 minutes, then they had 8 minutes of excise\(^8\) with intensity between
medium to high, and ended the test with 35 minutes of rest. Their results are
shown in Figure 2.3. During the 35 minutes of rest after exercise, we observe a
slow and almost linear decrease in HR (the lower part of Figure 2.3), and $HR_{\text{min}}$
almost reaches its pre-exercise value after 35 minutes (the end of the dataset).
However, how long time it takes $HR_{\text{min}}$ to reach normal values after exercise,
depends on how hard and long the exercise is. This phenomena is connected to
excess usage of oxygen after exercise, due to removal of lactate and increased
body temperature [10] [25] [38].

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\(^8\)They did a step test, repeated climbing on a bench.
2.6 Beat-to-beat variations in heart rate

There are two different parts of the nervous system\(^9\) that regulate HR up and down with different frequencies. In the field of Heart Rate Variability (HRV)-analysis on beat-to-beat recordings of HR, relevant statistics (such as standard deviation) is computed, and Fourier frequency analysis is applied to predict the balance between the nervous systems that control the heart of an individual. Beat-to-beat recordings of HR measure the time between two subsequent R-waves, known as the R-R interval. R-waves are recognized as the highest peaks in an ECG-signal, as shown in Figure 2.4.

![R-R interval](image)

**Figure 2.4:** A sketch of a typical ECG signal showing the R-R interval between two subsequent R-waves. R-R intervals are used in HRV analysis.

A high HRV is recognized as high variation in time between subsequent heart beats (large variation in subsequent R-R intervals). Short term HRV analysis is used by all the big manufacturers of training computers, like Garmin, Polar and Suunto. They estimate physiological parameters both during and after workouts, like recovery time and lactate threshold. However, the validity of short term HRV analysis in sport applications is still under discussion. More research is needed in this field before HRV gives accurate measurements of physiological parameters during exercise due to limited knowledge and limited precision in HRV-readings [20] [22] [63].

2.7 External factors that might affect heart rate

A lot of factors that are not directly connected to exercise intensity, may also affect properties of HR. Those factors are in some cases possible to control, in other cases not. The disadvantage is that they might introduce unexpected behaviour of HR, or at least more complex behaviour. Some drugs, like beta blockers used

\(^9\)The two nervous systems that regulates HR are the sympathetic nervous system and the parasympathetic nervous system.
against heart disease, lowers HR_{min} \cite{13}. On the other hand, chemical stimulants like caffeine and nicotine, elevates HR_{min} \cite{13}. Other factors that can affect properties of HR are dehydration, poor nutritional status, emotional stress, fright (causing a release of adrenaline), illness, altitude (lowered oxygen in air), hot or cold environments, among other things \cite{13}.

### 2.8 Summary of heart rate properties

To summarize this chapter, some aspects of HR dynamics might be of interest to extract information about physical condition, such as HR_{min} and time constants in the HR dynamics. In addition, since nonlinearities are introduced at high intensities, it might be possible to detect the onset of nonlinearities at a given workload to extract information about cardiovascular fitness.

In the upcoming sections, we will look at physiology aiming to explain the different aspects of HR dynamics. When the underlying processes of HR regulation are known, we are much more capable of developing a model that behaves according to properties of HR. A model based on physiological principles should make us able to extract information of interest from different parts of the system. According to the theory in this chapter, we aim for time constants of HR and HR_{min} to predict physical condition, and the onset of nonlinearities in HR response to predict cardiovascular fitness.
Chapter 3

Physiology related to heart rate properties

The heart is a muscle responsible for pumping blood around in the body. How fast the heart is pumping or contracting is known as heart rate (HR). HR is governed by feedback mechanisms from the entire body. From the heart, blood is transported through arteries\(^1\) to deliver vital oxygen to almost every cell in the body, before the blood is pushed towards the heart again through veins\(^2\). The system responsible for oxygen delivery in the body is known as the circulatory system. The circulatory system consist of the heart, lungs, vessels and blood, and is illustrated in Figure 3.1. In the upcoming sections I will go through the most important mechanisms in the regulation of HR, and look at factors that may affect HR. It’s a lot of physiology, but there are some important physiological concepts that are necessary to understand the rationale of a mathematical model based on physiological principles. In most cases, the explanations covered in this chapter do not fully replicate the most detailed physiological understanding. I have attempted to keep it as simple as possible without loosing the main message.

3.1 The heart

The heart consists of four chambers connected to two different circulatory main paths. One path delivers oxygen rich blood to cells in the body, while the other path leads blood through the lungs for the deoxygenated blood\(^3\) to pick up new oxygen. If the heart functions properly, about the same amount of blood passes through both circulatory paths in a specific direction at all times.

To move blood in the circulatory system, the heart has to contract. To initialize a contraction, we have something known as the sinoatrial node (SA

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\(^1\) arteries - vessels that leads blood out of the heart
\(^2\) veins - vessels that leads blood into the heart
\(^3\) deoxygenated blood - blood that not carries oxygen
node), which is localized in one of the heart chambers\textsuperscript{4}. The SA node cells are connected to the autonomic nervous system, which in turn is connected to the brain.

![Circulatory System Diagram](image)

**Figure 3.1:** My own sketch of the circulatory system. Red paths indicates that the blood is saturated with oxygen ($O_2$), while blue paths indicates that the blood has released oxygen to muscles and organs around in the body. We observe that oxygen rich blood leaves the left ventricle into arteries that transport blood to all parts of the body. The flow of blood out of the heart, is known as cardiac output (CO). When oxygen take parts in the production of energy in the body, it’s converted to carbon dioxide ($CO_2$). $CO_2$ and blood is transported back to the heart through veins. In the upper path in the figure, deoxygenated blood passes through the lungs to pick up new oxygen, and $CO_2$ leaves the body through breathing. We also note the SA node placed on the right atrium that initiates every heart beat. The SA node is connected to the nervous system, where different stimuli in the body determine how often the SA node should initiate a heart beat.

\textsuperscript{4} *The right atrium*
3.1.1 Maximal beat frequency (HR$_{\text{max}}$)

The heart consists only of excitable cells, with the ability to propagate an electrical signal [39]. When the SA node initiates an electrical signal into the excitable heart cells at the right atrium, the electrical signal spreads throughout the heart, which thereafter contracts in a specific manner for optimal pumping efficiency. However, excitable cells need some time to reset before a new contraction [39]. This leads to a physiological maximal limit for HR for fully functioning heart contractions. However, maximal HR (HR$_{\text{max}}$) may vary a lot between subjects, and decreases slowly with age [52]. HR$_{\text{max}}$ usually lies between 160 and 220 bpm, and simple formulas based on statistics are developed to estimate HR$_{\text{max}}$. One such formula is presented by Nes et al. [52] as: $211 - 0.64 \times \text{age}$ bpm with a standard error of 10.8 bpm. This model can be used to predict HR$_{\text{max}}$ without doing a physical test. However, we observe the large standard error in this model (about 10% of HRR$^6$), and a physical test is necessary to discover the true HR$_{\text{max}}$ of a subject to desired precision. The model can be a backup alternative if a physical test to obtain HR$_{\text{max}}$ is impossible for a subject.

3.1.2 Cardiac output

The volume of blood pumped per heart contraction is known as the stroke volume. The stroke volume is recognized as the amount of blood ejected per beat from the left ventricle$^7$, with unit ml/beat [31]. Since the heart is a muscle, endurance training increases the size of the heart, leading to a bigger stroke volume [45] [6] [48]. In addition, cardiac output (CO) is defined as (stroke volume)$\times$(heart rate), and tells us the amount of blood the heart pumps per minute (l/min) [31]. This means that a trained heart is able to pump more blood per time than an untrained heart. In addition, since the heart of a trained person is bigger, fewer heart beats are necessary to deliver the same amount of oxygen to the body. How HR and stroke volume changes with increasing CO are shown in Figure 3.2. We observe from the green line in Figure 3.2 that CO increases superlinear with HR. HR accounts for a much greater proportion of the increase in CO during strenuous exercise than the increase in stroke volume does [31]. Since the content of oxygen (per volume) is close to constant in arterial blood leaving the heart [57], an increase in CO means more delivered oxygen to the body.

3.1.3 Minimum beat frequency (HR$_{\text{min}}$)

The heart has a physiological limited minimum beat frequency (HR$_{\text{min}}$). At total rest (typically lying on the couch) the use of oxygen is at an absolute minimum.

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$^5$The time to reset excitable cells is known as the refractory period.

$^6$Heart rate reserve - difference between HR$_{\text{min}}$ and HR$_{\text{max}}$ in a subject

$^7$See Figure 3.1.
in skeletal muscles. In this case, the heart will reduce CO to a minimum to not waste energy. Hence, the flow of blood through muscles is not any higher than necessary. Since the heart of trained athletes is bigger than for untrained people, it follows directly from CO = (stroke volume) × (heart rate) that athletes should have lower values for HR_{min} than untrained. Highly trained endurance athletes can obtain a HR_{min} as low as 30 – 40 bpm, while untrained people can have a HR_{min} as high as 100 bpm [5] [13].

### 3.1.4 The heart: summary

As described in this section, the heart is pumping blood according to the need of oxygen in cells in the body. CO is the factor that is adjusted according to the demand of oxygen delivery. As we have seen from Figure 3.2, the delivery of oxygen (CO) increases superlinear with HR. We have also seen how HR_{max} depends on age, but with large variations among subjects. A physical test is therefore necessary to obtain the real value of HR_{max} to required precision. When HR_{max} is found, we can assume that this value is a constant\(^8\), at least for a specific movement pattern. HR_{max} is believed to be independent of cardiovascular fitness and physical condition. HR_{min} is on the other hand related to cardiovascular fitness

\(^8\)The decrease in HR_{max} with age is so slow (0.64 bpm per year on average according to the formula by Nes et al. [52]) that this is a fair assumption.
and physical condition, and is therefore of great interest in the development of a model. $HR_{\text{min}}$, or at least some kind HR at rest, is an attribute we possibly can extract from HR data. The difference between $HR_{\text{min}}$ and $HR_{\text{max}}$ is referred to as Heart Rate Reserve (HRR).

### 3.2 Regulation of heart rate

An unstimulated SA node will spontaneously initiate heart beats\(^9\) [61]. However, the autonomic nervous system is connected to the heart through the SA node, and can stimulate the SA node to change HR from as low as 30 bpm to as high as 220 bpm in some subjects. Regulation of the autonomic nervous system is an unconscious process, and can be divided into two different systems, the sympathetic nervous system and the parasympathetic nervous system [31]. Both systems are connected to the heart, and both systems give stimuli to the heart at all times. HR increases when sympathetic stimulus on the SA node dominates parasympathetic stimulus. HR decreases when parasympathetic stimulus dominates sympathetic stimulus. In this way, the balance between the two systems can quickly regulate HR.

The regulation of sympathetic and parasympathetic activity in the heart is primarily controlled by the brain, which in turn collects feedback from all parts of the body through nervous systems and different receptors. The two most important receptors that affect HR during physical activity are baroreceptors and chemoreceptors.

#### 3.2.1 Baroreceptors

Baroreceptors are able detect changes in pressure inside vessels in the circulatory system. Baroreceptors are often called “stretch receptors” since they are sensitive to stretching. The pressure changes inside vessels during activity, and baroreceptors are important to recognize those changes. Baroreceptors are localised in the walls of large systemic arteries, mainly close to the heart and around the throat to prevent heart failure and brain damage [31]. When the pressure rises in large arteries, baroreceptors are stretched, which causes them to transmit signals through nerves to the brain. From the brain, signals are sent back through the autonomic nervous system to regulate the pressure towards normal levels. The regulation of pressure is primarily done by adjusting CO (higher/lower HR), and by constriction/dilation of arteries and veins by the sympathetic nervous system in noncritical parts of the circulatory system, like vessels in arms during cycling [31].

\(^9\)The frequency without any stimulus is about 100 bpm [61].
3.2.2 Chemoreceptors

Chemoreceptors are responsible for maintaining a proper concentration of $O_2$ (oxygen), $CO_2$ (carbon dioxide) and $H^+$-ions (protons) in the body tissue. Chemoreceptors are primarily localized in the brain, but are also located around the throat and close to the heart (just as baroreceptors). Due to their location, chemoreceptors are always in close contact with arterial blood. The concentration of $O_2$ is usually within normal values in arterial blood, but the concentration of $H^+$-ions may increase during heavy exercise due to production of lactate [31]. Chemoreceptors are connected via nerves to the respiration center in the brain which regulates breathing frequency. An increase of $H^+$-ions in arterial blood should therefore increase muscle activity in the chest during respiration [60], which in turn affects HR. It’s not only chemoreceptors that control respiration, but a full explanation of respiratory regulation is still uncompleted in physiological research [61].

3.2.3 Regulation of heart rate: summary

The most important thing to note in this section, is how baroreceptors can detect changes in pressure and tell the brain to change HR rapidly to prevent hazardous levels of blood pressure. Due to this, there should at least be one component in HR dynamics that changes fast to changes in workload. This is also in accordance to the finding by Fujihara et al. [24], where HR changed within 2 seconds after onset of exercise. Chemoreceptors also play an important role, since they contribute to increase the muscle activity in large muscles in the chest during respiration when the chemical composition of arterial blood is changed. It’s reasonable to assume that changes in the chemical composition of arterial blood is slower than changes in pressures, since the blood has to be transported all the way from muscles, via veins, heart and lungs (recall Figure 3.1), and then to arteries where the blood reaches chemoreceptors. Hence, chemoreceptors might contribute to a somewhat slower component.

3.3 Oxygen transport from lungs to muscles

In previous sections we looked at properties of the heart and how HR is regulated. However, we have not looked at why HR needs to be regulated during exercise. In summary, it’s all about the delivery of oxygen to the body tissue for production of energy used by body cells. When there is lack of oxygen in parts of the body, the heart will respond by increasing CO. The usual way to measure oxygen delivery during exercise, is to measure $VO_2$ ($l/(min\cdot kg)$) in a laboratory test. $VO_{2max}$ is the maximal amount of oxygen the circulatory system can deliver per time per mass to the body at maximal load, and is often used as a predictor of
cardiovascular fitness.

### 3.3.1 Partial pressure of oxygen and hemoglobin

In mixed gases, each type of gas has a *partial pressure* that contributes to the total pressure. The individual pressure exerted by a particular gas within a mixture of gases is known as its partial pressure [61]. We recognize the partial pressure of \( O_2 \) as \( PO_2 \). In the air surrounding us, there is a partial oxygen pressure. There is also a partial pressure of oxygen in the blood. When breathing, air flows into the lungs due to lowered air pressure when the lungs stretch. Since \( PO_2 \) usually is higher in air than in blood, oxygen diffuses through the walls into the blood passing by inside the lungs. The same thing happens to \( CO_2 \), but in the opposite direction.

The blood consists of red blood cells. Inside red blood cells we have *hemoglobin* (Hb). Hb is able to bind oxygen given by the reaction equation [61]:

\[
0_2 + Hb \rightleftharpoons Hb0_2 .
\]  

(3.1)

Oxygen bound to Hb *do not* contribute to \( PO_2 \) in blood, only oxygen dissolved in blood contributes. However, as \( PO_2 \) rises in blood inside the lungs, equation 3.1 is driven to the right since the availability of \( O_2 \) increases on the left side of the equation. In this way, Hb works as a reservoir for oxygen in blood. In fact, about 97-98% of the oxygen transported with the blood is bonded to Hb in arterial blood [61] [31], and fraction of Hb bond to oxygen (\( Hb0_2\% \)) in arterial blood remains quite constant\(^{10}\) even during strenuous exercise [57]. In addition, chemical changes in the blood, such as lowered pH\(^{11}\), reduces the ability of Hb to bind oxygen [61].

The relationship between \( PO_2 \) in blood and \( Hb0_2\% \) is shown by the *dissociation curve(s)* in Figure 3.3. Figure 3.3 also shows how lowered pH affects the dissociation curve. The important thing to observe from Figure 3.3 is the plateau for high values of \( PO_2 \), before the curve drops (from right to left) for lower values of \( PO_2 \). This is a direct effect of equation 3.1. When \( PO_2 \) is above a given threshold, a further increase in \( PO_2 \) doesn’t bind more oxygen to Hb, since Hb on the left side of equation 3.1 is saturated. When \( PO_2 \) decreases, equation 3.1 is driven to the right, but only a small amount of oxygen is released from Hb until \( PO_2 \) reaches about 40 mm Hg, were a significant portion of oxygen is released from Hb.

\(^{10}\)A small drop in \( Hb0_2\% \) in arterial blood has been observed in trained subjects at maximal intensity [57].

\(^{11}\)When the concentration of \( H^+ \)-ions increases, the pH is lowered. Low pH is referred to as “sour” or “acidic”.
3.3.2 Release of oxygen from hemoglobin

After blood has passed through the lungs, it’s transported back to the heart and pumped out via arteries to the rest of the body. Vessels have a fork structure with smaller and smaller diameter down to the smallest vessels named capillaries. When the blood reaches muscle cells (or any other living cell in the body), we get diffusion of oxygen from blood inside capillaries into cells, due to lower $PO_2$ in cells than in arterial blood.

$PO_2$ is lower in muscle cells than in arterial blood since some of the oxygen inside cells is used in glycolysis in the production of adenosine triphosphate (ATP). ATP is the energy source essential to every muscle contraction. It follows from Figure 3.3 that if cells have low metabolism\textsuperscript{12}, there will only be a small drop in $PO_2$ inside them, such that Hb leaving the cells is still almost fully saturated with oxygen. However, if the cell metabolism is high and $PO_2$ inside cells is lower than 40 mm Hg, Hb will release large amounts of oxygen to the blood, which lets oxygen diffuse into cells. We then observe a lowered $HbO_2\%$ in blood leaving the cells. In other words, if the intensity of muscle work is low, the drop in $PO_2$

\textsuperscript{12}Metabolism is connected the chemical processes inside cells that produce essential energy (ATP).
is not that big compared to arterial blood, and $HbO_2\%$ remains high. When the intensity of muscle work increases above a threshold that reduced PO\(_2\) below about 40 mm Hg in the cells, a much higher drop $HbO_2\%$ may be observed.

As shown in Figure 3.3, local elevation of muscle acidity (lowered pH) facilitates further release of oxygen to the muscle cells. Also, the reaction given by equation 3.1 is facilitated by increased temperature in muscles with high metabolism, since metabolism produces a lot of heat [61]. If strenuous exercise is sustained, we get lowered pH and increased temperature in the muscle, shown as a large drop in $HbO_2\%$ in blood leaving the muscle.

### 3.3.3 Own reflections based on theory in this section

We can look upon $HbO_2\%$ as the ability of oxygen in blood. As long as the cells have sufficient access to oxygen through diffusion from the blood, the cells should be able to produce ATP and perform work at the same effort. If there’s not enough oxygen dissolved in the blood to deliver enough oxygen to the active cells, Hb starts to release oxygen to the blood. Since $HbO_2\%$ might drop (from right to left) when a kind of threshold\(^{13}\) of cell metabolism is reached, a significant drop in $HbO_2\%$ might indicate which workload a subject can remain at for a long time.

The blood pH is continuously lowered above a certain (high) intensity due to accumulation of lactate. An intensity where $HbO_2\%$ already is lowered, should give a continuous drop in $HbO_2\%$ for continuous lowered pH, even though the intensity is constant. This is due to the right-shift in dissociation curves shown in Figure 3.3. Theoretically, the drop in $HbO_2\%$ will eventually level out towards 0 when the right-shift of the dissociation curve is very large (high pH), or if the metabolism is very high in the muscle cells (low PO\(_2\)). When the pH continues to fall inside active muscles, the pH will reach a point where the pH will inhibit muscles to perform sufficient contractions to remain at the same effort.

If we are able to measure $HbO_2\%$ in the most active muscle in an activity type, such as a muscle in the legs during cycling, we could possibly detect the threshold workload/power where the subject can remain at the same effort for a long time.

### 3.4 Muscles and blood pressure

As described in previous sections, blood saturated with oxygen is transported through vessels to deliver oxygen by diffusion into living cells. The oxygen is essential to produce ATP necessary for all cell functions. During exercise, the

\(^{13}\)Where $PO_2$ has dropped to about 40 mm Hg, ref. Figure 3.3.
need for oxygen in highly active cells increases dramatically, which is the main reason for increased HR during exercise.

Vessels inside highly active muscles are able to adjust oxygen delivery locally by expanding or *vasodilate*. This increases the flow of blood locally in muscles a few tenfold times compared to resting values [31] [14]. When the flow of blood through a muscle increases, a rapid drop in arterial pressure is recognized by baroreceptors as explained in section 3.2, which in turn tells the heart to pump faster. Since the pressure inside arteries must remain within normal values to push blood through the circulatory system, all vessels in the body cannot expand at the same time due to an upper limit in CO\textsuperscript{14}.

![Figure 3.4: A sketch of how the flow of blood increases locally with increasing metabolism the tissue [31]. When the metabolism increases inside a muscle, lack of oxygen make vessels expand inside the muscle, which lowers the arterial blood pressure. Baroreceptors recognize this drop in pressure, and tell the heart to beat faster. Increased CO keeps the arterial pressure within normal values.](image)

Psychological factors may affect blood pressure. It’s clear that HR increases when we start exercising due to increased metabolism in active muscle cells, but also psychological stress or fright may effect HR vastly. The reason for this is an alarm reaction reflex, which provides an excess of arterial pressure that can immediately supply blood to the muscles that might need to respond instantly to cause flight from danger. This in turn will demand an increased CO, such that the heart must beat faster.

\textsuperscript{14}The upper limit in CO is roughly 4-7 times resting values, depending of cardiovascular fitness.
The most important things to note from this section is that muscles are able to adjust blood flow locally both due to workload and psychological stress, which leads to rapid drop in pressure, followed by increased HR.

### 3.5 Muscles and metabolism

The three main sources of energy in food is fat, carbohydrates and proteins. However, for the body to make use of this energy, it has to be converted to adenosine triphosphate (ATP), as mentioned in section 3.3. Before the energy is converted to ATP, it can mainly be stored in two different ways, as fat or glycogen. Glycogen are long chains of glucose (sugar). The storage of fat may last for days without refill of nutrition, while the glycogen storage may only last for about an hour \[9\]. Unused proteins and excess carbohydrates are converted and stored as fat.

#### 3.5.1 Sources of ATP

How the body chooses to produce ATP depends on the energy demand in active muscles, assuming that the storage of glycogen is not empty. Fat is used as a source of energy all the time, but the body tends to use more fat than usual at medium exercise intensity, as shown in Figure 3.5. Since the breakdown of glycogen, glycolysis, may happen both with and without oxygen present, glycogen can be used as a source of ATP in two different ways. If there is oxygen present, we have *aerobic glycolysis*. If there is lack of oxygen, we have *anaerobic glycolysis* \[31\]. There are more than one theory about what’s happening during glycolysis, and we won’t go into every detail. A good discussion on the different theories is written by Bruce L. Gladden \[27\] (2010).

As seen in Figure 3.5, aerobic glycolysis decreases exponentially with increasing intensity of the working muscles, while anaerobic glycolysis rises exponentially with intensity \[31\]. Aerobic glycolysis is a completed reaction, while anaerobic glycolysis is a preliminary state due to the end products. The end product of aerobic glycolysis is 36 ATP units, $CO_2$ and $H_2O$, while anaerobic glycolysis produce 2 ATP, $H^+$-ions and lactate, as shown in Figure 3.6. However, even if the use of glucose is far from optimal\[15\] in anaerobic glycolysis, the maximal rate of ATP production is much faster in anaerobic glycolysis than in aerobic glycolysis. This leads to approximately 2.5 times more production of ATP per unit time in anaerobic glycolysis \[31\].

\[15\]2 ATP units in anaerobic glycolysis vs. 36 ATP units in aerobic glycolysis.
Figure 3.5: The figure shows a sketch of sources of ATP at different exercise intensities [31]. At low intensities, when oxygen availability is high in the muscles, aerobic glycolysis is the dominating source. At high intensities, when oxygen availability is low in the muscles, anaerobic glycolysis is the dominating source. The shape of the anaerobic glycolysis line (red line) is connected to the activation of fast-twitch muscle fibres. The shape of the aerobic glycolysis line (blue line) is connected to the activation of slow-twitch muscle fibres. ATP obtained from fat (green line) is highest at medium intensity, but gives a significant contribution at all intensities. Oxygen isn’t necessary for breakdown of fat. Oxygen is therefore only used in aerobic glycolysis (blue line).

3.5.2 Different types of muscle fibres

At low intensities when oxygen is accessible to all muscle cells, almost all glycolysis is aerobic. However, this is not only due to sufficient oxygen, but also depends on the muscle fibres involved in the mechanical work. To simplify, we only distinguish between types of muscle fibres, slow-twitch\textsuperscript{16} and fast-twitch\textsuperscript{17}. In the process of making ATP, mitochondria inside cells are necessary in aerobic glycolysis. In slow-twitch fibres, we have 2-3 times more mitochondria than in fast-twitch fibres, making aerobic glycolysis much more common than anaerobic glycolysis in slow-twitch fibres [55]. It’s therefore possible, from a modelling viewpoint, to assume that fast-twitch fibres always produce lactate when ATP is formed, while slow-twitch fibres never produce lactate when ATP is formed. When the demand of muscle force increases, more fast-twitch fibres are activated, giving rise to more anaerobic glycolysis, and consequently $H^+$-ions and lactate [27].

It should be mentioned that the proportion of slow-twitch and fast-twitch fibres are known as Type I muscle fibres\textsuperscript{16} and Type II muscle fibres\textsuperscript{17}.

\textsuperscript{16}Slow-twitch muscle fibres are known as Type I muscle fibres

\textsuperscript{17}Fast-twitch muscle fibres are known as Type II muscle fibres
fibres in different muscles vary from person to person, and has not been shown
to change with athletic training. The proportion of different muscle fibres is
therefore determined by genetics [31]. The average proportion between slow-
twitch and fast-twitch fibres is approximately 50/50 in both legs and arms [59]
[62], but proportions from 82/18 (long distance athletes) to 37/63 (sprinters) are
measured in different athlete sports [31].

3.5.3 Metabolism and heat production

Metabolism is defined to be the sum of all chemical reactions in all cells of the
body, but we can also refer to high metabolism in single cells or groups of cells
(muscles). Most of the chemical reactions, such as during glycolysis, produce a
lot of heat. In fact, heat is the end product of almost all the energy released in
the body. On average, as much as 35% of the energy available from food becomes
heat during the formation of ATP, and even more is lost to heat when ATP is
transformed to something functional in the cells. This means that optimally no
more than 27% of the energy from food is actually used to do functional work
such as muscle contractions [31]. In addition, about 75% of all of the energy used
for muscle work is further converted to heat overcoming friction in vessels and
muscles. The heat liberated by the body is therefore highly proportional to the
consumption of oxygen [61] [31].

In the body there is always a basal metabolism due to organ functions. In
addition, the body must produce heat to keep the body core temperature about
37°C. If the body core temperature is above normal, the body will try to release
heat through increased blood flow to the skin and sweating, among other things.

Heavy physical activity may increase the metabolism tenfold, while diges-
tion only increases the metabolism with a few percent [31]. Due to the higher
metabolism in the body during activity than at rest, more heat is released in the
chemical reactions to form ATP. If the exercise is light, the metabolism increases
only a little, and the temperature rise would therefore be negligible. The body
core temperature will on the other hand increase noticeably if the exercise is hard
for a long time, or extremely hard for a short time. The body would then not
have time to release excess heat from the production of ATP. From chemistry we
know that increased temperature speeds up chemical reactions, leading to higher
metabolism. In other words, if we perform strenuous exercise that increases the
body core temperature, there will be an elevated metabolism in the body due to
the elevated temperature after we have stopped exercising.

3.5.4 Body temperature analog

About 60% of the body weight in adults is water [31]. If we think of the body
as a boiler with water able to release heat to the surroundings at (constant)
temperature, we can think of metabolism as heat from a hotplate. We assume that the hotplate at minimum gives the water a temperature at 37°C. Water has high specific heat capacity, which means that water can hold a lot of energy. This implies that it takes a long time to change the temperature in water, compared to air with low specific heat capacity for example.

If the heat from the hotplate is elevated only a little, the temperature would increase only a little before we slowly reach a steady-state. If we on the other hand turn up the heat from the hotplate a lot, the temperature will increase a lot, and the increase will be faster, before it slowly reaches the steady-state temperature. If we again we turn up the hotplate, but now at maximum heat. The temperature might rise very quickly since the supplied heat is very high, and the water would reach a maximum steady-state temperature due to the release of heat to surrounding air. What all the three experiments have in common, is that after the heat is turned to minimum, all of them slowly release the excess heat to the surroundings toward 37°C. If the temperature of the surroundings is lowered, heat is faster released from the water.

The analog above is supposed to make it easy to understand how different exercise intensities might rise the body core temperature. As long as the exercise intensity is low, the body core temperature should remain almost constant, such that there is little excess temperature initiated metabolism. The higher the exercise intensity is, the faster is the body core temperature elevated. When the temperature is elevated, it takes a long time before the metabolism in the body reaches basal values. How long time it takes before the temperature goes back to 37°C after exercise, depends on the environmental temperature and clothing. As long as temperature initiated metabolism exists, the heart must beat faster to deliver the increased demand of oxygen\footnote{A similar concept is often referred to as Excess Post-exercise Oxygen Consumption (EPOC), which is a merging of all effects that might cause elevated oxygen consumption after exercise, such as increased body core temperature and aerobic lactate removal.} \cite{25, 38}. A study on children measured approximately 10 additional heart beats per celsius degree above basal body core temperature \cite{18}. This gives us an idea of how much the temperature might affect HR.

### 3.5.5 Muscles and metabolism: summary

There are a lot of things in this section that are relevant for a mathematical model. The shape of the red line from Figure 3.5, is highly connected to activation of fast-twitch muscle fibres and production rate of lactate at different intensities. The slow-twitch fibres produce little lactate compared to the faster ones, but dominate in the muscle work at low intensities. Since oxygen isn’t necessary for breakdown of fat, the usage of oxygen to form ATP (which affects HR) is only connected to glycolysis. We also note the almost equal distribution of slow-twitch
and fast-twitch muscle fibres at average in humans. In addition, high metabolism at high intensity may elevate the body core temperature, and build up a long lasting excess usage of oxygen during and after exercise. This is a relatively slow process that might give rise to an important component in a HR model.

### 3.6 Lactate and the threshold concept

As mentioned in the previous section, when there is lack of oxygen in highly active muscles, lactate is produced. If the concentration of lactate is high locally in the muscle, we usually feel pain. This is not due to the lactate, but the \( H^+ \)-ions, one of the other byproducts in anaerobic glycolysis, as shown in Figure 3.6. A higher concentration of \( H^+ \)-ions lowers the pH which disturbs processes related to contraction in muscle cells [26]. Because of the highly linear relationship between production of lactate and \( H^+ \)-ions, we can measure lactate as an estimate of muscle acidity (lowered pH) [58]. Lactate at increasing workload during exercise has been measured for a long time, and it’s well known that measured lactate concentration rises exponentially with workload.

![Figure 3.6: My own simplified illustration of the two pathways in glycolysis.](image)

Aerobic glycolysis is usual in slow-twitch fibres, while anaerobic glycolysis is usual in fast-twitch fibres. While the aerobic path is a completed one-way reaction, the anaerobic path is reversible and only a preliminary state due to the end products \( H^+ \) and lactate. We observe that 2 ATP is the result of the anaerobic path, while we get 36 ATP for the aerobic path. Nevertheless, the anaerobic path is much faster, and may produce more ATP per time. When the intensity is reduced, and the availability of oxygen increases, lactate is transformed back into pyruvate. This pyruvate is either transformed back into glucose and stored as glycogen, or used as a source to produce ATP through the aerobic path inside mitochondria. Both ways remove the excess \( H^+ \)-ions that make the muscles acidic [31].
3.6.1 Lactate as a source of ATP

Lactate is often looked upon as a limiting factor in high intensity training. However, lactate production reduces $H^+$-ions when there is lack of oxygen, as shown in Figure 3.6, where we get 2 $H^+$-ions instead of 4 $H^+$-ions. Lactate also works as an energy buffer, making muscles able to maintain at high effort much longer than without lactate production. Since the process of anaerobic glycolysis is reversible, lactate may be used as an energy source in aerobic glycolysis if oxygen is present, or stored as glycogen for later use.

If the production rate of lactate is low, the little lactate produced is used as an energy source locally in other muscle cells where oxygen is present [10]. When the production of lactate is high, lactate is transported into blood passing through the muscle, and transported back to the heart. The heart, the liver, and less active muscles with a lot of oxygen present, are in turn able to use lactate as an energy source when acidic blood is transported back into arteries. In this way, the blood gets rid of lactate and excess $H^+$-ions, keeping the arterial blood lactate concentration as low as possible. Since red blood cells don’t have mitochondria, they are only able to produce ATP anaerobically. Therefore, we always have a basal concentration of lactate about 1 mmol/l in arterial blood [54].

3.6.2 Transport and removal of lactate

Lactate in arterial blood (or capillary blood) can easily be measured with small hand held devices. At rest, we should always measure a concentration close to the basal concentration of 1 mmol/l. Red blood cells produce lactate all the time, while the same lactate diffuses out of the blood, keeping the concentration of lactate constant.

When we start exercising so hard that lactate is transported from highly active muscles into the blood, we may after a little time measure lactate concentrations above the basal concentration in arterial blood. To prevent accumulation of lactate in the blood, more lactate diffuses into the heart, the liver and skeletal muscles with oxygen present, so that the flux of lactate into the blood equals the flux of lactate out of the blood. In this way, the concentration of lactate is kept constant even though the production is high in some muscles.

It’s important to point out that oxygen used in removal of lactate, ref. Figure 3.6, comes in addition to the oxygen demanded by the active muscles. The body will try to keep the lactate concentration as low as possible by using lactate as an energy source. We emphasize that lactate both can be used as an energy source to produce ATP (which consumes oxygen), or be stored as glycogen for later use (not using oxygen). We don’t know how large fraction of the lactate that is removed by aerobic glycolysis, or if this fraction changes with intensity. This makes it complicated to estimate the amount of oxygen used in breakdown of lactate. We also recall from section 3.2 how chemoreceptors detect lowered pH
in arterial blood to regulate respiration, which causes even more usage of oxygen.

![Figure 3.7](image.jpg)

**Figure 3.7:** The figure shows typical results from a lactate profile test. In a common procedure, the subject runs for about 4 minutes at a given workload, before the lactate is measured (usually in the fingertip) in the short break for about 1 minute. This procedure is repeated until lactate starts to increase exponentially. The measured lactate is shown as blue dots in the figure, where the x-axis shows the workload the subject has completed before lactate was measured. The lactate threshold is often said to be 4 mmol/l, but may vary between subjects. In addition, there is no standard procedure to calculate the threshold from the lactate profile test. In this case, assuming that the lactate threshold is exactly at 4 mmol/l, the threshold power ($p_T$) would for this subject be about 280 watt, as shown by the red stippled line.

### 3.6.3 Lactate threshold and threshold power

There is a maximal rate of how much lactate the blood is able to get rid of. At some point for increasing workload, the production rate of lactate exceeds the removing rate from the blood. This point is known as *Maximal Lactate Steady State workload* (MLSSw) [10], or we could simply name it $p_T$, as in “threshold power” in cycling. Below $p_T$, the lactate concentration in arterial blood reaches a steady-state after some time. Above $p_T$, lactate will accumulate, and a drop in pH locally and in arterial blood eventually make us unable to remain at the same effort. We name the highest possible steady-state lactate concentration $La_T$, where we define $La_T$ to occur at the exact same workload as $p_T$.

A study on elite cyclists shown a $La_T$ of about 4.5 ±1.0 mmol/l [8]. However, there are large individual variations in $La_T$, ranging from 2 – 8 mmol/l in capillary blood [10]. Although $La_T$ may vary substantially among people, it’s widely accepted to use 4 mmol/l as the threshold value for lactate in the literature [32].
Capillary finger blood samples are often used when lactate is measured during activity, and gives a good measurement of arterial blood lactate [66].

### 3.6.4 Removal of lactate at different intensities

Since lactate might be used as an energy source, studies have shown that exercise involving large muscle groups (like cycling), affects how fast lactate is removed [53]. A study by Belcastro and Bonen [7] (1975) investigated how fast lactate was removed during cycling between rest and intensities above \( p_T \). They found an optimal removal rate at 32% of \( VO_{2\text{max}} \), as shown in Figure 3.8.

![Figure 3.8](image)

**Figure 3.8:** From the figure we observe how the removal of lactate is low at rest (10% of \( VO_{2\text{max}} \)). The maximal removal of lactate occurs at 30 – 40% of \( VO_{2\text{max}} \). At high intensities about 70 – 90% of \( VO_{2\text{max}} \), the lactate may accumulate, such that the removal is zero, Belcastro and Bonen [7] (1975).

We also observe from Figure 3.8 that the removal of lactate is relatively slow at rest\(^\text{19}\), and the intensity of exercise must be about 60 – 70% of \( VO_{2\text{max}} \) before the removal of lactate is less than at rest. The removal rate of lactate is shown to be independent of cardiovascular fitness, both at rest or at any given absolute workload [21].

### 3.6.5 Lactate and the threshold concept: summary

There are several interesting concepts to note from this section from a modeling viewpoint. The most important is how the heart delivers an additional amount of

\(^{19}\)About 10% of \( VO_{2\text{max}} \) equals rest
Section 3.6 Lactate and the threshold concept

Oxygen because of lactate production, in addition to the oxygen used to perform work by active muscles. Lactate has a basal concentration in blood, which rises exponentially above a specific workload. The fact that lactate is removed faster at low to medium intensities than at rest, is also important to understand lactate dynamics. Lactate dynamics are highly nonlinear, as described in the text.

Because of the considerable effect on oxygen demand in the body caused by lactate [34], it might be reasonable to introduce a component in a HR model with similar properties. The workload threshold, $p_T$, is a predictor of cardiovascular fitness. The test described in Figure 3.7 is the traditional (but cumbersome) way to predict $p_T$. However, if we recall subsection 3.3.3, a measure of $HbO_2\%$ might be an alternative way to measure $p_T$. We might be able to construct and tune a mathematical model to predict $p_T$ at the expected workload in different subject, under the assumption that $p_T$ occurs at the same intensity in all subject.
Chapter 4

Previous work on heart rate modelling

In recent years, a few scientists have tried to develop mathematical subject-independent models to simulate HR for some sort of intensity input. In this section I will present the most relevant research.

4.1 A model by Cheng et al. (2008)

Cheng et al. [15] (2008) presented a model formulated as a system of two nonlinear differential equations with treadmill speed as input, combined with a linear main formula that computed HR for treadmill exercise. Their model was given by:

\[ \dot{\nu}_1(t) = -a_1 \nu_1(t) + a_2 \nu_2(t) + a_2 p(t)^2 \]
\[ \dot{\nu}_2(t) = -a_3 \nu_2(t) + \phi(z(t)) \]
\[ z(t) = \nu_1(t), \quad \phi(z(t)) = \frac{a_4 \nu_1(t)}{1 + e^{-(\nu_1(t) - a_5)}} \]
\[ \nu(t) = a_6 \dot{\nu}_1(t) + \nu_{\text{min}}, \]

where \( \nu \) is modelled HR and \( p \) is the workload (treadmill speed) applied to the system at time \( t \). The model was loosely connected to possible physiological processes, where one component (\( \nu_1 \)) was assumed to be fast and connected to nervous systems central response to exercise, while the other component (\( \nu_2 \)) was slower and assumed to be connected to several peripheral effects in the body, leading to a slow upward drift in modelled HR for medium to high intensity. However, six parameters (\( a_1, ..., a_6 \)) with unclear physiological meaning were obtained from the mean of six different subjects, since the goal of their study was to design a treadmill controller system. The model didn’t extract individual information from HR data, and the model was only demonstrated for light to medium exercise intensity.
4.2 A model by Lefever et al. (2014)

Lefever et al. [43] (2014) presented a time-variant\footnote{Time-variant means that something do change in time. Time-invariant means that something doesn’t change is time.} model specifically developed for cycling with power as input. This model used a multivariable dynamic transfer function, with two free parameters that continuously were adjusted to fit the data. The general form of their model was:

\[
\nu(t) = L(z^{-1})p(t) + \xi(t),
\]  

(4.3)

where \(\nu\) is modelled HR, \(L\) is the transfer function, \(p\) is input power and \(\xi\) is the uncertainty. The fit to the HR data was very good in the presented results \((R^2 = 0.89 \pm 0.07)\), but the two free parameters changed significantly during the exercise, and had no physical interpretation. In addition, when two parameters are changed at once, we risk that the change in one of the parameters affects the change in the other parameter. They also tried to fix the free parameters, but concluded that their time-variant model was significant better to fit HR data than a time-invariant model.

4.3 A model by Zakynthinaki (2015)

Zakynthinaki [65] (2015) presented a model developed for treadmill running aiming to predict cardiovascular fitness. The model was given by a differential equation consisting of a product of three factors:

\[
\dot{\nu}(\nu, \nu(0), \lambda, p, t) = f_{\min}f_{\max}f_D
\]

\[
f_{\max}(\nu, \lambda) = 1 - e^{-\left(\frac{\nu - \nu_{\max}}{\alpha_1}\right)^2}
\]

\[
f_{\min}(\nu, \lambda) = 1 - e^{-\left(\frac{\nu - \nu_{\min}(\lambda)}{\alpha_2}\right)^2}
\]

\[
f_D(\nu, \nu(0), p, \lambda, t) = -d(\lambda)(\nu - D(\lambda, p, t)),
\]  

(4.4)

where \(\nu\) is modelled HR and \(p\) is the workload input (treadmill speed). Two of the factors \((f_{\min} \text{ and } f_{\max})\) faded out the derivative of HR towards minimum and maximal HR, which prevented the model to get non-physiological values for HR. The third factor \((f_D)\) was a “demand” function with treadmill speed as input, that controlled the dynamics between the two extremals. \(f_D\) was a sum of a linear component and a nonlinear lactate component, with a common time constant \((d)\) controlled by one parameter \(\lambda\). The nonlinear lactate component implemented a slow drift in modelled HR towards \(HR_{\max}\), as long as the intensity was above the threshold workload (treadmill speed). \(\lambda\) was optimized to make the model
fit the HR data as good as possible, and could take values between 0 and 1. \( \lambda \) was assumed to reflect cardiovascular fitness, where 1 was excellent.

The results lack statistical power since the model only was applied to one person. In addition, the model was somewhat ad hoc, since there were different expressions for the lactate component under activity and recovery, and it was unclear how the model would behave with changing and discontinuous workload input. The model was only applied to one step up or one step down in the article.

4.4 A model by Mazzoleni et al. (2016)

In 2016, a model was published by Mazzoleni et al. [46]. This model was developed specific for cycling with power \((p)\) and cadence \((\omega)\) as input. The model was constructed as a nonlinear differential equation with a mathematical approach, and was able to predict HR response without knowing anything about the fitness of the subject a priori. The model was based on the model by Zakynthinaki [65] (2015) described above, but the nonlinearities from the lactate model by Zakynthinaki were replaced with a second order multivariable Taylor series expansion \((f(p, \omega))\). In addition, the model incorporated a steady-state value of HR below \(HR_{\text{max}}\) for all exercise intensities. Their model was formulated as:

\[
\begin{align*}
\dot{\nu} &= A \left( \nu - \nu_0 \right)^\alpha \left( \nu_x - \nu \right)^\beta \left( D - \nu \right)^\gamma \\
\dot{D} &= B \left( f(p, \omega) - D \right)^\eta \\
f(p, \omega) &= c_0 + c_1 p + c_2 \omega + c_3 p^2 + c_5 p \omega,
\end{align*}
\]

where \(\nu\) is the modelled HR. The results in the article are very impressive, since the model fits the HR data very good \((R^2 = 0.90 \pm 0.05)\). In addition, the parameters were time-invariant. They also concluded that a model with cadence as input, gave a better estimate than a model only taking power as input. However, due to the mathematical approach, there were as much as eleven free parameters that had to be optimized to make the model fit the HR data as good as possible. The free parameters had no obvious physical interpretation, and more work was needed to extract valuable information of the HR response from the optimized parameters.

4.5 Summary of previous models

All present work on HR modelling have strengths and limitations. The challenge is to develop a mathematical model that fits HR data well, and at the same time
extracts physical interpreted parameters from the HR data that are proven to say something about physical condition and/or cardiovascular fitness, preferably without knowing anything about the cardiovascular fitness of the subject a priori. In the development of a new mathematical model, there are a lot of inspiration and ideas to obtain from the present work mentioned above. We want our mathematical model to be based on physiological principles, since this seems like the most advantageous approach for extracting physiologically interpreted parameters from HR data. As explained in chapter 2, resting HR and time constants of the system might be of interest to predict physical condition. If we are able to predict $p_T$ from HR data after cycling workouts, we might also extract the cardiovascular fitness of the subject.
Chapter 5

Mathematical and numerical tools for data analysis

5.1 Linear response theory

Linear response theory is an important field in physics and engineering. It’s used in everything from quantum mechanical systems to the study of electrical circuits, but also in a lot of other areas, such as heat and pressure systems, NMR spectroscopy and seismology. The strengths of linear systems are features and properties that are much simpler than in the nonlinear case, and a lot of mathematical techniques, such as Laplace transform and Fourier transform, can be availed for simple mathematical analysis. The theory in this section is found in a compendium by Johansen and Måløy [37] (2015).

5.1.1 Properties of LTI-systems

We often want to look at the special case where the system dynamics remain constant at all times. Such systems are known as Linear Time-Invariant systems or simply LTI-systems. “Linear” means that the system responds with the same relative change for all sizes of stimulus or excitations \( e(t) \).

If the response \( r(t) \) of an LTI-system happens immediately to an excitation, it’s mathematically expressed as:

\[
r(t) = h \cdot e(t)
\]

where \( h \) is a constant. In most cases, this is not the response we observe for physical systems. Usually, there is some delay between the excitation and the observed response. Instead of \( h \) being a constant as in equation 5.1, it can be some sort of “memory”-function or transfer function \( h(t) \). \( h(t) \) weights the contribution to the response from present and earlier excitations in time. The more realistic (but still linear) physical response, can then be written as:
\[ r(t) = \int_{-\infty}^{t} h(t - \tau)e(\tau)d\tau . \]  
(5.2)

The integral above is a \textit{convolution integral}. For intuition, we can physically think of this integral as a reversed and shifted \( h(t) \)-function sliding from \(-\infty \) to \( t \) through \( e(t) \) along the \( \tau \)-axis. In most practical situations, the integral limit starts from 0. Since the actual computation of equation 5.2 often is done by a computer, we should also present the numerical expression:

\[ r[t] = \sum_{\tau = -\infty}^{t} h[t - \tau]e[\tau] , \]  
(5.3)

where the solution is a finite sum.

Linearity also implies that multiple independent stimuli (at the same time) can be added up due to the \textit{principle of superposition}, to give the same total response as the different stimuli would have caused individually. In a more formal way, the principle of superposition is given as:

\[ r(\alpha u + \beta v) = \alpha r(u) + \beta r(v) . \]  
(5.4)

Also, if the system is linear, we can actually integrate the response from a short\(^1\) impulse to obtain the step response. We can then compare the scaled\(^2\) step response with the integrated impulse response to verify that they are the same [24].

"Invariant" means that the system properties are independent of time, which in our case would mean that time constant of the system don’t change in time (time-invariant). If we apply \( e(t) \) and let the system reach a steady-state, and then remove \( e(t) \), we should observe the same response both ways, only in opposite vertical directions. A plot of the upward response together with the horizontal mirrored downward response, is possible to check if they are the same to investigate time-invariance. For a system to be time-invariant, \textit{causality} is a necessity. Causality implies that a given response only is dependent on excitations present and past, not future excitations. Mathematically this is given as:

\[ h(t) = 0 \quad \forall t < 0 . \]  
(5.5)

At last, an LTI-system has to be stable. To ensure stability, the system has to fulfil the following criteria:

\[ \|e(t)\|_{\infty} = \sup\{|e(t)|\} < \infty \]
\[ \|r(t)\|_{\infty} < \infty . \]  
(5.6)

\(^1\) Short compared to time constants of the system.
\(^2\) The step response must have the same integral as the impulse response.
In words, equation 5.6 tells us that as long as the excitation \( e(t) \) on the system is finite, the system response \( r(t) \) will be finite, which secures stability of the system.

### 5.1.2 Common strategies for obtaining \( h(t) \) of an LTI-system

Figure 5.1 shows a typical LTI-system. As seen from the figure, the excitation is transformed by \( h(t) \) to a response. In the lower part of the figure, we can see a typical step response and impulse response from bicycle experiments, where a power input from the pedals are transformed to a HR response. However, \( h(t) \) is unknown, but there are different strategies to obtain \( h(t) \). If we use experimental strategies, we can use step excitation or pulse excitation.

![Figure 5.1](image)

**Figure 5.1:** The upper part of the figure shows a typical LTI-system. An excitation \( e(t) \) is transformed by \( h(t) \) to an observed time-delayed response \( r(t) \). \( e(t) \) above can represent a short bicycle sprint (power input) and \( r(t) \) is a typical observed HR response. \( h(t) \) is unknown, but can be estimated through experiment or numerical curve fitting. In the middle of the figure, a typical step response for a bicycle experiment is shown, while the lower part of the figure shows a typical impulse response.

In the case of step-excitation, we assume an abrupt change \((\Delta e)\) in excitation, and keeping this excitation until the response has reached steady-state at time \( t \). This gives the following:

\[
r(t) = \Delta e \int_0^t h(t - \tau)d\tau .
\]

From equation 5.7 we have that \( h(t) \) is given by:
So, if we perform a step-excitation experiment and record the response, we can use equation 5.8 and the derivative of the response to estimate $h(t)$ for the system.

In the case of pulse-excitation, we again assume an abrupt change ($\Delta e$) in excitation, but this time only for a very short time ($\epsilon$) before we decrease the excitation again. We want the pulse to be as short as possible, and at least much shorter than the time constant of the system. This gives the following integral:

$$ r(t) = \Delta e \int_0^\epsilon h(t - \tau)d\tau . $$

We see from equation 5.9 that the response is obtained from an integral over $h(t)$ for a short time. Under the assumption that $\epsilon$ is much smaller than the time constant of the system, $h(t)$ is essentially constant over the integral. From equation 5.9 we have that $h(t)$ is given by:

$$ h(t) = \frac{r(t)}{\Delta e} . $$

This means that, if we perform a short enough excitation on the system, we can use equation 5.10 to directly compute $h(t)$ from the response.

### 5.1.3 Alternative strategy for obtaining $h(t)$ of an LTI-system

In the theory above, $h(t)$ is carried out from experiments directly. In some cases, for example in a bicycle experiment with power as input and HR as output, the two methods above might give us some challenges. In step-excitation experiments, we need to find $r'(t)$, but the HR response might be noisy and give unstable derivatives along the curve. In pulse-excitation experiments, we avoid derivation of noisy data, but the pulse has to be short compared to the system response, which might be a challenge in a typical bicycle experiment. Instead of the approximate expressions for $h(t)$ given by equation 5.8 and equation 5.10, we could use the general expression equation 5.2 and perform a numerical deconvolution to obtain $h(t)$. However, a noisy signal might cause troubles for a numerical solver, with the risk of getting meaningless results.

A solution to the challenge just described, is to guess the shape of $h(t)$ on a phenomenological basis. We can then perform a numerical convolution using this $h(t)$ according to equation 5.10, and optimize necessary parameters with a computer program. In this way, we have no troubles with noisy data and an approximate function for $h(t)$ can be obtained from any response data, assuming that $h(t)$ is chosen properly. We don’t get the exact $h(t)$ for the linear system, but might get a good approximation with optimized parameters.
In the simplest case, where \( r(t) \) looks like a linear first order system we may choose \( h(t) \) to be:

\[
h(t) = \gamma e^{-\frac{t}{\tau}}.
\]  
(5.11)

If \( r(t) \) is more complicated and acts like a linear second order system, we can choose \( h(t) \) to be:

\[
h(t) = \gamma(e^{-\frac{t}{\tau_1}} - e^{-\frac{t}{\tau_2}}).
\]  
(5.12)

With the second order expression, we are able to get a much better fit in smooth transitions. \( \tau \)-coefficients in the expressions above, might be considered as the time constants of the system. If a first order \( h(t) \) gives a good approximation, there is probably one underlying time constant that controls the response. If a second order \( h(t) \) gives a good approximation, there are probably two underlying time constants that control the response. The optimization should be performed on \( \alpha \) and \( \tau \)-values in the guessed \( h(t) \)-function, and in this way discover the time constants \( (\tau) \) of the system. If a second order expression for \( h(t) \) doesn't give a good fit, there might be more than two underlying time constants. In that case, we can construct more complicated \( h(t) \)-functions with more \( \alpha \)-values and \( \tau \)-values, with the cost of more complexity in the construction of \( h(t) \) and more time-consuming optimization.

### 5.2 Numerical solution of Ordinary Differential Equations

In physics, we usually describe dynamical systems in terms of one or more differential equations. We distinguish between a Partial Differential Equation (PDE) and an Ordinary Differential Equation (ODE). PDEs are often used to describe systems changing in time and space, such as heat distribution and wave motion, while ODEs often are used when the system only is changing in time. For our purposes, we only need ODEs since we don’t have a space dimension. ODEs with first derivatives only, is known as first order ODEs, and the general form and the corresponding initial condition are given by equation 5.13:

\[
y'(t) = f(t, y(t)), \quad y(0) = y_0.
\]  
(5.13)

The right side of the equation is usually referred to as the right-hand side (RHS), and \( f \) is the function we have to develop to describe the system behaviour.

#### 5.2.1 Euler’s method

To solve ODEs numerically, we need a numerical integrator that computes the development in small discrete time steps \( \Delta t \). The simplest numerical integrator
is known as Euler’s method, and is derived directly from the definition of the derivative:

\[ \frac{y(t + \Delta t) - y(t)}{\Delta t} = f(t, y(t)) \]  

\Rightarrow y(t + \Delta t) = y(t) + \Delta tf(t, y(t)) + \mathcal{O}((\Delta t)^2). \]  

The last term in equation 5.15 indicates that the local error of the estimates in each step is proportional with $(\Delta t)^2$, and can be obtained through Taylor expansion. In other words, for every time step we estimate the development of the time series, the local error is accumulating to a global error. In the case with Euler’s method, we have to take extremely short time steps to keep the global error of the estimate low. If the global error becomes too large, we jeopardize that the solver becomes unstable and the solution may go to infinity. The global error of Euler’s method is proportional to $\Delta t$, and the method is then said to be of 1st order.

### 5.2.2 Fourth order Runge-Kutta

In numerical integration, there will always be some sort of error in the estimate, and a lot of different numerical integrators are developed with different strengths and weaknesses. Euler’s method has the strength of being extremely fast, but has a weak precision. The most used numerical integrator in physics is probably Fourth order Runge-Kutta (RK4) given in equation 5.16 [49]:

\begin{align*}
    k_1 &= f(t, y(t)) \\
    k_2 &= f(t + \Delta t/2, y(t) + k_1 \Delta t/2) \\
    k_3 &= f(t + \Delta t/2, y(t) + k_2 \Delta t/2) \\
    k_4 &= f(t + \Delta t, y(t) + k_3 \Delta t) \\
    y(t + \Delta t) &= y(t) + \frac{\Delta t}{6} (k_1 + 2k_2 + 2k_3 + k_4) + \mathcal{O}((\Delta t)^5). 
\end{align*}  

Compared to Euler’s method, RK4 uses four different slopes with different weights to compute the value in the next time step. We notice from equation 5.16 that the local error of RK4 goes as $(\Delta t)^5$, with a global error of 4th order. We get a substantial improvement in accuracy with RK4 compared to Euler’s method when using a small $\Delta t$, with the cost of more computations per time step. However, the error also accumulates with RK4, and in long-term simulations, the error might become large and make the solution unstable.
### 5.2.3 Long term simulations

In long-term simulations, it’s important to keep the error as low as possible. Optimally, we should use a **symplectic** integrator. Symplectic integrators are designed in a way that prevents the error of accumulating\(^3\), although the local error may have a low order of accuracy. A widely used symplectic integrator is the **Verlet algorithm** with local error of 2\(^{nd}\) order and low computational cost. However, all symplectic integrators require coupled equations from second order ODEs, and our system only consist of first order ODEs. Since we aren’t able to use symplectic integrators, we are stuck with non-symplectic integrators such as Euler’s method and different Runge-Kutta methods.

### 5.2.4 Gill’s method

An alternative version of RK4 is **Gill’s method**. This is only a modification of RK4, trying to incorporate round-off errors by weighting the slopes differently [3]:

\[
\begin{align*}
  k_1 &= f(t, y(t)) \\
  k_2 &= f(t + \Delta t/2, y(t) + k_1 \Delta t/2) \\
  k_3 &= f(t + \Delta t/2, y(t) + \Delta t(\frac{1}{2}(-1 + \sqrt{2})k_1 + (1 - \frac{1}{2}\sqrt{2})k_2)) \\
  k_4 &= f(t + \Delta t, y(t) + \Delta t(-\frac{1}{2}\sqrt{2}k_2 + (1 + \frac{1}{2}\sqrt{2})k_3)) \\
  y(t + \Delta t) &= y(t) + \frac{\Delta t}{6}(k_1 + (2 - \sqrt{2})k_2 + (2 + \sqrt{2})k_3 + k_4) + \mathcal{O}((\Delta t)^5).
\end{align*}
\]

A comparison of numerical solvers applied on long-terms simulations, showed that Gill’s method gives stable results much longer than RK4 but with the same short term accuracy [17]. This makes Gill’s method more suitable for our ODE system.

When solving ODEs, we might experience unstable solutions. Equations that give unstable solutions for some numerical solvers, unless the numerical time step is very small, are known as **stiff equations**. A stiff equation often has rapid changes in the solutions, that can be a consequence of rapidly changing input data, such as power from bicycle experiments. **Matlab** offers many different functions to solve ODEs. If the input data is changing rapidly, a **stiff solver** is often necessary to get stable results.

An appropriate function for solving stiff ODEs with **Matlab** is **ode15s**. **ode15s** uses variable order solvers and adaptive time steps. However, in some cases **ode15s** can be slow, even when the stability of the problem might not be a big

\(^3\)Symplectic integrators are often said to conserve the initial energy of the system, and are widely used in simulations of orbital motion.
Figure 5.2: (a) The figure shows a comparison of the numerical solution between the built in Matlab ODE-solver (ode15s) and our own numerical ODE-solver implementing Gill’s method (ODEGill). All parameters are fixed. $\Delta t = 1$ in our own solver, while the time step in ode15s is changing. (b) The figure shows the absolute value of the difference in each solution point between the two solvers. As seen from the figures, the solutions are approximately identical in the two solvers.

problem. Little control of the time step is also a drawback. To deal with those problems, I implemented my own numerical ODE-solver, using Gill’s method with fixed time steps. The implementation can be found in section B.5. The step length requirement is that the time steps are less than the characteristic time of the system. In our case, the solution was always stable as long as the time steps were set to 1 second, but usually also with 2 seconds time steps. All simulations in this thesis are done with 1 second time steps.

5.3 Numerical optimization of free parameters

Since our goal is to extract information from HR data, we need a strategy. One such strategy is to develop a mathematical model with some free parameters, that possesses the same characteristics as the system being modelled. If the model successfully catches the system behaviour, the model may reproduce the recorded system response for the same input. However, for the model to reproduce the data, the free model parameters must be chosen properly.

The natural way to obtain the best parameter values, is to try all combinations of parameter values, compare the modelled response with the actual response for all those combinations, and use an error estimate to pick the parameter combination that gives the lowest error. Of course, it’s impossible to examine all combinations of parameter values (even for only one parameter), since that would give infinitely many combinations. However, a lot of algorithms have been
developed to effectively search for the optimal combination of parameters to a given precision. Such algorithms are known as optimization algorithms.

5.3.1 Properties of optimization algorithms

In the simplest case, optimization algorithms use gradients at the solution to determine in what direction to change the parameters, and how big the parameter changes should be. If the change in the solution is below a predefined value for a little change in the parameters (small gradient at the solution for all parameters), the algorithm stop further searching. If there is only one or two parameters, the algorithm should accurately find the best combination of parameters to desired precision. If we get more parameters to optimize, things become more difficult, and we risk that the solver doesn’t find the true optimal parameter combination.

The difference between optimization algorithms are how they change parameters during the search for optimal parameters, how they try different combinations, and their rule to stop further searching. To reduce the risk of obtaining the wrong optimal combination of parameters, a proper initial guess of the parameters is important. Some algorithms also offer the ability to constrict the range of the parameter values, which often makes the algorithm faster. Optimization of multiple parameters is often very time consuming, and we should always put in some effort to make the optimization as fast as possible.

5.3.2 Computing the standard deviation of the standard errors in fitted parameters

Matlab offers a lot of different functions to optimize parameters. The function I have chosen to use, is a function named fmincon. fmincon is a gradient-based method which offers constrained parameters, and has behaved stable and fast for our problem specification with HR data. In addition to the optimal parameters, fmincon returns the gradient and Hessian matrix at the solution for each of the parameters. These gradient values should be small if the solver has found a minimum, while the diagonal elements of the Hessian matrix can be used to evaluate the sensitivity of different parameters at the solution. We have that the diagonal of the inverse Hessian matrix are the variances ($\sigma^2$) of the optimized parameters [56]. If we name the Hessian matrix $H$, we formally have that:

$$C = H^{-1},$$

where $C$ is the covariance matrix. The variance of the parameters are given by:

---

4I used fmincon with the default Interior-Point algorithm, and tolerance criteria 'TolFun'=10e-16.

5The inverse of the Hessian matrix is often referred to as the covariance matrix, which is a symmetric matrix that says something about the correlation between the parameters.
\[ \sigma_i^2 = C_{i,i}, \]  
(5.19)

where \( i \) is the number of parameters. From the variance we can compute the standard deviation (SD) of the standard errors in the fitted parameters:

\[ SD_i = \sqrt{\sigma_i^2}. \]  
(5.20)

In addition, when optimal parameters are found, we can keep the all parameters fixed except one to evaluate the sensitivity of this parameter. This parameter can be varied around the optimal parameter to investigate how much the solution change. To evaluate how much the solution change, we need an estimate of the error.

---

**Figure 5.3:** The figure shows our procedure to extract parameters from experimental HR data. A main program (red blocks) calls an optimization program (yellow block). The optimization program initializes (green blocks) the routine to repeat in the optimization (blue blocks) for different combinations of free parameters. The optimization gets initial values of free parameters and parameter bounds, which are provided into the built in *Matlab* optimization algorithm *fmincon*. The *fmincon* minimizes the r-value (returned by blue blocks), and the optimization finishes when the stop criteria is reached (small changes in gradient at the solutions). The optimal parameters are then returned to the main program.
5.3.3 Error estimate and goodness of fit

When the optimization algorithm evaluates how good the model fits the data for different parameter combinations, it must have an error estimate \( r \) to minimize. A lot of different error estimates can be applied, but the most common is probably the least squares method. This is simply given as [56]:

\[
r = \sum_{i=1}^{n} (y(t_i) - f(t_i))^2 ,
\]

with \( r \) being the sum of the squared errors at all points in the solution. \( y(t_i) \) is the actual response of the system in point \( i \), while \( f(t_i) \) is the estimate of \( y(t_i) \) in the same point. The optimization algorithm should make \( r \) as small as possible.

Sometimes, some parts of the data might be more important than others, and we wish the optimization to weight those important parts the most. An example could be a dataset where some parts have a lot of important dynamics, while other parts may have much noise or little dynamics. The easiest solution to this problem is to apply a weight function to the error estimate. The error estimate we obtain then is given by:

\[
r = \frac{\sum_{i=1}^{n} \omega(t_i)(y(t_i) - f(t_i))^2}{\sum_{i=1}^{n} \omega(t_i)}.
\]

\( \omega(t_i) \) is the weight function, where we are free to chose the shape. As an example, we can chose \( \omega(t_i) = 10 \) at important parts of the data, \( \omega(t_i) = 1 \) at unimportant parts of the data, and \( \omega(t_i) = 0 \) at parts of the data with a lot of noise. In addition, it’s also possible to thin the data in parts with little dynamics or noise to give more weight to parts with more dynamics. An advanced problem specific algorithm to do this could be developed, but it can be challenging to distinguish between important dynamics and noise.

To decide how good the model actually fits the data with optimal parameters, the coefficient of determination (usually denoted as \( R^2 \)) is often applied. Coefficient of determination is given by [56]:

\[
R^2 = 1 - \frac{\sum_{i=1}^{n} (y(t_i) - f(t_i))^2}{\sum_{i=1}^{n} (y(t_i) - \bar{y})^2}.
\]

Here, \( y(t_i) \) is the actual response of the system in point \( i \), while \( f(t_i) \) is the estimate of \( y(t_i) \) in the same point. \( \bar{y} \) is the mean of all \( y(t_i) \)-values. We recognize the numerator as \( r \) given in equation 5.21. \( R^2 \) can obtain values between 0 and 1, where 1 indicates a perfect fit.

The optimization algorithm will search for the combination of parameters that minimizes the error estimate, but we want large values of \( R^2 \). Since we want to optimize with respects to \( R^2 \), we must optimize only the last term of \( R^2 \) (in other words skip “1–” in equation 5.23).
5.4 Filtering of data

Collections of biological data might be noisy, but different techniques can be applied to reduce this noise. When much of the noise is removed, the underlying information appears clearer. Reducing the sampling frequency or downsampling the data might reduce some noise, but the best way to do it, is to use a frequency filter. A frequency filter has the property that we (to some degree) can decide which frequencies in the data we want to keep, and which frequencies we consider as noise. At the same time, we have to be careful with which frequencies we remove, since we rarely know exactly what is noise. If we remove too many of the frequencies, we risk removing valuable information.

![Butterworth low-pass filter transfer functions](image)

**Figure 5.4:** The figure shows Butterworth low-pass filters of different order $n$. We observe the smooth and almost flat passband in the white area to the left, and the order dependent decay in the stopband in the grey area to the right. Here, the cutoff frequency is $\omega_c = 1$, which we observe as a break point in the filter.

A widely used frequency filter is the Butterworth filter [42]. This filter is known for being very flat in the passband, as shown to the left in Figure 5.4. The passband is the range of frequencies we want to have left after the signal has been filtered. The frequency band we want to let out, is known as the stopband. A perfect filter should let all wanted frequencies through with the same sensitivity (flat passband), and stop all unwanted frequencies. This is however impossible.

If only high frequencies are of interest, we should use a high-pass filter that lets high frequencies through. If only low frequencies are of interest, we would choose a low-pass filter. If we don’t want high or low frequencies, we should use a
bandpass filter. Which filter we choose dependents on the data we want to filter. In our case with biological data, it’s highly likely that we get high frequency noise in the data. Then we have to choose a low-pass filter. The normalized transfer function for a Butterworth low-pass filter is given by equation 5.24 [42]:

\[
G(\omega) = \frac{1}{\sqrt{1 + (\omega/\omega_c)^{2n}}},
\]  

(5.24)

where \(G\) stands for gain, \(\omega\) is frequency, \(\omega_c\) is the cutoff frequency, and \(n\) is the order of the filter. A plot of equation 5.24, with \(n = 1, \ldots, 5\) and \(\omega_c = 1\), shows typical Butterworth low-pass filters, where a low value of \(G(\omega)\) implies low passing of frequencies. The white area to the left of Figure 5.4 is the passband, restricted by the cutoff frequency \(\omega_c\), while the the grey area to the right is the stopband. We observe the almost flat passband, as desired. The steepness of the stopband is determined by the order of the filter, where a higher order gives a steeper stopband. The stopband is reduced by \(20 \times n \text{ dB/decade}\).
Chapter 6

Sensors

6.1  *Garmin Premium* heart rate chest strap

We were using a *Garmin premium chest strap* to record HR during cycling experiments. The strap is carried around the chest, with two areas with rubber where electrodes are localized. The electrodes are able to detect the electrical signal originating from the SA node by measuring the R-wave from a heart contraction. A small computer unit is attached to the strap to process the data detected by the electrodes. The computer unit computes means of R-R intervals to calculate HR given in unit *beats/min*, but the algorithm by *Garmin* for computing HR is proprietary. The calculated HR is transmitted every second to a *Garmin* device (*Garmin Edge 1000*) via ANT+\(^1\), and then displayed and stored locally on the device. Experiments by others have shown good accuracy for HR chest straps compared to reference data from ECG \((R^2 = 0.99)\) [4].

![Garmin premium chest strap](image)

*Figure 6.1:* Garmin premium chest strap

\(^1\)Short distance wireless technology.
6.2 **Garmin Vector** power and cadence pedals

We used *Garmin Vector pedals* to record power and cadence during cycling experiments. The pedals use *Piezoresistive String Gauges* to detect changes in electrical resistivity when mechanical strain is applied. Eight string gauges are placed inside the pedal to detect the slope of the pedal bending, which correlates very well to the power applied to the pedal. We tightened the pedals with recommended torque (34-40 N-m) and followed other instructions in the manual [2] to get correct readings from the pedals. *Garmin* claims power accuracy within ±2 %, which is precise enough for our purposes. The estimated power and other metrics are transmitted to a *Garmin Edge 1000* via ANT+.

![Figure 6.2: Garmin Vector pedals](image)

6.3 **Moxy** muscle oxygen instrument

We were using *Moxy NIRS monitor* to estimate oxygenation locally in muscle tissue continuously during experiments. "NIRS" stands for *Near-Infrared Spectroscopy*. The *Moxy* unit was attached to the skin, and it must be adequately covered to shut out surrounding light. On the part of the monitor that is in contact with the skin, there is a near-infrared-light emitter which emits light with wavelengths from 630-850 nm, which can penetrate about 2 cm into biological tissue. There are also two detectors at 12.5 mm and 25 mm from the emitter to receive the emitted signal that has travelled through the tissue.

Hemoglobin bound to oxygen (oxyhemoglobin) have a different absorption spectra than hemoglobin not bound to oxygen (deoxygenoglobin), as shown in Figure 6.3. In other words, oxyhemoglobin and deoxyhemoglobin absorb different amounts of light for different wavelengths. *Beer-Lambert law* is given as:

$$\log \frac{I_0}{I_1} = elc.$$  \hspace{1cm} (6.1)
Figure 6.3: Hemoglobin bound to oxygen (oxygenated Hb, red line) has a different light absorbance spectra than hemoglobin not bound to oxygen (deoxygenated Hb, blue line) [1]. We observe that deoxyhemoglobin absorbs more light at low wavelengths than oxyhemoglobin. At the longest wavelengths emitted from Moxy, oxyhemoglobin absorbs a little more light than deoxyhemoglobin. Moxy is able to analyze the light that has traveled through tissue, and estimates the ratio between oxyhemoglobin and deoxyhemoglobin to predict the fraction of Hb bound to oxygen ($HbO_2\%$).

Here, $I_0$ is the intensity of emitted light, $I_1$ is the intensity of detected light, $\epsilon$ is (in this case) molar absorptivity\(^2\) of oxyhemoglobin or deoxyhemoglobin, and $l$ is the length of the path the light has traveled through the tissue. See the right part of Figure 6.4 for an overview of different quantities in Beer-Lambert law.

To us, $c$ is the number of interest in equation 6.1, which is the molar concentration of oxyhemoglobin or deoxyhemoglobin in the tissue. Moxy knows $I_0$ and $\epsilon$, detects $I_1$ for four different emitted wavelengths, and then uses Beer-Lambert law to calculate the molar concentration of oxyhemoglobin and the total molar concentration of hemoglobin. The ratio between these two quantities gives an estimate of percentage of hemoglobin bound to oxygen in muscle tissue.

We referred to fraction of hemoglobin bound to oxygen in blood as $HbO_2\%$ in section 3.3. The equivalent to $HbO_2\%$ in muscle tissue with a mix of venous and arterial blood, is named $SmO_2$ by the Moxy-developers. $SmO_2$ can hold values from 0-100%. Since there is a mix of arterial and venous blood in muscles, the readings by Moxy cannot tell us anything about $HbO_2\%$ in arterial or venous

\(^2\)Molar absorptivity tells us how chemical species absorb light at different wavelengths, and values are found experimentally and available in literature.
blood distinctively, but the expected drop in $Hb_0^2\%$ in venous blood at high intensities, should be observed as a drop in the overall $Hb_0^2\%$ ($SmO_2$). However, there are many complications due to different light travel paths, as shown to the left in Figure 6.4. The details about $SmO_2$ is calculated by Moxy is proprietary, but the most important physics about how it works should be covered in this section.

Figure 6.4: The figure to the left illustrates how Moxy works. Light is emitted and travels through skin, fat and muscle tissue, before some of the light is collected by Moxy at two different travel lengths. The combination of fat and muscle tissue complicates the measure of $SmO_2$, but Moxy claims that their sophisticated algorithm can handle such challenges [1]. The figure to the right illustrates how light is absorbed in muscle tissue, and clarifies different physical quantities used in Beer-Lambert law in equation 6.1.

In the simplest case, only two wavelengths need to be emitted in NIRS to measure concentration of oxyhemoglobin, for example 760 nm and 850 nm. At 760 nm, deoxyhemoglobin has higher absorbency than oxyhemoglobin, as seen from Figure 6.3. At 850 nm, oxyhemoglobin has higher absorbency than deoxy-hemoglobin. The difference in detected signal/light intensity (signal at 760 nm minus the signal at 850 nm) will change with changes in the concentration of oxyhemoglobin, and the sum signal/light intensity (signal at 760 nm plus the signal at 850 nm) will change with changes in overall hemoglobin concentration [47]. The ratio between these quantities would then be a simple estimate of the quantity named $SmO_2$ by the Moxy-developers.

The Moxy unit should be attached to the most active muscles for the specific activity to obtain the most relevant information of muscle oxygenation. In cycling we attached Moxy to the calf, or more precisely Gastrocnemius. The Moxy-developers have suggested Vastus Lateralis, on the outer thigh, but readings in this position gave inconsistent results in our experiments. It should be mentioned that if the layer of fat where the monitor is attached is close to or more than 2 cm thick, readings of $SmO_2$ are not possible. This was however not a problem for us. The signal received by the detectors is processes by the computer inside Moxy, before the data is stored locally and optionally transmitted via ANT+ to an ANT+ receiver.
6.4 \textit{Lactate Pro 2} lactate measure instrument

To measure lactate concentration in capillary blood, we used \textit{Lactate Pro 2} (LT-1730) by Arkray. The subject gets a little sting in a finger, and we squeeze a little drop of blood\footnote{Only 0.3 \(\mu l\) of blood is needed per sample.} out of this finger. A disposable strip is plugged into \textit{Lactate Pro 2} and then brought into contact with the drop of blood to collect a blood sample. The strips contain a reagent that reacts with lactate in the blood sample, producing a small electrical current that is proportional to the lactate in the blood sample. \textit{Lactate Pro 2} uses this current to calculate the lactate concentration with good accuracy, shown in independent verification experiments (overall standard error of 3.3\%) \cite{11}. However, no accuracy information is given by the manufacturers.

There are different methods for measuring lactate concentration in blood since blood consists of both blood cells and blood plasma. This may lead to confusion, since basal values and threshold values for lactate concentration may vary among measuring methods. Some lactate instruments measure lactate concentration in
blood plasma only, some in blood cells, and other in both blood cells and blood plasma (whole blood) [23]. \textit{Lactate Pro 2} measures whole blood lactate concentration, and shows good accuracy compared to reference measurements [30]. The well-known basal and threshold lactate concentrations around 1 mmol/l and 4 mmol/l respectively, used in most literature on lactate, are based on lactate concentration in whole blood. \textit{Lactate Pro 2} should therefore estimate comparable values to values in most literature.

### 6.5 \textit{Braun ThermoScan 5} IR thermometer

As a measure of body temperature during exercise, we used \textit{Braun ThermoScan 5} (IRT 6020) IR thermometer. The unit has a probe that is inserted into the ear canal, and the ear (tympanic) temperature is measured immediately when a button is pushed. Measured body temperature may vary substantially between measurement method and where on the body the temperature is measured. The absolute value of the temperature is of little importance to us, since we are only interested in relative changes in body temperature. However, since the inner ear shares blood supply with the temperature control center in the brain, \textit{Braun} claims that IR measurements in the ear gives a precise and responsive estimate of the real core temperature in the body (body core temperature).

![Braun ThermoScan 5 IR thermometer](image)

\textit{Figure 6.7:} \textit{Braun ThermoScan 5}

IR thermometers work such that infrared (IR) light is collected by the probe inserted into the ear canal. The wavelength of the received IR light is calculated to give a direct measurement of the temperature. Under the assumption that the room temperature is between 10-40°C, \textit{Braun} claims in the manual an accuracy of ±0.2°C and a clinical repeatability of ±0.14°C.
Chapter 7

Test protocols and standard tests

7.1 General protocol

7.1.1 Formalities and information about participants

The criteria for participating in the study was being a male who exercises at least once a week. To participate in the study, each subject had to read and accept a consent form (ref. Appendix C), which described how personal data is treated and their right to withdraw from the study at any time. When signing the consent form, the subjects also confirmed that they didn’t have any known heart disease. We got approval to perform experiments on humans by Regional komite for medisinsk og helsefaglig forskningsetikk REK sør-øst-Norge.

A second scheme was filled out (ref. Appendix D), where the subjects described their short term and long term physical activity, and ranked their own cardiovascular fitness (independent of activity) from 1-10, with 10 as world class. Some subjects didn’t do cycling in their training regularly, while some did. The participants ranged from good cardiovascular fitness to world class athletes in cross-country skiing. We consciously chose subjects who exercise regularly, since some of the physical tests were very exhausting. This was to prevent recruited subjects from not being able to complete different tests. A summary of personal information of participants in the study is given by Table 7.1. The "MAP"-value will be explained in the next section.

7.1.2 Experimental setup

The tests were performed in a laboratory at University of Oslo, with good possibilities for regulating the room temperature with a large window. The subjects were able to by preference to open or shut the window to regulate temperature, so all tests were performed in comfortable temperatures about 15-20°C to prevent freezing or overheating. All tests were performed on the same road bicycle.
Table 7.1: The table summarized personal information about subjects that participated in the study. "MAP" is a quantity obtained from experiments. "Own ranking" are how subjects rated their own cardiovascular fitness independent of activity.

(Errida) placed on a cycle roller (Tacx Satori) with a magnetic brake on the back wheel. The experimental setup is shown in Figure 7.1.

Figure 7.1: To the left we have a picture of the experimental setup during laboratory tests. To the right we see a picture of a subject during a test. We observe the placement of Moxy at the calf and the screen in front of the subject.

Since we used a traditional bicycle without the possibility of fixing resistance, the subjects themselves had to keep track of the power they applied to the pedals. The resistance during tests was regulated by the gears on the bicycle by the subjects themselves, and they were at all times free to choose which cadence felt
natural for them to achieve optimal performance. In this way, the experimental setup was very similar to the situation we face in outdoor cycling.

To make it easy for the subjects to follow the desired intensity/power in the test protocol, we used a software named Peripedal. Peripedal made us able to construct predefined test protocols on screen. Peripedal showed present power applied to the pedals and the desired power at the same time on a screen in front of the subjects. All other metrics collected during the experiments were also shown in real-time to the subjects.

Before each test, Moxy was carefully placed on one of the subjects calves. Placing of Moxy is explained in more detail in section 6.3. The electrodes on the HR chest strap were humidified to get stable readings of HR from the beginning of the exercise. The power and cadence pedals were calibrated using Garmin Edge 1000 before each test. Data was collected and stored by Peripedal during laboratory experiments. As a backup, data was also collected and stored by Garmin Edge 1000 and Moxy. Since the data from Moxy couldn’t be stored directly on Garmin Edge 1000, we had to synchronize the recording of data at the beginning of each test between the two units. We also experienced that small parts of data stored locally on Moxy could disappear without any reason. We therefore preferred to collect data with Peripedal. However, Peripedal cannot be used in the field since that would require a laptop, so we had to use Garmin Edge 1000 and Moxy during outdoor tests.

7.2 MAP-test

Our MAP-test was inspired by a protocol developed by Kuipers et al. [41] (1985), and aimed to determine a MAP-value and HR$_{\text{max}}$. MAP stands for Maximal Aerobic Power, and was defined as the highest power obtained in our MAP-test protocol. The value of MAP was assumed to be the power output that maximized HR for a given subject, and a protocol similar to the protocol by Kuipers et al., was verified to work (in the sense of obtaining MAP) in the field (compared to laboratory tests) by Gonzalez-Haro et al. [29] (2007).

Our MAP-protocol was a "ramp-test". Before the start of each test, the subject was resting by sitting on the bicycle for 2 minutes, where the median HR the last minute was considered to be the approximate HR$_{\text{min}}$ while sitting. The test started with 10 minutes at 100 watt workload as warm-up, and then the first step was also at 100 watt for 2.5 minutes (150 seconds), before we increased the demanded power with 25 watt each 2.5 minutes until exhaustion. The subjects had to look at the current power on the screen and try as good as possible to meet the demanded workload, shown by Peripedal on the screen in front of them. MAP was calculated at the last step, adding the fraction completed of the last step to the previous completed step. The formula for computing MAP yields:
\[ \text{MAP} = p_{\text{prev}} + 25 \times \frac{t_{\text{step}}}{150}, \]  

(7.1)

where \( p_{\text{prev}} \) = "demanded power on last completed step", and \( t_{\text{step}} \) = "time completed on last step". As a simple example, if the subject completed 30 seconds on the step with 325 watt as demanded power, the calculated MAP-value would be: \( 300 + 25 \times \frac{30}{150} = 305 \) watt. In Figure 7.2 the MAP-test protocol is shown for a subject obtaining a MAP-value of 350 watt, just completing the step at 350 watt.

**Figure 7.2:** The figure shows the MAP-test protocol for a subject that obtains a MAP-value equal to 350 watt. After 10 minutes of warm up, the test increases the demanded workload with 25 watt every 2.5 minutes. The subject tries to complete as many steps as possible until exhaustion. If the subject isn’t able to fulfil the demanded workload within 5 watt on average on the present step, the test is aborted and the MAP-value is computed. The highest measured HR during the test is assumed to equal HR\(_{\text{max}}\). Before the start of each test, the subject rests by sitting on the bicycle for 2 minutes, where the median HR the last minute is considered to be HR\(_{\text{min}}\).

If the subject was not able to fulfil the demanded power on the last step, but continued pushing, the value of MAP was calculated at the point of this step where the demanded power was not fulfilled within 5 watt on average. The reason for steps of 2.5 minutes, is that we wanted HR to stabilize on each step,
at least below $p_T$. The average HR on the last 60 seconds of each step was defined as the steady-state HR for the subject on the corresponding step. In addition, ear temperature was measured\(^1\) with *Braun ThermoScan 5* before and after the warm-up, and after that every 2.5 minutes (after each step) to get a corresponding temperature to each steady-state HR.

From the results of this test we are able to plot HR steady-state values against power, to explore how the HR responds to increasing power. We also obtain the MAP-value and $HR_{\text{max}}$ that are individualized input parameters in our model, and the MAP-value was used in later experiments to customize intensity for different subjects. In addition to the HR response with increasing intensity, we also explore how the muscle oxygen changes in the calf of the subjects, with the hope of finding a pattern that might detect $p_T$, as outlined in section 3.6. Since we collect ear temperature after each step, we are able to plot temperature against time or power to investigate how the temperature changes during exercise. The MAP-value also predicts the cardiovascular fitness of different subjects, which could be an important factor to HR response and muscle oxygen readings.

### 7.3 Depletion-test

Our *Depletion-test* was very similar to the MAP-test, but aimed at investigating different properties of the HR response. In the Depletion-test, we wanted to investigate the long term HR response at a constant intensity above $p_T$. To verify that the subject actually had been above $p_T$, lactate was measured\(^2\) before and immediately\(^2\) after the test. Before the start of the test, the subject was resting sitting on the bicycle for 2 minutes, where the median HR the last minute was considered to be the approximate $HR_{\text{min}}$ while sitting. The Depletion-test started with a warm-up for 10 minutes at 100 watt, then the first step was at 100 watt for 2.5 minutes, before we increased the demanded power with 25 watt each 2.5 minutes. However, this time we were not increasing the demanded power until exhaustion. From the MAP-value obtained in the MAP-test, we computed the workload that equaled $0.9 \times \text{MAP}$, a workload we assumed to be above $p_T$. When the demanded workload reached the step below $0.9 \times \text{MAP}$, this step was completed, but the next step only increased to a workload of $0.9 \times \text{MAP}$ with "unlimited" duration. The test was aborted if the subject didn’t remain at $0.9 \times \text{MAP} \pm 5$ watt on average the last 30 seconds. Ear temperature was measured with *Braun ThermoScan 5* before and after the warm-up, and after that every 2.5 minutes until end of the test.

We can clarify the protocol with an example. If we assume that the subject got a MAP-value of 350 watt on the MAP-test, we get $0.9 \times \text{MAP} = 315$ watt. This

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\(^1\)Temperature was only measured in some of the experiments, since we didn’t have access to the IR thermometer in the beginning of the study.

\(^2\)Immediately means in this case less than 1 minute after end of test.
means that the subject at the Depletion-test should complete all step up to 300 watt (including 300 watt), before the subject is encouraged to keep a workload of 315 watt for as long as possible. Under the assumption that the workload of the last step is above $p_T$, the subject will eventually (in typically less than 20 minutes) be exhausted. A typical Depletion-test for a subject with MAP-value at 350 watt is shown in Figure 7.3.

![Figure 7.3](image)

**Figure 7.3:** The figure shows the Depletion-test protocol for a subject with MAP-value equal to 350 watt. After 10 minutes of warm up, the test increases the demanded workload with 25 watt every 2.5 minutes, until the subject reaches the last step below $0.9 \times \text{MAP}$. After that, the subject has to remain at the same workload ($0.9 \times \text{MAP}$) as long as possible until exhaustion. The test is aborted when the subject isn’t able to remain at $0.9 \times \text{MAP}$. The inherent $\text{HR}_{\text{max}}$ should theoretically be the same as in the MAP-test. An estimate of the resting HR while sitting on the bicycle ($\text{HR}_{\text{min}}$), is measured two minutes before the start of the test.

From the Depletion-test we obtain important information about HR dynamics at high intensity with a workload above $p_T$, with much longer duration than each step of the MAP-test. The Depletion-test will discover if HR stabilizes or increases toward $\text{HR}_{\text{max}}$ (found in the MAP-test) for a workload above $p_T$. It’s therefore important to us, from a modelling perspective, to investigate how HR behaves above $p_T$. We recall from chapter 4 that Mazzoleni et al. [46] (2016) assumed that HR reaches a steady-state below $\text{HR}_{\text{max}}$ for all exercise intensities. Since the increase in lactate is continuously above $p_T$, and since lactate might introduce nonlinearities, this assumption needs further investigation. If we find HR to not stabilize above $p_T$, we can take advantage of this property to predict
Section 7.4 Threshold-test 69

cardiovascular fitness. In addition, the ear temperature data makes us able to explore how the temperature changes at a constant workload (0.9×MAP) above $p_T$.

### 7.4 Threshold-test

The *Threshold-test* was very different from the two tests described above. The aim for this test was to investigate how the muscle oxygen in the calf behaves just above and below what we assume is $p_T$, obtained from the MAP-test. The test also got some more dynamics than the other tests, which makes it easier to spot trends in collected data.

![Threshold-test protocol](image)

**Figure 7.4:** The figure shows the Threshold-test protocol for a subject with MAP-value equal to 350 watt. The blue lines indicate steps with a workload at 0.7×MAP, while red lines indicate steps with a workload at 0.9×MAP. The subject should be below $p_T$ at blue lines, and above $p_T$ at red lines. The warm up and cool down procedure is equal, so the test protocol is symmetric.

Before the start of the test, the subject was resting sitting on the bicycle for 2 minutes, where the median HR the last minute was considered to be the approximate HR$_{min}$ while sitting. The test started with a 2.5 minutes step at 0.25×MAP. The next step was 2.5 minutes at 0.5×MAP. After this short warm-up, we started the high-intensity sequence that was supposed to be a little below $p_T$ (at 0.7×MAP) and a little above $p_T$ at (0.9×MAP), with steps lasting for 5 minutes. $p_T$ was assumed to be at roughly 0.8×MAP, according to results obtained from the MAP-test. After this sequence around $p_T$, the intensity were
stepped down opposite from what we did in the start of the exercise. How the test
looks like for a test person with a MAP-value of 350 watt is shown in Figure 7.4.

The Threshold-test gives valuable information on how the HR response and
muscle oxygen acts around $p_T$. Also, if there are trends and nonlinearities in the
collected HR data, the response in our symmetric intensity profile would not be
symmetrical when "horizontally mirrored" as mentioned in section 5.1.
Chapter 8

Results from standard tests

8.1 Results from MAP-test

8.1.1 HR data from MAP-test

Figure 8.1a shows raw data from a single MAP-test. The red line is HR, while the grey line is the corresponding power. The short black lines show where the steady-state values of HR are computed, which is the last minute of each step. In this particular dataset, we can observe a little overshoot in HR response in step transitions, especially at the first steps with low workload, before HR reaches a steady-state a little below. At the last completed step (350 watt), it’s unclear if HR reaches a steady-state.

Figure 8.1: (a) A plot of raw HR and power data for one subject during the MAP-test. (b) The normalized steady-state HR for all subjects (n=13) during the MAP-test.

In Figure 8.1b, the steady-state values of all 13 MAP-tests are plotted together. Dots indicate the normalized steady-state values of HR, corresponding
to the black lines in Figure 8.1a. The plot of HR is normalized with respect to heart rate reserve (HRR) given by:

$$\overline{HRR} = \frac{HR - HR_{\text{min}}}{HR_{\text{max}} - HR_{\text{min}}}.$$  \hfill (8.1)

In equation 8.1, $HR_{\text{min}}$ is the value obtained while resting before the MAP-test, and $HR_{\text{max}}$ is the maximal value of HR during the MAP-test. From Figure 8.1b, most of the responses look quite linear. The error bars illustrate the standard deviation in HR the last minute of each step, which looks fairly small at most points for all datasets.

To further investigate the linear relation between HR and power, we can plot raw data of HR and power from all MAP-tests into a histogram, and plot normalized HR against normalized power. Normalized power is given by:

$$\bar{p} = \frac{p}{\text{MAP}}.$$  \hfill (8.2)

A histogram of normalized HR ($\overline{HRR}$) versus normalized power ($\bar{p}$) is shown in Figure 8.2a. The \textit{Matlab} code to make the histogram was borrowed from Øyvind Nøstdahl Glesersen at the University of Oslo \cite{28}. The colour intensity indicates the count of observations in each box of the histogram, while the colour is MAP-value divided by the body mass of the subject. Green colours indicate subjects with better cardiovascular fitness than subjects with red colours. The white line in Figure 8.2a indicates a perfect linear relation between HR and power from rest (0 watt) to MAP. As we observe, most of the MAP-tests give us an almost linear behaviour all the way to MAP, with a weak curvature to the right close to MAP. Figure 8.2b. The response looks the same for subjects with good cardiovascular fitness (green) and a less good cardiovascular fitness (red).

![Normalized HR data for all subjects (n=13) during the MAP-test against normalized power.](a)

![Relative SmO2 data for all subjects (n=13) during the MAP-test against normalized power.](b)

\textbf{Figure 8.2:} (a) Normalized HR data for all subjects (n=13) during the MAP-test against normalized power. (b) Relative $SmO_2$ data for all subjects (n=13) during the MAP-test against normalized power.
8.1.2 SmO\textsubscript{2} data from MAP-test

In Figure 8.2b, SmO\textsubscript{2} data from all MAP-tests (n=13) are plotted against normalized power. Due to large differences in absolute values in SmO\textsubscript{2} readings among different subjects, we had to do some scaling to extract valuable information. The scaling of SmO\textsubscript{2} was done by:

$$\text{Relative } SmO_2 = \frac{SmO_2 - \text{median}(SmO_2)}{100} + 1. \quad (8.3)$$

The subtraction of the median in equation 8.3 removes the relative differences in SmO\textsubscript{2} between subjects. We divide by 100 since the unit of SmO\textsubscript{2} is %, and add "1" as a baseline value. This means that Figure 8.2b shows relative changes in SmO\textsubscript{2} from the baseline at "1" at low intensities.

As we observe from Figure 8.2b, SmO\textsubscript{2} is almost constant until we reach \(\bar{p} = 0.8\), marked with the white vertical line. After \(\bar{p} = 0.8\), it looks like SmO\textsubscript{2} on average starts to drop until the subjects are exhausted. Not all subjects get the clear drop at \(\bar{p} = 0.8\), which is shown as a right-shift in the relative change after \(\bar{p} = 0.8\) for some subjects. The response looks almost the same for subjects with good cardiovascular fitness (green) and a less good cardiovascular fitness (red), but it seems like the drop in SmO\textsubscript{2} is more consequently around \(\bar{p} = 0.8\) for the subjects with best cardiovascular fitness in this study.

![Figure 8.3: (a) Relative ear temperature change during the MAP-test for a few subjects (n=5) against normalized power. (b) Cadence for all subjects (n=13) during the MAP-test plotted against normalized power.](image)
the standard error of ±0.2°C as specified by the manufacturers of the IR thermometer. Before and after the 10 minute warm up, between the first and second data point in each series, we observe little relative change in temperature, and the standard errors overlap in all datasets. The temperature seems to increase quite linear roughly between \( \bar{p} = 0.4 \) and \( \bar{p} = 0.7 \) for all subjects. Around \( \bar{p} = 0.7 \) we observe a steeper increase in temperature than at lower intensities for three of the subjects, while the remaining two have a pretty flat response. The relative change in temperature is roughly between 1-2°C. More intuitively, we could plot temperature against time instead of normalized power, but this was evaluated to be very similar and gave less information. The red and yellow line in Figure 8.3a had considerable shorter duration than the other results (≈ 10 minutes). The remaining datasets had almost the same duration.

Figure 8.3b shows how the cadence varied against normalized power in the MAP-test. All subjects increased the cadence at higher intensities, on average from about 65-85 rpm, which is on pair with the expected optimal cadence from a muscle activation viewpoint [44]. We also observe that the subjects with lowest measured cardiovascular fitness (red) tended to keep both higher and lower cadence than the subjects with best cardiovascular fitness.

8.2 Results from Depletion-test

8.2.1 HR data from Depletion-test

From the Depletion-test we have many results that are quite similar to results from the MAP-test. In Figure 8.4a, we see the raw data of HR and power from one single subject during the Depletion-test, the same subject as in Figure 8.1a. As earlier, the grey line is power, the red line is HR, and the short black lines are the steady-state value of HR the last minute of each step. We make the same observation as earlier, with a small overshoot in HR after step transitions at low intensities. At high intensities, HR seems to not stabilize, and we get a upward drift at constant workload at 0.9×MAP for this subject.

The normalized HR from all 7 Depletion-tests is shown in Figure 8.4b, just like the data from the MAP-test in Figure 8.1b. The reason why two of the lines (red and purple) are separated from the rest of the datasets, is because there was a large gap (roughly 100 watt) in MAP-values, leading to significantly higher intensity at the different workloads for two of the subjects.

From Figure 8.4b it’s hard to see where the last step at 0.9×MAP starts, and we only see the steady-state values.
Figure 8.4: (a) A plot of raw HR and power data for one subject during the Depletion-test. (b) The normalized steady-state HR for all subjects (n=7) during the Depletion-test.

8.2.2 HR step data from Depletion-test

To investigate the HR response at 0.9×MAP for all the subjects, we can plot HR data only from the last step. The results are shown in Figure 8.5, and the subject colour is the same in Figure 8.4b and Figure 8.5. The HR responses in Figure 8.5 are normalized as in Figure 8.1b with equation 8.1, where HR\(_{\text{max}}\) is the value obtained in the MAP-test and HR\(_{\text{min}}\) is the value found before the start of the Depletion-test. The reason for this is that HR\(_{\text{max}}\) is assumed to be inherently the same in both the MAP-test and the Depletion-test, while HR\(_{\text{min}}\) is allowed to change rapidly from day to day. In Figure 8.5 we have used raw data that is filtered with a 2\(^{nd}\) order low-pass Butterworth filter with normalized cutoff frequency \(\omega_c = 0.04\), as presented in section 5.4. The vertical stippled line in Figure 8.5 marks 2.5 minutes into the last step, the same length as previous steps in the test. The lower horizontal stippled line indicates the normalized HR value that corresponds to 0.9×MAP if we assume a linear response in HR versus power all the way to MAP (as suggested by results from the MAP-test), while the upper horizontal line marks HR\(_{\text{max}}\) from the MAP-test. The duration for each subject at the last workload at 0.9×MAP, is seen from the x-axis in Figure 8.5.

We observe from Figure 8.5 that all subjects reached a normalized HR above the expected HR at 0.9×MAP. We observe that some subjects started well below 0.9×MAP, while others were above before they started the last step. Five of the subjects had a large upward drift during the last step, while two of the subjects (purple and dark blue line) had little upward drift. One subject (orange line) reached HR\(_{\text{max}}\), and even got a HR just above HR\(_{\text{max}}\) obtained in the MAP-test. Some of the other subjects (light blue line, yellow line and dark red line) did not reach a steady-state, but the maximal HR was below HR\(_{\text{max}}\). The rest of the subjects (dark blue, purple and green line) reached a steady-state HR below
Figure 8.5: Smoothed and normalized HR response for all subjects (n=7) on the last step at 0.9×MAP at the Depletion-test.

HR\textsubscript{max}, but above the expected 0.9×MAP-line. All subjects were above the lactate threshold. The lactate measured immediately after the Threshold-tests (in mmol/l) was: 12.2 (dark blue), 21.7 (orange), 14.6 (yellow), 14.6 (purple), 7.4 (green), 19.4 (light blue) and 11.2 (dark red).

8.2.3 \textit{SmO\textsubscript{2}} and temperature data from Depletion-test

The \textit{SmO\textsubscript{2}} data from all Depletion-tests plotted against normalized power is given by Figure 8.6a. The \textit{SmO\textsubscript{2}} data is treated as earlier in the MAP-test, using equation 8.3. We clearly see a drop in \textit{SmO\textsubscript{2}} for many of the subjects when workload is kept constant at 0.9×MAP. There is a large variation in the \textit{SmO\textsubscript{2}} response at low intensities, but this is not so important since we are mostly interested in what happens above \(\bar{p} = 0.8\). We cannot see any clear differences between the subjects with respect to measured cardiovascular fitness (MAP/weight), but one subject (orange in the plot) didn’t get a drop in \textit{SmO\textsubscript{2}} as the other subjects did at \(\bar{p} = 0.9\).

Figure 8.6b shows a plot of all 4 Depletion-tests where temperature was measured with \(±0.2\text{°C}\) error bars. Subject colours are consistent with Figure 8.4b and Figure 8.5. None of the subjects changed ear temperature significantly during the 10 minute warm up (between first and second point for each dataset), but had a slow and almost linear increase from roughly \(\bar{p} = 0.25\) to \(\bar{p} = 0.85\). We clearly see an increase in temperature at \(\bar{p} = 0.9\) for three of the subjects, while one subject (purple line) didn’t have a significant change in temperature. The
8.3 Results from Threshold-test

8.3.1 HR data from Threshold-test

The results from the Threshold-test are quite different from the MAP-test and Depletion-test. Figure 8.7a shows the HR response for one subject during the Threshold-test, the same subject as in Figure 8.1a and Figure 8.4a. The red line shows raw HR data, while the grey line shows the raw power data. We observe that HR seems to stabilize at the three steps corresponding to 0.7×MAP, while it’s unclear if HR stabilizes at the two steps corresponding to 0.9×MAP. The short black lines show the mean value of HR the last minute on the steps with workload 0.7×MAP, and HR seems to reach a higher steady-state value for each of the steps. Even though the power profile of the Threshold-test is the same up and down, HR is much higher at the same workloads during cool down compared to the warm up.

If we plot the mean of all 5 Threshold-test datasets, we get Figure 8.7b. The red line is the normalized mean HR for all datasets, while the grey line is the normalized mean power for all datasets. Both lines are gently smoothed with
a Butterworth low-pass filter. The red shade over and under HR is the 95%-confidence interval for the mean of HR responses, using a t-table from statistics with df=5 (degree of freedom). The mean HR looks quite similar to the single HR response in Figure 8.7a, and the confidence interval is quite small at high intensities.

![Figure 8.7](a) A plot of raw HR and power data for one subject during the Threshold-test. (b) Normalized mean of HR for all subjects (n=5) during the Threshold-test with a 95% confidence interval for the mean. The grey line shows the power profile in both figures.

### 8.3.2 SmO$_2$ data from Threshold-test

We also want to look at SmO$_2$ data from the Threshold-test. Raw data of SmO$_2$ for the same subject as in Figure 8.7a, is shown in Figure 8.8a (blue line). In this subject we observe that SmO$_2$ increases from $\approx 70\%$ in the beginning of the test, before SmO$_2$ seems to stabilize for SmO$_2 \approx 80\%$. When the workload is altered between $0.7 \times$ MAP and $0.9 \times$ MAP, we observe that SmO$_2$ changes. SmO$_2$ drops to SmO$_2 \approx 65\%$ during both steps at $0.9 \times$ MAP, and SmO$_2$ doesn’t seem to stabilize during the 5 minutes the steps last. When the workload is equal to $0.7 \times$ MAP, SmO$_2$ increases back to the value it had before the drop. When the workload is reduced to $0.5 \times$ MAP and $0.25 \times$ MAP during the cool down, SmO$_2$ increases to SmO$_2 \approx 90\%$, which is much higher than during the warm up at the same workloads.

The dataset we justed looked at is from the subject in the study that got most consistent readings of SmO$_2$ during all standard tests. The absolute values of SmO$_2$ varied among subjects. In some subjects SmO$_2$ never reached a steady-state at the beginning of the test, and SmO$_2$ could both drop and increase in this phase for different subjects. In one subject we observed no drop in SmO$_2$ during the first step at $0.9 \times$ MAP, but all subjects had a clear drop in SmO$_2$ during the
second step at $0.9 \times \text{MAP}$. All subjects had a huge increase in $\text{SmO}_2$ during cool down. The mean of $\text{SmO}_2$ from all Threshold-tests are shown in Figure 8.8b, and the separate datasets can be found in section A.1 (Figure A.1). In Figure 8.8b we used equation 8.3 to "normalize" each dataset before we computed the mean of them, but added 0.7 instead of 1 in equation 8.3 to get a more intuitive $y$-axis, with $\text{SmO}_2$ ranging from approximately 0.6 to 0.9. The blue line shows the mean of $\text{SmO}_2$ data, while the grey line is the mean of normalized power, both smoothed with a Butterworth low-pass filter. The blue shaded area is the 95\%-confidence interval for the mean of the $\text{SmO}_2$ data, which is quite wide due to much variation in response among different subjects. We observe in Figure 8.8b that the drop in $\text{SmO}_2$ on average is weak during the first step with workload $0.9 \times \text{MAP}$, but the drop is significant during the second step at $0.9 \times \text{MAP}$. After the last step at $0.7 \times \text{MAP}$ $\text{SmO}_2$ increases to a value higher than at the beginning of the test.
Chapter 9

Linear analysis of heart rate response

As mentioned in chapter 2, earlier experiments have revealed nonlinearities in HR response during exercise. These nonlinearities are assumed to mainly be a consequence of lactate production and elevated body core temperature. Some refer to the nonlinearities as a “slow component”, like Cheng et al. [15] (2008). This implies that they attempted to model all nonlinearities in one differential equation. It’s in our interest to explore nonlinearities at different intensities, to get a visual idea of how and when nonlinearities are introduced in HR response. From this visual impression, we can evaluate if it seems reasonable to put all nonlinear effects in one component.

9.1 Fitting a nonlinear system with a linear model of 2^nd order

The HR response from a test completed by only one subject is shown by the blue line in Figure 9.1b. The y-axis is scaled with respect to $HR_{max}$ for this subject. Baseline workload was set to $0.25 \times MAP$ to reduce noise in HR at the lowest intensities and ensure that the Garmin Vector pedals were activated from the start of short impulses. This made us able to produce impulse responses comparable to Fujihara et al. [24] (1973) mentioned in chapter 2. The test protocol is given by:

1. 2 minutes warm up at baseline
2. A 10 second impulse at $1 \times MAP$ was repeated 5 times every 2 minutes with baseline power between impulses
3. Two 5 minute steps at $0.5 \times MAP$ were performed with 7 minutes at baseline power after each of them
4. Two 5 minute steps at 0.9×MAP were performed with 7 minutes at baseline power after each of them.

Figure 9.1: (a) shows a 1st and 2nd order linear fit to the mean of five impulse responses, where the blue line is the mean. The mean response is assumed to catch the underlying linear dynamics. The 2nd order linear fit is somewhat better than a 1st order. (b) shows the convolution of power input using the 2nd order linear function with optimal parameters as transfer function \( h(t) \). We observe a good fit with the linear model at low intensities, but the linear model clearly fails at high intensities.

In section 5.1 linear response theory was presented. From other research and our own results, it’s obvious that the response is nonlinear. I mentioned different tests to verify an LTI-system. Linearity could be verified by integration of impulse responses to obtain step responses with the same integral. Our result when doing this was noisy and little successful. Time invariance can be investigated by plotting the upward step response against the horizontally mirrored downward response. The two 5 minute steps at 0.9×MAP in Figure 9.1b showed that the downward response obviously is slower than the upward response, in contrast to the two steps at 0.5×MAP where the response is almost the same in both directions. In addition, stability is secured since the power obviously is less than \( \infty \).

If we wrongly assume that our system is an LTI-system, we can obtain the transfer function \( h(t) \) for the system. However, \( h(t) \) can be hard to compute directly from noisy data, as explained in section 5.1, but a solution to this problem was suggested. By using a transfer function as given by equation 5.11 or equation 5.12, we are able to optimize parameters to fit the convolution of the power input against the actual HR response.

In Figure 9.1a I have collected the HR response from the five impulses in Figure 9.1b. The impulses are shown as grey lines, while the blue line is the...
mean of them which hopefully represents the underlying HR response in the noisy data, which we are interested in. The y-axis is scaled with respect to the maximal change in HR for the mean of the responses. The red line in Figure 9.1a shows a 1\textsuperscript{st} order fit using equation 5.11 with optimal parameters, where the time constant is found to be $\tau_1 = 42.8 \pm 4.8$ s. The green line in Figure 9.1a shows a 2\textsuperscript{nd} order fit using equation 5.12 with optimal parameters, where the time constants are found to be $\tau_1 = 24.7 \pm 1.7$ s and $\tau_2 = 7.7 \pm 0.8$ s. $\tau_1$ controls the decay speed, while $\tau_2$ is connected to the delay in response observed at the beginning of the impulse. From the coefficients of determination given in Figure 9.1a, we see that the 2\textsuperscript{nd} order fit ($R^2 = 0.98$) is considerably better than the 1\textsuperscript{st} order fit ($R^2 = 0.85$), especially in the beginning of the response. The decay time constant for the 2\textsuperscript{nd} order fit ($\tau_1 = 24.7 \pm 1.7$ s) seems to catch the HR-decay much better than the 1\textsuperscript{st} order fit, where the slope is too flat. I therefore choose to use the 2\textsuperscript{nd} order linear function as our transfer function $h(t)$. The coefficient in $h(t)$ is given by $\tau_1 = 24.7$ s, $\tau_2 = 7.7$ s and the scaling factor $\gamma = 0.0201$ (also found in the optimization). Our transfer function is therefore given by:

$$h(t) = 0.0201 \times (e^{-\frac{t}{\tau_1}} - e^{-\frac{t}{\tau_2}}). \quad (9.1)$$

The convolution of the power input using our transfer function $h(t)$ given by equation 9.1, is shown by the red line in Figure 9.1b. I have added 0.36 to the baseline which can be considered as the normalized HR\textsubscript{min} (HR/HR\textsubscript{max}). Since our system cannot start at zero, (and since we didn’t measure a value for HR\textsubscript{min} in this experiment), a normalized resting value at approximately 0.36 seems to give the best fit. Our system cannot start at 0 when HR is scaled with respect to HR\textsubscript{max} instead of HRR.

### 9.2 Evaluation of possible model components

As seen from Figure 9.1b, the convolution fits the short impulses very well. The fit to the steps at $0.5 \times \text{MAP}$ is not that bad neither. Since the upward and downward response is almost the same at $0.5 \times \text{MAP}$ steps, our linear time-invariant model fits the data well in transitions, but overshoots slightly at steady-state. The most interesting observations are spotted on the last two steps at $0.9 \times \text{MAP}$. The linear model overshoots a lot at high intensity, stabilizes when HR hasn’t, drops faster than the actual response and drops much below the actual response at baseline workload. The value of $R^2$ is therefore low (0.57). This clarifies how nonlinearities are introduced at high intensities. Since our linear model fits the data well at short impulses and at low intensity, a linear component with fast dynamics seems necessary.

On higher intensities we have to deal with slower decay in transitions and the non-steady-state behaviour observed at $0.9 \times \text{MAP}$ in Figure 9.1b, but also...
in Figure 8.7b. It’s likely that this is a result of lactate production, as suggested by Zakynthinaki [65] (2015) among others, but also supported by the theory presented in this thesis. It seems reasonable to include a component with dynamics similar to lactate production in the body, assumed to have slower dynamics than the fast linear component.

At last we have to deal with elevated HR after the steps at $0.9 \times \text{MAP}$. This effect is clearly shown in Figure 9.1b and Figure 8.7b, and gives rise to a third component. Since HR isn’t elevated after steps at low intensity ($0.5 \times \text{MAP}$), the third component shouldn’t build up considerably at low intensities. The elevated HR also seems to have very slow dynamics, since HR seems to almost stabilize at an elevated value in Figure 9.1b. This is assumed to be in connection with elevated temperature, as explained in section 3.5.

From the analysis in this chapter and the experimental results showed in the previous chapter, it’s reasonable to construct a HR model with three components: one fast component with linear behaviour at low intensities, one slower component with dynamics similar to lactate acting on higher intensities, and one very slow component that builds up at high intensities. This is in contrast to earlier models where they have attempted to collect all nonlinear effects in one component, like Cheng et al. [15] (2008), Zakynthinaki [65] (2015) and Mazzoleni et al. [46] (2016). How the three components are constructed in our new model is explained in detail in the next chapter.
Chapter 10

Our new mathematical model to simulate heart rate

As a first comment to our model, it’s important to point out that the superior task for the heart is to deliver oxygen to the body. When different receptors send information to the heart via the nervous system, it’s usually to regulate HR to meet the demand of oxygen around in the body. However, the heart will not beat any faster than necessary to meet the oxygen demand. This model is based on physiological principles related to regulation of HR, where modelled HR is detonated as \( \nu \). We can through optimization against HR data obtain the optimal values of the free parameters incorporated in the model. The free parameters are chosen to be \( \tau_L \), \( \bar{p}_T \) and \( \nu_{min} \). \( \tau_L \) is an attempt to measure the speed of HR dynamics connected to physical condition. \( \nu_{min} \) is a measure of the basal HR at rest, and is also connected to physical condition. \( \bar{p}_T \) on the other hand is tuned to be a constant fraction \( \kappa = 0.8 \) of MAP, as indicated by Figure 8.2b, when MAP is known. If \( \bar{p}_T \) is found to be larger than \( \kappa \) in an optimization when MAP is supplied into our model, it predicts better cardiovascular fitness.
To avoid confusion:

We have established the threshold power to be $0.8 \times \text{MAP}$.

- $p_T$ is the threshold power with unit watt. $p_T = 0.8 \times \text{MAP}$ is therefore the threshold power with unit watt.

- $\bar{p}$ is normalized power without physical units, normalized with respect to MAP. $\bar{p} = 0.8$ is therefore a fraction 0.8 of MAP.

- $\bar{p}_T$ is the normalized threshold power without physical units, normalized with respect to MAP. We have:

$$\bar{p}_T = \frac{p_T}{\text{MAP}} = 0.8 = \kappa \quad (10.1)$$

Our model optimizes the normalized threshold power $\bar{p}_T$. The important observation is that $\bar{p}_T \neq \kappa$ for other values than MAP. For the correct value of MAP as input to the model, the model is adjusted to obtain $\bar{p}_T \approx \kappa$ in the optimization.

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10.1 Components

Our new mathematical model for simulating HR dynamics is the sum of three different components; a fast component $\nu_L$ with time constant $\tau_L$, a somewhat slower component $\nu_G$ with time constant $\tau_G^1$, and a very slow component $\nu_M$ with time constant $\tau_M$:

- $\nu_L$ is physiologically assumed to be connected to the oxygen supply in highly active muscles (like the legs in cycling) for production and refill of the ATP storage in the same muscles, according to the aerobic path in Figure 3.6. The $L$ in $\nu_L$ refers to the local supply of oxygen to the working muscles.

- $\nu_G$ is much more nonlinear than the first component and is physiologically assumed to be highly connected to the production and removal of lactate. The $G$ in $\nu_G$ refers to the global supply of oxygen that contributes to aerobic removal of lactate in the whole body, as explained in section 3.6.

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$^{1}\tau_G$ is not specified in our model, but is the inherent time constant of $\nu_G$. 

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$^a$We assume the MAP-value obtained from the MAP-test to be the “correct” MAP-value.
• The last component, $\nu_M$, is assumed to work with a lot slower time constant than the two other components. $\nu_M$ is physiologically connected to increased use of oxygen due to elevated body temperature that speeds up chemical reactions, as explained in section 3.5. The $M$ in $\nu_M$ refers to the increased supply of oxygen in the body due to increased overall metabolism.

We have $\tau_L < \tau_G < \tau_M$. $\nu_L$ should catch the fast changes in HR, while $\nu_G$ should handle non steady-state behaviour and the slower decay in HR observed in experimental data at high intensities. $\nu_M$ is supposed to take care of the slow component that builds up during exercise at high intensities. A sketch of how the model roughly is supposed to work is illustrated in Figure 10.1, according to the findings in chapter 9.

**Figure 10.1:** The figure shows a sketch of how our model is supposed to behave at different intensities. At the first low intensity step at $0.5 \times \text{MAP}$, it’s only $\nu_L$ that contributes significant to the change in the modelled HR ($\nu$). At the high intensity step at $0.9 \times \text{MAP}$, both $\nu_G$ and $\nu_M$ contributes significant, and gives a slower decay in $\nu$ than after the step at $0.5 \times \text{MAP}$. Grey blocks show the power applied to the system.

### 10.2 Component distribution

Each component has a model-fixed possible maximal contribution: $\nu_{L_{\text{max}}}$, $\nu_{G_{\text{max}}}$ and $\nu_{M_{\text{max}}}$, as fractions of heart rate reserve (HRR). The sum of maximal contributions therefore equals the difference between $\nu_{\text{min}}$ and $\nu_{\text{max}}$. In other words, $\nu_L$, $\nu_G$ and $\nu_M$ are at all times added upon $\nu_{\text{min}}$, and might add up to $\nu_{\text{max}}$ if the exercise is long and hard enough. To make it clear, we can write up the following equations:
\[ \nu = \nu_{\text{min}} + \nu_{L} + \nu_{G} + \nu_{M} \]  
(10.2)

\[ \nu_{\text{max}} = \nu_{\text{min}} + \nu_{L_{\text{max}}} + \nu_{G_{\text{max}}} + \nu_{M_{\text{max}}} \]  
(10.3)

\( \nu_{\text{min}} \) is one of the parameters we are going to optimize as a prediction of resting heart rate (HR\(_{\text{min}}\)).

When our model is constructed as given in equation 10.2 and equation 10.3, we prevent the system from obtaining non-physiological values. At the same time we are able to adjust the time constants of the components independently. We are also able to define the behaviour and shape of the three components to behave as expected according to experimental data and theory. However, the distribution between different the components is something we have to choose ourselves.

### 10.2.1 Choosing the value of \( \nu_{M_{\text{max}}} \)

In Figure 9.1b we assumed that HR\(_{\text{min}}\) were roughly \(0.36 \times HR_{\text{max}}\). If we normalize with respect to HRR instead of HR\(_{\text{max}}\), we can investigate how much HR is elevated after the steps at \(0.9 \times \text{MAP}\) compared to the beginning of the exercise to roughly measure the size of \( \nu_{M_{\text{max}}} \). When doing this we find \( \nu_{M_{\text{max}}} \) to be approximately 0.1 of HRR. By comparing HR at the end of the first step at \(0.7 \times \text{MAP}\) with HR at the end of the last step at \(0.7 \times \text{MAP}\) in Figure 8.7b (marked with black lines), we also find \( \nu_{M_{\text{max}}} \) to be approximately equal to 0.1 of HRR on average. The threshold-test was strenuous for such a long time that it’s reasonable to define 0.1 of HRR as the maximal value of \( \nu_{M} \) (\( \nu_{M_{\text{max}}} \)). In addition, we recall from subsection 3.5.4 that earlier research suggested approximately 10 additional heart beats per celsius degree above the baseline temperature. Temperature data from MAP-tests and Depletion-tests showed a change in temperature about 0.6-1.8\(^{\circ}\)C above baseline temperature. Since 0.1 of HRR is roughly 10-15 bpm for most subjects, \( \nu_{M_{\text{max}}} = 0.1 \) seems to approximately be in accordance with other research.

### 10.2.2 Choosing the values of \( \nu_{L_{\text{max}}} \) and \( \nu_{G_{\text{max}}} \)

If the contribution is fixed among the components we would have 90\% of HRR remaining to distribute among \( \nu_{L_{\text{max}}} \) and \( \nu_{G_{\text{max}}} \). However, we want the distribution to be dynamic such that \( \nu_{\text{max}} \) also can be obtained at a very high intensity for a short time, even though the time constant of \( \nu_{M} \) is very slow. This means that we want the sum of \( \nu_{L_{\text{max}}} \) and \( \nu_{G_{\text{max}}} \) to be equal to HRR when \( \nu_{M} = 0 \), giving \( \nu_{L} \) and \( \nu_{G} \) the possibility to add up to \( \nu_{\text{max}} \). We can formulate the dynamic distribution as follows:
\[ \nu_{M_{\text{max}}} = \text{constant} \quad (10.4) \]

\[ \nu_{L_{\text{max}}} = \nu_{L_{\text{max}}} - \frac{\nu_M}{2} \quad (10.5) \]

\[ \nu_{G_{\text{max}}} = \nu_{G_{\text{max}}} - \frac{\nu_M}{2} \quad (10.6) \]

We just argued for \( \nu_{M_{\text{max}}} \) to be 0.1 of HRR, such that the constant in equation 10.4 is set equal to 0.1. However, we also need values for \( \nu_{L_{\text{max}}} \) and \( \nu_{G_{\text{max}}} \).

From subsection 3.5.2 we know that the distribution between slow-twitch and fast-twitch muscle fibres on average is approximately 50/50 in humans. For simplicity we suggested that fast-twitch fibres always produce lactate, while slow-twitch fibres never produce lactate. Under this assumption, all of the oxygen transported inside muscles is used by slow-twitch fibres only, while the remaining oxygen is used in the whole body during breakdown\(^2\) of lactate produced by fast-twitch fibres (or due to elevated body core temperature). From this reasoning, it seems reasonable to divide the fraction of HRR equally between \( \nu_{L_{\text{max}}} \) and \( \nu_{G_{\text{max}}} \).

If we define our modelled HRR to be \( \nu_R (\nu_{\text{max}} - \nu_{\text{min}}) \) we get the (dynamic) component distribution: \( \nu_{L_{\text{max}}} = 0.5\nu_R \), \( \nu_{G_{\text{max}}} = 0.5\nu_R \) and \( \nu_{M_{\text{max}}} = 0.1\nu_R \). The shape and other details of the three components will be described in the upcoming sections.

### 10.2.3 Physiological interpretation of dynamical distribution

We also have to try to give a physiological interpretation of the dynamical distribution of maximal component contribution given by equation 10.4, equation 10.5 and equation 10.6. When the body temperature is normal, we can assume that the body prioritizes delivering blood to highly active muscles, as explained in section 3.4. The body should also prioritize delivery of blood to other muscles and organs that are able to remove lactate to keep the lactate concentration as low as possible, as mentioned in section 3.6. When the body core temperature is elevated, there is an increased flow of blood to the skin to transport heat to the surface of the body, as mentioned in section 3.5. This means that some of the cardiac output (CO) that could be used in muscles and organs, instead has to transport heat to the surface. The increased flow of blood to the skin reduces the ability of delivering oxygen to muscles and organs important for the activity. However, the increased temperature also speeds up chemical reactions in less important parts of the body, so the contribution from \( \nu_M \) to \( \nu \) if justified. For simplicity we assume that the reduction in \( \nu_{L_{\text{max}}} \) and \( \nu_{G_{\text{max}}} \) is equal due to

\(^2\)Removal by aerobic glycolysis.
introduction of \( \nu_M \), which explains why we divided \( \nu_M \) by 2 in equation 10.5 and equation 10.6.

10.3 The fast component \( \nu_L \)

The fast component \( \nu_L \) is assumed to reach a steady-state for all intensities when the time approaches infinity. The steady-state of \( \nu_L \) is from now on named \( D_L \). \( \nu_L \) is assumed to be the only component that contributes at low intensities, which implies that \( D_L \) must be linear at low intensities to comport the linear behaviour in the MAP-test in section 8.1. This is further supported by the linear behaviour we found at low intensities in Figure 9.1b and by the results from Fujihara et al. [24] (1973). Figure 9.1b indicated a small nonlinear behaviour already at 0.5×MAP, and substantial nonlinearity at 0.9×MAP. We can therefore assume that \( D_L \) is less than linear when the intensity is above 0.5×MAP, since other components start to contribute to \( \nu \). If \( D_L \) doesn’t start to level out around 0.5×MAP, the sum of components would be more than linear, which is a contradiction to the linear steady-state response up to 0.8×MAP we found in the MAP-test.

10.3.1 Steady-state function of \( \nu_L \)

We assume that accumulation of lactate and elevated body core temperature introduces nonlinear components. We presented a drop in \( SmO_2 \) as an alternative way to identify the lactate threshold (or threshold power) in section 3.3. Results from the MAP-test in section 8.1 indicated a threshold power \( \bar{p}_T \) at \( \bar{p} = 0.8 \) (\( \kappa \)). If we recall Figure 3.7, the value of \( p_T \) given by the stippled red line at the x-axis corresponds to a lactate concentration of 4 mmol/l at the y-axis. As shown in Figure 3.7, the lactate concentration is close to the basal value at 1 mmol/l for low workloads, hence there is little violation of the linear assumption. In addition, our own measurements of temperature during the MAP-test and Depletion-test in section 8.1 and section 8.2 show little increase in body core temperature at low intensities.

Since the total response below \( p_T \) is assumed to be the sum of three components, the total steady-state response should be a straight line up to \( \bar{p} = 0.8 \) as shown in section 8.1. Therefore, it’s reasonable to construct the steady-state function \( D_L \) to be less than linear when \( D_L \) approach \( p_T \). In addition, due to the formulation of the model with components with limited contribution, \( D_L \) must level out towards \( \nu_L^{\text{max}} \) at 1×MAP for the model to possibly reach \( \nu^{\text{max}} \) at the MAP-test. \( \nu_L^{\text{max}} \) can be interpreted as a maximal rate of oxygen consumption by aerobic glycolysis in highly active muscles. Since there is a limited amount of oxygen that can be transported locally to a muscle per time, this is a fair assumption. A muscle can’t use more oxygen than the maximal delivered amount,
and the heart won’t beat faster than necessary when the local delivery of oxygen is at a maximum.

From the argumentation above, $D_L$ is in our model given by:

$$D_L(p) = \nu_{Lmax} \times 2 \left( \frac{1}{1 + e^{-\frac{\bar{p}}{\alpha_L}}} - 0.5 \right).$$

(10.7)

equation 10.7 is a logistic function with power as input, where the shape is determined by $\alpha_L$. A plot of the normalized equation 10.7 is shown in Figure 10.2. As we see in Figure 10.2, the response is approximately linear at low intensities up to 0.4×MAP (red stippled line), and almost 1 when we approach 1×MAP (black stippled line). $\alpha_L = 0.2$ was chosen to give the desired shape of $D_L$, with linear shape at low intensities and $D_L = \nu_{Lmax}$ at MAP. We note that $D_L(p) \to \nu_{Lmax}$ when $p \to \infty$. This is a mathematical weakness of equation 10.7, because $\nu_{Lmax}$ can’t be obtained for any realistic power. However, the value of $D_L$ is about 99% of $\nu_{Lmax}$ at MAP, and the error is negligible in our estimates. We could adjust $D_L$ to be even closer to 1 at MAP, but that would give an unwanted steeper response at low intensities.

**Figure 10.2:** The figure illustrates the shape of the steady-state function $D_L$ for the fast component $\nu_L$ given by equation 10.7. The red stippled line shows the desired linear behaviour at low intensities, while the black stippled line illustrates where we want $D_L$ to reach 1. $\alpha_L = 0.2$ in equation 10.7. $\nu_{Lmax} = 1$ for visual purposes.

**10.3.2 The equation of $\nu_L$**

Up till now, we have only mentioned the steady-state function $D_L$, but not the actual expression for $\nu_L$. $\nu_L$ is designed as a first order differential equation with
$D_L$ as input. $\nu_L$ is given by:

$$\dot{\nu}_L(p) = \frac{1}{\tau_L} (D_L(p) - \nu_L).$$  \hspace{1cm} (10.8)

We observe that $D_L$ determines the steady-state value that $\nu_L$ converges towards in an exponential manner, with a time constant $\tau_L$ controlling the speed of the dynamics. $\tau_L$ is one of the physiological parameters we want to extract through optimization against HR data, to say something about the speed of the HR dynamics to predict physical condition.

### 10.3.3 Summary of $\nu_L$

To summarize, $\nu_L$ is assumed to predict the increase in HR due to increased delivery of oxygen in highly active muscles. In other words, $\nu_L$ tells us how much $\nu$ must increase or decrease due to oxygen used to produce ATP in the legs during cycling. As long as the intensity of exercise is low and remains within the aerobic domain, roughly below $0.5 \times \text{MAP}$, this is the dominating component in the contribution to $\nu$. This behaviour is shown to the left in Figure 10.1.

### 10.4 The slower component $\nu_G$

As shown in Figure 3.6, lactate can both consume oxygen in aerobic glycolysis or be converted back to glycogen without using oxygen. We believe that the accumulation of lactate introduces the non-steady-state behaviour at high intensities above $p_T$ which we observed in Figure 8.5 and Figure 8.7b. We also believe that breakdown of lactate is the reason for the slower decay in HR after strenuous periods during exercise. How large fraction of lactate that is used to produce ATP at different times during exercise is unknown, and it would be wrong to set $\nu_G$ equal to accumulated lactate. However, $\nu_G$ will in our model adapt many of the same properties as the lactate dynamics, like a steady-state value for workloads below $p_T$, and divergence for workloads above the same threshold.

#### 10.4.1 Input function of $\nu_G$

As with the fast component $\nu_L$, $\nu_G$ also has a steady-state function, but in a different way. For $\nu_L$ we had a steady-state function $D_L$ that abruptly changed with power, and the delay in $\nu_L$ was incorporated by $\tau_L$ in equation 10.8. For $\nu_G$, the delay is incorporated in a differential equation $G(p,G)$, where the solution $G$ is input to $\nu_G$. $\nu_G$ is therefore the steady-state function itself up to a given threshold ($G = 1$).
The G-function is developed with theory about lactate dynamics as a basis. The desired properties of G are mentioned in section 3.6 about lactate, and can be summarized in the following points:

1. G should reach a steady-state for all workloads below $p_T$, $G \rightarrow \text{constant}$ $\forall p \in [0, p_T]$ when $t \rightarrow \infty$.

2. G should diverge for all all workloads above $p_T$, $G \rightarrow \infty$ $\forall p \in (p_T, \infty)$ when $t \rightarrow \infty$.

3. The dynamics of G should be dependent of power according to results by Belcastro and Bonen [7] (1975), as shown in Figure 3.8.

4. G should have a basal value above 0 at rest, $G > 0$ when $p = 0$.

How the model of the G-function is developed is explained in detail in section 10.6.

**10.4.2 Steady-state function of $\nu_G$**

Assuming that $G$ is computed, $\nu_G$ is given by:

$$\nu_G(G) = \nu_{G_{\text{max}}} \times (1 - e^{-\frac{G - G_0}{\alpha_G}}).$$

(10.9)

Equation 10.9 is an exponential function with $G$ as input, where the shape is determined by $\alpha_G$. A plot of the normalized equation 10.9 is shown in Figure 10.3. As we see in Figure 10.3, the response is somewhat linear at low values of $G$, but starts to level out rapidly when we approach $G = 1$ (black stippled line). $G_0 = 0.25$ was simply a result of the scaling of G. The lactate threshold is at 4 mmol/l and the basal lactate is 1 mmol/l. Hence, we divided both the threshold and the basal lactate by four to scale $G$ with respect to the threshold where $G$ isn’t able to reach a steady-state anymore. $\alpha_G = 0.82$ was chosen to make $\nu_G \approx \nu_{G_{\text{max}}}$ for reasonable values of $G$.

$\alpha_G$ has a great influence on the value of $\bar{p}_T$ obtained in an optimization. When MAP for a subject is known and supplied into our model, we want our model to find $\bar{p}_T = \kappa$ in the optimization of a dataset from this subject. Since all subjects had completed a MAP-test, the MAP-value for all subjects was known. $\alpha_G$ was therefore used to adjust our model such that the optimization algorithm found approximately $\bar{p}_T = \kappa$ for all subject in different experiments.

We note that $\nu_G(G) \rightarrow \nu_{G_{\text{max}}}$ when $G \rightarrow \infty$. $G \rightarrow \infty$ can in theory be obtained in the model, but not in real life. The G-model is adjusted such that the values of $G$ never become unreasonably large. This implies that $\nu_{G_{\text{max}}}$ can’t be obtained in our model, but $\nu_G$ is about 99% of $\nu_{G_{\text{max}}}$ at $G = 4$, and the error is therefore negligible in our estimates. $\nu_{G_{\text{max}}}$ can be interpreted as the maximal rate of aerobic lactate removal.
10.5 The slow component $\nu_M$

$\nu_M$ is assumed to be of little importance as long as the intensity of exercise is low and the surrounding temperature is below uncomfortable values. If the intensity is somewhat higher, the body temperature elevates, and $\nu_M$ stays elevated for a long time after exercise compared to $\nu_L$ and $\nu_G$, as explained in section 3.5. Our own measurements of temperature during the MAP-test and Depletion-test in section 8.1 and section 8.2 shows a faster increase in body core temperature at workloads around and above $\bar{p} = 0.8$ for some subjects. $\nu_M$ is constructed to rapidly build up during heavy exercise, and to give a slow downward drift for a long time afterwards. If we look at Figure 9.1b and Figure 8.7b again, we see an elevated HR after the high intensity steps. This elevated HR must eventually revert back to the values before the exercise, but this take a long time. This is the effect we want to take care of with $\nu_M$. The desired dynamics of $\nu_M$ are illustrated in Figure 10.1.

10.5.1 Input function of $\nu_M$

As with $\nu_G$, the slow component $\nu_M$ is the steady-state function itself, with $M$ as input$^3$. The $M$-model takes power as input and incorporates the time constant of $\nu_M$ ($\tau_M$) in the same way as the $G$-model did in $\nu_G$. The $M$-function is constructed to fulfil three criteria:

$^3M$ is a model for temperature initiated metabolism.
1. $M$ must reach a steady-state for all workloads $p$, $M \to \text{constant}$ $\forall p \in [0, \infty)$ when $t \to \infty$.

2. $M$ should have slow dynamics, $\tau_M \gg \tau_G > \tau_L$.

3. $M$ can obtain values larger than 1.

Details about the construction of the $M$-function are explained in section 10.7.

10.5.2 Steady-state function of $\nu_M$

Assuming that $M$-values are known, we need an expression for $\nu_M$. Our hypothesis is that as long as the intensity is low, the small increase in temperature/metabolism doesn’t give a significant rise in HR. Elevated body core temperature speeds up chemical reactions which might cause an elevated usage of oxygen, such that the heart must beat faster. As long as the intensity is low, the rise in body core temperature might be too low to speed up chemical reactions significantly. When the intensity rises, the temperature/metabolism might rise so much that oxygen demand increases. However, as with $\nu_L$ and $\nu_G$, the values of $\nu_M$ must reach a maximal value since the body temperature is prevented from increasing to critical values.

To get the desired behaviour of $\nu_M$, we choose a logistic function ("S-curve") given by:

$$\nu_M(M) = \nu_{M\text{max}} \times \left(\frac{1}{1 + e^{-\frac{(M-M_0)}{\alpha_M}}} \right). \quad (10.10)$$

We observe from equation 10.10 that $\alpha_M$ controls the steepness of the logistic function, while $M_0$ determines how much the metabolism $M$ must increase before $\nu_M$ starts to contribute significant in the model. $\alpha_M = 0.12$ and $M_0 = 0.6$ was chosen to give the desired behaviour with little contribution from $\nu_M$ if the exercise had been light, according to the temperature results from the MAP-test and Depletion-test. A plot of the normalized $\nu_M$ given by equation 10.10 is shown in Figure 10.4. The black stippled line in Figure 10.4 shows the value of $M_0$. We observe that $\nu_M \approx 1$ when $M = 1.2$. A metabolism larger than 1.2 doesn’t increase $\nu_M$ further. $\nu_M$ will stay elevated at $\nu_{M\text{max}}$ for a long time for high values of $M$ due to the slow dynamics of $M$.

10.6 Mathematical model for the $G$-function

A few mathematical models have been suggested to simulate lactate dynamics, with varying complexity and accuracy. The most interesting model was, from our viewpoint, a model published by John F. Moxnes and Kjell Hausken [50] (2009). Their model was a differential equation that focused on flux of lactate in and out
Figure 10.4: The figure illustrates the shape of $\nu_M$. The black stippled line shows the value of $M_0$ that adjusts when the $\nu_M$ start to contribute in the model. $\alpha_M = 0.12$ and $M_0 = 0.6$ in equation 10.10. We observe that $\nu_M \approx 1$ when $M = 1.2$. $\nu_{M_{\text{max}}} = 1$ for visual purposes.

of a lactate "pool". They suggested a two-compartment model for the lactate pool. The blood pool was one compartment, while the rest of the body was the second compartment.

The model by Moxnes and Hausken inspired our model of the $G$-function, but there are several differences. We emphasize that the $G$-function is not assumed to simulate lactate in the blood, but to have many of the same properties. The reason is that many of the nonlinearities in HR are believed to be a consequence of accumulated lactate. You should not be confused when we talk about lactate and $G$ at the same time, since $G$ has all the same properties as lactate mentioned in this section. The $G$-function is constructed to model the increased need of oxygen due to breakdown of lactate through aerobic glycolysis. The values of $G$ are without units, and are defined to be relative to a defined threshold, with $G = 1$ at the threshold. The two-compartment idea, combined with a differential equation, is continued from Moxnes and Hausken, but the production and removal functions are completely different.

### 10.6.1 The basal production

First, to get the desired behaviour as explained in subsection 10.4.1, we need a basal production for balance in the differential equation. We name the constant production rate in the blood pool $p_0$. This is physiologically connected to the basal production of lactate by red blood cells, since they only can produce ATP through anaerobic glycolysis, as mentioned in section 3.6. $p_0 = 0.0025$ was chosen
to give the desired behaviour described in subsection 10.4.1 and assumed to be a constant. We have no theoretical basis for the value of $p_0$. In addition to the basal product of lactate, we want a production term depending on power and a removal term depending on both power and $G$.

### 10.6.2 Production term

As a first assumption, we assume that fast-twitch muscle fibres *always* produce lactate when activated, while slow-twitch muscles fibres *never* produce lactate. This is actually not a bad assumption, since a lot of theory claims that production of lactate is low in slow-twitch compared to fast-twitch muscle fibres due to the much higher content of mitochondria. From Figure 3.5 we see how the anaerobic glycolysis increases exponentially with intensity. Since anaerobic glycolysis is the only process that produces lactate, and we just defined that fast-twitch muscle fibres are the only contributors to the production of lactate entering the blood pool, the activation curve of fast-twitch fibres is supposed to have the same shape as the red line in Figure 3.5 [33]. Therefore, the production term in our model is given by:

$$f_{\text{prod}}(p) = e^{\frac{p}{p_T}} - 1.$$  

We observe that there is no production of $G$ if the power equals zero in equation 10.11. $p_T$ is the threshold power.

### 10.6.3 Removal terms

Our removal function is a little more complicated than the production term, since it’s a product of two functions. The first function is a function of power, and is physiologically connected to the fact that lactate might be used as a source to produce ATP, as shown in Figure 3.6. We believe that lactate is removed from the blood pool to produce ATP in a larger amount when the intensity rises, up to a certain maximal removal. It’s unclear if it’s the absence of mitochondria or the transport rate of lactate to uninhabited mitochondria in other parts of the body that is the limiting factor of removal, or any other reason, but it has been shown that lactate is removed faster during activity than at rest [7]. This is explained in section 3.6 and shown in Figure 3.8. If there hadn’t been a maximal removal of lactate, lactate wouldn’t accumulate as it clearly does.

We chose a exponential shape of the removal function that depends on workload. In addition, we assume that there always is a small basal usage of lactate as to produce ATP, named $r_0$, which is necessary to balance the equation at zero power. The first function in the removal function is therefore given by:

$$f_{\text{rem}}(p) = r_0 + (1 - e^{-\frac{p}{p_T}}).$$
We observe from equation 10.12 that $f_{\text{rem}}(p) = r_0$ if $p = 0$, so this part of the removal function cannot be zero. $r_0 = 0.17$ was adjusted to give the desired behaviour described in equation 10.4.1 and assumed to be constant. We have no theoretical basis for the value of $r_0$.

The second of the two functions in the removal function is a function of $G$ itself. This is physiologically connected to the availability of lactate to use in production of ATP. When a certain concentration of lactate is reached, a higher concentration will not lead to further increase in removal, since the tissue already has enough lactate available to remove at a maximal rate. This function has an exponential shape as the first removal function and is given by:

$$f_{\text{rem}}(G) = 1 - e^{-\frac{G}{\alpha}}.$$  \hspace{1cm} (10.13)

$G$ is restricted to always be larger than zero, so that equation 10.13 always is larger than zero. $\alpha$ is connected to how fast the maximal removal is reached for increasing $G$ by adjusting the break point of equation 10.13. As mentioned in section 3.6, the lactate removal at rest seems to be independent of cardiovascular fitness. Hence, $\alpha$ is considered a constant. We have chosen $\alpha = 0.3$ since this gave the desired/best behaviour when we tested the model, but we have no theoretical basis for the exact value of this parameter.

The total removal function is a product by the two functions mentioned above. The total removal function is therefore given by:

$$f_{\text{rem}}(p, G) = (r_0 + (1 - e^{-\frac{p}{\tau}}))(1 - e^{-\frac{G}{\alpha}}).$$  \hspace{1cm} (10.14)

We note that equation 10.14 never can be zero for all combinations of $p$ and $G > 0$. We multiply the two terms since if there is no $G$ to remove, it wouldn’t help to increase the intensity $p$ to remove $G$. Conversely, if $G$ is high, the removal rate will vary with $p$ as desired.

### 10.6.4 The complete $G$-model

If we collect all the terms presented in this section, we end up with the full ODE to solve for $G$:

$$\dot{G}(p, G) = p_0 + \frac{1}{\tau_p}(e^{\frac{p}{\tau_p}} - 1) - \frac{1}{\tau_r}(r_0 + (1 - e^{-\frac{p}{\tau}}))(1 - e^{-\frac{G}{\alpha}}).$$  \hspace{1cm} (10.15)

In equation 10.15 $\tau_p$ is a time constant for the production term, while $\tau_r$ is a time constant for the removal term. If we write equation 10.15 on a compact form, we get:

$$\dot{G}(p, G) = p_0 + \frac{1}{\tau_p}f_{\text{prod}}(p) - \frac{1}{\tau_r}f_{\text{rem}}(p, G).$$  \hspace{1cm} (10.16)

We will use equation 10.16 to find the values of $\tau_p$ and $\tau_r$ that give the desired steady-state from $p = 0$ up to $p = p_T$. 
10.6 Mathematical model for the $G$-function

![Graphs of the production and removal functions](image)

Figure 10.5: (a) A plot of equation 10.11 for $p_T = 0.8 \times \text{MAP}$. (b) A plot of equation 10.12 for $r_0 = 0.17$ and $p_T = 0.8 \times \text{MAP}$. (c) A plot of equation 10.13 for $\alpha = 0.3$. (d) A plot of equation 10.14 for the same parameter values as in (b) and (c).

### 10.6.5 Balanced parameters for steady-state behavior

Our first criteria is that $G$ should be stable at rest. $p = 0$ and $G = G_0$ gives $\dot{G}(0, G_0) = 0$:

\[ 0 = p_0 + \frac{1}{\tau_p} f_{\text{prod}}(0) - \frac{1}{\tau_r} f_{\text{rem}}(0, G_0) \]

\[ 0 = p_0 - \frac{1}{\tau_r} f_{\text{rem}}(0, G_0) \]

\[ \tau_r = \frac{f_{\text{rem}}(0, G_0)}{p_0}. \]  

(10.17)

Our second criteria is that $G$ should stabilize at the threshold $p_T$. $p = p_T$ and
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\[ G = G_T \] gives \( \dot{G}(p_T, G_T) = 0: \]

\[
0 = p_0 + \frac{1}{\tau_p} f_{prod}(p_T) - \frac{1}{\tau_r} f_{rem}(p_t, G_T)
\]

\[
-\frac{1}{\tau_p} f_{prod}(p_T) = p_0 - \frac{1}{\tau_r} f_{rem}(p_T, G_T)
\]

\[
\tau_p = \frac{f_{prod}(p_T)}{\frac{1}{\tau_r} f_{rem}(p_T, G_T) - p_0}. \tag{10.18}
\]

For the parameter values given in this chapter (which is collected in Table 10.1), we get \( \tau_r \approx 38.5 \) s and \( \tau_p \approx 97.1 \) s.

Figure 10.6: (a) shows how the \( G \)-model behaves for different workloads \( \bar{p} \) over long time, with \( \bar{p}_T = \kappa = 0.8 \). We see that all workloads below \( \bar{p}_T \) gives a steady-state, while workloads above \( \bar{p}_T \) give a diverging value of \( G \). (b) shows how the \( G \)-model decays for different workloads below \( \bar{p}_T \). The workload is equal to \( \bar{p}_T \) on the left side of the black stippled line. We observe that the decay is fastest for the workloads from \( \bar{p} = 0.1 \) to \( \bar{p} = 0.5 \).

10.6.6 Tests of the \( G \)-model

Using the expressions for \( \tau_r \) for \( \tau_p \) found in equation 10.17 and equation 10.18 respectively, should secure that the \( G \)-model stabilizes at rest and at the threshold \( p = p_T \). This is not mathematically proven, but is illustrated in Figure 10.6a for \( \bar{p}_T = \kappa = 0.8 \). We observe from the purple line for \( \bar{p} = 0.8 \) that \( G \) goes toward 1, which is the threshold. For workloads above \( \bar{p}_T \), like the green line with \( \bar{p} = 0.85 \), \( G \) diverges. From the blue line at very low workload with \( \bar{p} = 0.2 \), we see that \( G \) actually decreases a little\textsuperscript{4}. This is a result of chosen parameters in the model,

\textsuperscript{4}The lactate concentration can probably decrease a little below basal concentration at low intensities at the beginning of the exercise according to own experience when measuring lactate.
and other choices of parameters values could prevent this, but that also disturbed other properties. However, this is of very little importance since the \(G\) is barely below the basal value. The two remaining workloads \(\bar{p} = 0.1\) (red line) and \(\bar{p} = 0.2\) (yellow line) stabilize below for \(p_T\) as desired.

In Figure 10.6b I have set \(\bar{p}_T = \kappa\) and applied \(\bar{p} = \kappa\) on the left side of the black stippled line until \(G\) almost has reached the threshold at 1. On the right side of the black stippled line we apply different workloads. We observe that the dark blue line that equals rest and the light blue line that equals \(\bar{p} = 0.7\) have the slowest decay. The fastest decays are observed for workloads from \(\bar{p} = 0.1\) to \(\bar{p} = 0.5\). This is the desired behaviour according to lactate removal in Figure 3.8.

![Figure 10.7:](image)

**Figure 10.7:** The figure shows how the \(G\)-model behaves for different values of \(\bar{p}_T\). We have applied \(\bar{p} = 0.8\) on the left side of the black stippled line, and \(\bar{p} = 0\) on the right side of the black stippled line. If \(\bar{p} > 0.8\), the \(G\)-model will not stabilize.

In Figure 10.7 I have applied \(\bar{p} = 0.8\) on the left side of the black stippled line, and \(\bar{p} = 0\) on the right side of the black stippled line. In this figure I have changed \(\bar{p}_T\). When \(\bar{p}_T = \kappa\) as in Figure 10.6a and Figure 10.6b, \(G\) goes towards 1 as shown by the yellow line. If \(\bar{p}_T\) is above \(\kappa\), \(G\) stabilizes below 1. If \(\bar{p}_T\) is below \(\kappa\), \(G\) diverges. This is the property we take advantage of when we optimize \(\bar{p}_T\) in our model. When we do an optimization of free parameters, the model hopefully detects at which workload HR doesn’t stabilize, and reflects this in the value of \(\bar{p}_T\). If the value of \(\bar{p}_T\) is different among datasets, this can indicate changes in cardiovascular fitness, under the assumption that HR doesn’t stabilize above \(p_T\).

### 10.7 Mathematical model for the \(M\)-function

The \(M\)-function is constructed on a phenomenological basis. \(M\) are some sort of estimate of elevated basal metabolism caused increased body core temperature.
We assume that the increased metabolism reaches a steady-state for all intensities. Since metabolism is highly connected to increased temperature in the body, and since the temperature in the body will not diverge, it’s reasonable that the metabolism stabilizes. The maximal metabolism in the body will constrict itself since we become tired and musculature becomes acidic. In addition, as explained in section 3.5, the dynamics of the increased metabolism is very slow compared to the two other components in the model. According to this, the model for $M$ is a simple differential equation given by:

$$\dot{M}(p) = \frac{1}{\tau_M} \left( \beta p - M \right).$$

(10.19)

We note that the differential equation goes toward $\beta p$, and $\tau_M$ determines how fast $M$ reaches this value.

We want $M$ to be able to reach a value larger than 1.2 at workloads around $\bar{p} = 0.8$. This gives us a "plateau" in $\nu_M$ given by equation 10.10, as shown in Figure 10.4. As an example, if we set $\beta = 1.5$, $M$ goes towards $1.5 \times \bar{p} = 1.2$, and $M$ will not be able to build up metabolism such that $\nu_M$ can stay elevated at $\nu_{M_{\text{max}}}$ for a period after heavy exercise. If we instead choose $\beta = 2$, $M$ goes towards $2 \times \bar{p} = 1.6$, and $M$ will keep $\nu_M$ elevated at $\nu_{M_{\text{max}}}$ for a period after hard training before it starts to decrease (for $M = 1.6$ down towards $M = 1.2$). Higher values of $\beta$ let $\nu_M$ be elevated at $\nu_{M_{\text{max}}}$ for a longer period after hard training before it starts to decrease.

The delay for high $M$-values can physiologically be interpreted as the time the body uses to reduce the body core temperature so much that the elevated body metabolism starts to decrease after exercise. However, we actually have no number or theoretical basis to decide how long this delay should be, and it
must be considered as a guess in our model. I have set $\beta = 2$. $\tau_M = 1500$ s was chosen to give the desired slow dynamic in the slow component $\nu_M$. This parameter value must also be considered as a guess to get the desired behaviour. $\tau_M$ should be dependent of environmental temperature and clothing, as explained in subsection 3.5.4, such that $\tau_M$ could probably be formulated as a function in a future model.

10.8 The complete model

From the MAP-test results in section 8.1, we have observed an almost linear behaviour all the way from the lowest workload up to MAP. Under the assumption that HR doesn’t stabilize above $p_T$, as indicated by Figure 8.5, the linear behaviour observed above $p_T$ in the MAP-test is assumed to be a consequence of the experimental setup\textsuperscript{5}. Our model doesn’t obtain a steady-state above $p_T$, such that $\nu$ will eventually reach\textsuperscript{6} $\nu_{\text{max}}$ for workloads above $p_T$. This is what the results in section 8.2 indicated for some subjects. How fast $\nu$ reaches $\nu_{\text{max}}$ is determined by how much the workload is above $p_T$. According to experimental data and theory, the components in our model are on a phenomenological basis constructed to behave as desired. The desired behaviour for our model described in this chapter, is shown for the MAP-test in Figure 10.9a and for the Depletion-test in Figure 10.9b. How the model performs on synthetic power profiles, laboratory

![Figure 10.9](image)

**Figure 10.9:** Figure (a) to the left shows the desired response of the different components during a MAP-test. We notice how the sum of the components gives a straight response all the way to MAP, where $\nu_{\text{max}}$ is reached. Figure (b) to the right shows the desired response of the different components during a depletion-test. We notice that the response is linear up to $0.9 \times \text{MAP}$ as in figure (a). After $0.9 \times \text{MAP}$, the response gets a break point, and the increase in response is completely controlled by $\nu_G$ toward $\nu_{\text{max}}$. The grey blocks behind show the power profile applied to the system.

tests and outdoor free ride tests, will be demonstrated in chapter 11.

\textsuperscript{5}Steps with duration of 2.5 minutes.

\textsuperscript{6}Or at least close to $\nu_{\text{max}}$. 


10.8.1 Steady-state below $p_T$ and table of parameter

According to linear behaviour observed from the MAP-test, and the assumption that HR stabilizes below $p_T$, we expect a linear HR steady-state response for workloads below $p_T$. From the drop in $SmO_2$ at $\bar{p} = 0.8$ in Figure 8.2b combined with the reasoning at the end of section 3.3, we chose $\kappa = 0.8$. If we plot the steady-state values of $\nu_L$, $\nu_G$ and $\nu_M$ with dynamical distribution and add them up, we get the results shown in Figure 10.10. The sum of the steady-states is expected to be a straight line from $\bar{p} = 0$ to $\bar{p} = 0.8$. The purple line in Figure 10.10 is the steady-state response, while the black stippled line is the desired behaviour. We see that our model with the current parameters behaves close to the desired behaviour. All parameter values are shown in Table 10.1.

![Steady-state functions of all the components, including dynamical distribution. The purple line is the total steady-state response, while the black stippled line is the desired steady-state response. The model seems to have the desired steady-state behaviour below $\bar{p} = 0.8$.](image)
### Table 10.1: Table of parameter values used in our model.

Our model computes with normalized units \((\text{HR}/\text{HR}_{\text{max}})\) and \((p/\text{MAP})\). Hence, most parameters are without units. The normalization of parameters with physical units is given in the last column.

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
<th>Unit</th>
<th>Normalization</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0.3</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>(\alpha_L)</td>
<td>0.2</td>
<td>none</td>
<td>([p/\text{MAP}])</td>
</tr>
<tr>
<td>(\alpha_G)</td>
<td>0.82</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>(\alpha_M)</td>
<td>0.12</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>(\beta)</td>
<td>2</td>
<td>none</td>
<td>([p/\text{MAP}])</td>
</tr>
<tr>
<td>(p_0)</td>
<td>0.0025</td>
<td>([1/s])</td>
<td>none</td>
</tr>
<tr>
<td>(r_0)</td>
<td>0.17</td>
<td>([1/s])</td>
<td>none</td>
</tr>
<tr>
<td>(G_0)</td>
<td>0.25</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>(M_0)</td>
<td>0.6</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>(\tau_M)</td>
<td>1500</td>
<td>([\text{s}])</td>
<td>none</td>
</tr>
<tr>
<td>(\nu_{L_{\text{max}}})</td>
<td>0.5</td>
<td>none</td>
<td>([\nu_L/\nu_R])</td>
</tr>
<tr>
<td>(\nu_{G_{\text{max}}})</td>
<td>0.5</td>
<td>none</td>
<td>([\nu_G/\nu_R])</td>
</tr>
<tr>
<td>(\nu_{M_{\text{max}}})</td>
<td>0.1</td>
<td>none</td>
<td>([\nu_M/\nu_R])</td>
</tr>
</tbody>
</table>
10.8.2 Our new mathematical model

The full model presented in this chapter is given by:

\[ \nu_{M_{\text{max}}} = \text{constant} \]

\[ \nu_{L_{\text{max}}} = \nu_{L_{\text{max}}} - \frac{\nu_{M}}{2} \]

\[ \nu_{G_{\text{max}}} = \nu_{G_{\text{max}}} - \frac{\nu_{M}}{2} \]

\[ D_{L}(p) = \nu_{L_{\text{max}}} \times 2 \left( \frac{1}{1 + e^{-\frac{p}{\nu_{L}}} - 0.5} \right) \]

\[ \dot{G}(p) = p_{0} + \frac{1}{\tau_{P}} (e^{\frac{p}{\nu_{G}}} - 1) + \frac{1}{\tau_{R}} (r_{0} + (1 - e^{-\frac{p}{\nu_{G}}})) (1 - e^{-\frac{G}{\alpha_{G}}}) \] (10.20)

\[ \dot{M}(p) = \frac{1}{\tau_{M}} (\beta p - M) \]

\[ \dot{\nu}_{L}(p) = \frac{1}{\tau_{L}} (D_{L}(p) - \nu_{L}) \]

\[ \nu_{G}(G) = \nu_{G_{\text{max}}} \times (1 - e^{-\frac{G-G_{0}}{\alpha_{G}}}) \]

\[ \nu_{M}(M) = \nu_{M_{\text{max}}} \times \left( \frac{1}{1 + e^{-\frac{(M-M_{0})}{\alpha_{M}}} \right) \]

\[ \nu = \nu_{\text{min}} + \nu_{L} + \nu_{G} + \nu_{M} \]

We note that the only input to this model is power. The two personalized parameters that is supplied a priori are HR\(_{\text{max}}\) and MAP. However, we will in section 12.3 explore the possibility of omitting MAP as a parameter known a priori. The modelled \( \nu \) is optimized against the actual HR. \( \tau_{L}, p_{T} \)\(^7\) and \( \nu_{\text{min}} \) are the free parameters we optimize.

\(^7\)We optimize the normalized quantity \( \tilde{p}_{T} \).
Chapter 11

Model tests

11.1 Test of model on synthetic standard tests

I will first test our model given by equation 10.20 on synthetic workload input. In Figure 10.1, Figure 10.9a, and Figure 10.9b in chapter 10 I roughly sketched how I wanted the model to behave according to theory and experimental results for different workload inputs.

How the model performs at synthetic standard tests described in chapter 7 is shown in Figure 11.1. In Figure 11.1 the free parameters are fixed to typical values; $\tau_L = 30$ s, $\bar{p}_T = 0.8$ and $\nu_{min} = 0.4$. Figure 11.1a shows how the model performs on a synthetic MAP-test, where the grey line shows the synthetic input power. We observe an almost linear response up to $HRR = 1$, but the model is slightly below 1 at the end of the test since all components aren’t maxed out at MAP. We have $\nu_L \approx 0.99\nu_{Lmax}$ at MAP as shown in Figure 10.2, and we have $\nu_G \approx 0.99\nu_{Gmax}$ at MAP since $G$ hasn’t increased enough to max out $\nu_G$ shown in Figure 10.3.

Figure 11.1b shows a synthetic Depletion-test, which should and does behave just like the synthetic MAP-test until the constant workload at $0.9 \times$ MAP. We observe that $\nu$ doesn’t stabilize at the last step as desired, and $\nu$ will go towards $\nu \approx 0.98HRR$. The reason is that $\nu_L \approx 0.98\nu_{Lmax}$ at $0.9 \times$ MAP in steady-state, while the other two components are approximately maxed out.

Figure 11.1c shows a synthetic Threshold-test, where the changes in $\nu$ are almost completely determined by $\nu_G$ at high intensities. We observe that the decay is somewhat slower than desired after the steps at $0.9 \times$ MAP. The last figure (Figure 11.1d) shows how our model behaves at two different step intensities ($0.5 \times$ MAP and $0.9 \times$ MAP), where $\nu_L$ completely dominates at low intensities, while $\nu_G$ and $\nu_M$ introduces slower dynamics and an elevated baseline at high intensities.

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11.2 Test of model on laboratory experiments

We just looked at how our model behaves with synthetic data and fixed parameters. We will now take a look at how it behaves with real data collected from experiments in the laboratory. An example is shown in Figure 11.2. We recognize this dataset from Figure 9.1b in chapter 9 (with a different normalization), so the protocol for this experiment has been presented. Figure 11.2a shows the experimental data (blue line) together with the modelled $\nu$ (red line). In the upper left, the optimized/fitted parameter values are given with standard deviation of the standard errors in them, together with an error estimate of the fit. The standard deviations and $R^2$ are computed as explained in section 5.3. We observe that our new model gives a much better fit of this dataset overall than the linear model.
in used in Figure 9.1b, both visually and by comparison of $R^2$ (0.97 vs. 0.57). However, the (2\textsuperscript{nd} order) linear model seems to fit the impulses at the beginning of the dataset better than our model.

We recall that we had to guess the normalized baseline heart rate in Figure 9.1b, since we had no measure of $HR_{\text{min}}$. I guessed this value to be 0.36. We observe from Figure 11.2a that the our new model find the same value to be 0.38±0.02.

![Figure 11.2](image)

**Figure 11.2:** (a) The figure shows the same dataset we investigated in chapter 9 and fitted with a 2\textsuperscript{nd} order linear model. In this figure I have instead fitted the data with our new model, which gives a much better fit than the linear model. (b) The contribution from different components in the fit.

### 11.3 Test of model in real life experiments

To test the model outdoors, two different subjects performed outdoor tests. Let us call one of the subjects S1, and the other subject S2. S1 and S2 agreed to keep the intensity low at flat and downward sections, but to increase the intensity in uphill sections, just like we would normally do when we cycling outdoors. They also agreed to keep the workload below MAP. Otherwise there were no restrictions.

Our first outdoor test, let’s call it T1, contained varying terrain with long flats, short hills and longer climb sections. This secured a lot of variation in HR and gave challenging datasets to fit our model to. S1 and S2 cycled the exact same route on T1 for comparison. T1 for S1 is given in Figure 11.3a, while T1 for S2 is given in Figure 11.4a. Both figures show the fitted parameters with standard deviations and $R^2$ coefficient (computed as described in section 5.3).

The next outdoor test, let’s call it T2, was completed only a couple of days later. S1 and S2 again cycled the exact same route as they did in T1 with the
same procedure, trying to copy T1 in intensity as good as possible. This made us able to explore variations in parameters for nearly identical exercises over a short period of time. We can also compare parameter values between S1 and S2. T2 for S1 is given in Figure 11.3b, while T2 for S2 is given in Figure 11.4b.

The last outdoor test, let’s call it T3, was only performed by S1. T3 followed a different route than T1 and T2, and contained a long climb section followed by a long downhill section. S1 kept the workload below MAP, but pushed constantly at high intensity during the climb section. This test gave less dynamics in HR, but is a very typical cycling workout. This gives us the opportunity to compare parameters between completely different workouts. The results from T3 by S1 are shown in Figure 11.3c. How the different components behave in the model during T3 test is shown in Figure 11.3d. In the upcoming chapter I will investigate and test the behaviour of the fitted parameters to evaluate their validity.

**Figure 11.3:** Results from all three outdoor tests by subject S1. (a): T1. (b): T2. (c): T3. (d): Component contributions during T3.
Figure 11.4: Results from both outdoor tests by subject S2. (a): T1. (b): T2.
Chapter 12

Study of optimized parameters

12.1 Reproducibility of \( \tau_L \) in the same dataset

In Figure 11.2a I fitted a laboratory test with short impulses and much HR-dynamics in the beginning. I found \( \tau_L = 23.0 \pm 4.4 \) s, where the standard deviation must be considered quite small and the estimate should have good precision. Since \( \tau_L \) is assumed to catch the fast changes in HR (and physiologically interpreted as a fast underlying time constant in HR response), it could be interesting to only fit our model to the short impulses at the beginning of the dataset. It’s reasonable to believe that this would give an even better precision in the estimate of \( \tau_L \). The result is shown in Figure 12.1.

In Figure 9.1a I fitted the mean of the same impulses as in Figure 12.1. For the mean I found \( \tau_1 = 24.7 \pm 4.8 \) s for the time constant related to decay speed in the 2\textsuperscript{nd} order linear fit. This value is almost the same as I found for \( \tau_L \) when we optimized the whole dataset with our new model (\( \tau_1 = 23.0 \pm 4.4 \) s). When I only fit the impulses with our new model without taking the mean of the impulses, as shown in Figure 12.1, the standard deviation is five times larger, and the value of \( \tau_L \) is a bit off the two other estimates. However, the value of \( \tau_L \) matches the time constants of the other two estimates within the standard deviation (\( \tau_1 = 11.9 \pm 20.0 \) s).

12.2 Reproducibility and sensitivity

To investigate the sensitivity of our parameters, we can use our goodness of fit coefficient \( R^2 \). For all five outdoor tests presented in section 11.3, I have found the optimal parameters shown in section 11.3 in the figures. After that I fixed two of the three optimized parameters, and varied the last one around the optimal value that maximizes \( R^2 \) (minimizes the error). This makes us able to see how sensitive the estimate is to changes in the parameter value that is being varied, and hence illustrates how sensitive the model is for this parameter. This was done
Figure 12.1: The figure shows a fit with our model of the short impulses in the dataset shown in Figure 11.2a. This make us able to compare the optimized $\tau_L$ for the the short impulses only and the whole dataset.

Figure 12.2: Red dots show the parameter values obtained in the optimization. (a) Visual illustration of the sensitivity of $\tau_L$ in T1 (blue line), T2 (red line) and T3 (yellow line) for S1. (b) Visual illustration of the sensitivity of $\tau_L$ in T1 (blue line) and T2 (red line) for S2.

for all three parameters $\tau_L$, $\bar{p}_T$ and $\nu_{\text{min}}$. All results are shown in the figures in this section. To compare sensitivity plots of each parameter between outdoor tests, equal parameters were placed in the same figure. Figures to the left are results from S1, while figures to the right are results from S2.

In Figure 12.2 we observe almost the same shape in sensitivity for $\tau_L$ in all
datasets for each of the two subjects. The shape is asymmetrical for both S1 and S2 and flatter for high values of $\tau_L$. The almost same behaviour is also observed for $\bar{p}_T$ in Figure 12.3. The asymmetry implies that the estimate is more sensitive to low values of the parameters, and it’s therefore more unlikely that the values are underestimated. For $\nu_{\text{min}}$, shown in Figure 12.4, the shapes are almost symmetric for both subjects. However, the shape is sharper for S2 (Figure 12.4b). Hence the estimate of $\nu_{\text{min}}$ is more more sensitive and precise for S1 than S2.

If we also look at the y-axis for all three parameters, we observe that $R^2$ is most sensitive to changes in $\nu_{\text{min}}$ overall. The estimate is less sensitive to higher
values of $\bar{p}_T$ than $\nu_{\text{min}}$, but is very sensitive to lower values of $\bar{p}_T$. There is no doubt that our estimate is least sensitive to $\tau_L$, but the estimate seems to be sufficiently sensitive to all three parameters.

### 12.3 Model prediction of $p_T$

According to the theory at the end of section 3.3 and our findings in section 8.1, where $SmO_2$ dropped at $\bar{p} = 0.8$, we assumed $\kappa = 0.8$ as a constant in the development of our model. In other words, the threshold power $p_T$ is always $0.8 \times \text{MAP}$. Our model was therefore constructed and parameters tuned, such that our model predicted $\bar{p}_T \approx \kappa = 0.8$ in the optimization when MAP was known (obtained from MAP-tests) and supplied as input. This was done at all Threshold-tests, outdoor tests, and some other test as well.

#### 12.3.1 Optimized value of $\bar{p}_T$ on Threshold-tests when MAP is known

The optimized $\bar{p}_T$-value for the five Threshold-tests processed in section 8.3 (all different subjects) is shown in Table 12.1. We observe the desired behaviour where $\bar{p}_T \approx \kappa$, and $\kappa$ is within the standard deviation for all subjects.

<table>
<thead>
<tr>
<th>Cand. nr.</th>
<th>$\bar{p}_T$</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.81</td>
<td>±0.03</td>
</tr>
<tr>
<td>2</td>
<td>0.82</td>
<td>±0.04</td>
</tr>
<tr>
<td>3</td>
<td>0.80</td>
<td>±0.02</td>
</tr>
<tr>
<td>4</td>
<td>0.79</td>
<td>±0.02</td>
</tr>
<tr>
<td>5</td>
<td>0.79</td>
<td>±0.06</td>
</tr>
</tbody>
</table>

**Table 12.1:** The table shows the estimated value of $\bar{p}_T$ with standard deviation at the Threshold-test for five different subjects. The MAP-value obtained from the MAP-test for each subject is given as input in the optimization, such that we expect $\bar{p}_T \approx \kappa = 0.8$.

means that our model predicts $\bar{p}_T$ to be approximately the same fraction of MAP regardless of the cardiovascular fitness of the subject. We emphasize that although our model is constructed to obtain $\bar{p}_T \approx \kappa = 0.8$ when MAP is supplied as input, it’s no matter of course that the optimized values of $\bar{p}_T$ in Table 12.1 are so close to $\kappa$ in five different subjects with significantly different cardiovascular fitness.
12.3.2 Prediction of $p_T$ when MAP is unknown

In theory, there is only one minimum to find in an optimization for a set of free parameters. Hence, the optimization algorithm should always find the same minimum regardless of the input value of MAP, which only is a constant multiplied with the free parameters $\bar{p}_T$. We have from equation 10.1:

$$p_T = \bar{p}_T \times \text{MAP}. \quad (12.1)$$

This means that the estimate of $p_T$ is only the product of the MAP-value supplied into the model and the optimized value of $\bar{p}_T$. If we supply MAP obtained from MAP-tests into our model, we expect the optimization algorithm to find $\bar{p}_T \approx \kappa$. In theory, since the optimization algorithm always should find the same minimum, we can supply any value of MAP into our model, and still obtain the same value of $p_T$. The optimization algorithm should adjust the optimal value of $\bar{p}_T$ according to the supplied value of MAP.

In Figure 12.5 I have supplied 300, 350, 380, 411, 450 and 500 watt as input MAP in the optimization for all five outdoor datasets in section 11.3. Estimates of $p_T$ for subject S1 are shown in Figure 12.5a, while estimates of $p_T$ for subject S2 are shown in Figure 12.5b. MAP equal to 380 watt and 411 watt was chosen since S1 obtained MAP=411 watt at the MAP-test, while S2 obtained MAP=380 watt on the MAP-test.

![Figure 12.5](image)

**Figure 12.5:** The figures show how the estimated $p_T$ (in unit [watt]) changes for six different input values of MAP in our model. The error bars show the standard deviation in $p_T$ for each estimate. **(a)** Estimated $p_T$ for S1 during T1 (blue dots), T2 (red dots) and T3 (yellow dots). **(b)** Estimated $p_T$ for S2 during T1 (blue dots) and T2 (red dots).

We observe in Figure 12.5 that both subjects get a downward drift in estimated $p_T$ for higher MAP values as input. In theory, if the same minimum is found in the optimization for all guesses of MAP, each dataset should get the same predicted $p_T$, such that the points with the same colours are aligned.
horizontally. I tried to increase the precision of the optimization algorithm in \texttt{fmincon} by setting the estimate tolerance less than $10^{-16}$, but the downward drift was visually unchanged. However, an input MAP that is roughly 100 watt off the actual MAP-value only gives 5-10 watt difference in estimated $p_T$ for both S1 and S2, and the difference is less than the standard deviation for each of the estimates, as seen from Figure 12.5. We observe less standard deviation for S1 than S2, as expected from the shape of the lines in Figure 12.3.

I should also comment on the differences in estimated $p_T$ at the outdoor tests with few days between. For S1 I found $p_T$ to be: T1: 347 watt, T2: 327 watt and T3: 318 watt (using MAP-value from MAP-test as input). For S2 I found $p_T$ to be: T1: 309 watt and T2: 325 watt (using MAP-value from MAP-test as input). That gives a variation of 29 watt in $p_T$ for S1, and a variation of 16 watt for S2. We will not validate these values, since that is not the intension of this thesis.
13.1 Our new model

We have seen different approaches in earlier work on HR modelling, but no one has earlier developed a model completely built on physiological principles. All parts of our model are connected to physiology through theory or reasoning that combines theory. A throughout research of HR properties and physiology connected to the same properties, made us able to introduce free parameters with a clear physiological interpretation. The models that disregarded the physiology behind the HR response but rather focused on complicated mathematics, were not able to give a physiological interpretation of optimized/free parameters. Hence, their results were difficult to interpret for people who want to extract information about their health. Although our new model is based on physiology and all parameters are time-invariant, our model seems to fits HR data on pair with or better than earlier models by comparison of $R^2$. However, for exact comparison of fit, the models should be applied on the same dataset.

Both Zakynthinaki [65] (2015) and Cheng et al. [15] (2008) distinguished between two components in their models. One was a fast and linear, while the other was nonlinear and mainly connected to production of lactate. However, none have presented a model that distinguishes between three components in the HR response as our model does. As we saw in chapter 9, it seems reasonable to divide the nonlinear response into two components, and keep the remaining component linear at low intensities were the nonlinear effects are small. The strength of decoupling the nonlinearities into two components, is the ability to control an additional time constant. While other models cannot distinguish between nonlinearities from lactate production and the much slower component connected to increased body core temperature, we are able to tell them apart in our model. This in turn makes it easier for the different components to contribute to the model where they should.

However, the complexity increases with three model components. We have
little knowledge of how many different processes in the body that contribute to nonlinearities in HR, and we don’t know exactly when the nonlinearities are introduced or how to tell them apart. Since the knowledge is limited, we have to do guesses based on our own small collection of data and reasoning based on physiology. For example, component $\nu_G$ in our model is connected to lactate, but we have no knowledge of how much of the lactate that takes part in aerobic glycolysis such that HR is being elevated, neither how much HR should increase for different concentrations of lactate or if this changes in time. In addition, we have no exact knowledge of the slow time constant for component $\nu_M$, other than that it’s very slow compared to the other components and seems to arise after heavy exercise. For $\nu_L$, $\nu_G$ and $\nu_M$ I had to manually try many different parameter combinations and component distributions, such that our components behaved as desired according to observations in our data. However, this also turned out to be a relatively successful approach ($R^2 = 0.97$) as seen in Figure 11.2a. Even though, the fit is not perfect, especially at short impulses.

### 13.1.1 Parameter $\tau_L$

Our fastest component $\nu_L$ was shaped and developed to contribute as a linear component at low intensities, and assumed to catch fast changes in HR responses due to local demand of oxygen. The related time constant $\tau_L$ was supposed to describe the speed of HR dynamics as a measure of physical condition. We recall from chapter 2 that a faster response was recognized as better physical condition, hence we assume a lower value of $\tau_L$ for better physical condition.

From the mean of short impulses in Figure 9.1a I found the time constant related to decay to be $\tau_1 = 24.7 \pm 4.8$ s, while the time constant obtained through optimization with our new model was $\tau_L = 23.0 \pm 4.4$ s. These are remarkably similar results, and indicates that our model probably is able to catch a underlying time constant of a fast component. From this we could assume that the estimate of $\tau_L$ would be even more accurate if we only fitted our model to the impulses, instead of the whole dataset. This was done in Figure 12.1, but I ended up with a much more inaccurate result for $\tau_L$ with large standard deviation, and the fit was actually poor on noisy step data. Hence, it would be no reason to weight parts of the data with more dynamics in the optimization to obtain more accurate values of $\tau_L$, as suggested in section 5.3. It therefore looks like slower and smaller transitions also are important in the computation of $\tau_L$ in our model.

The linear analysis of HR in chapter 9 showed that a 2nd order linear model with two time constants were better than a 1st order linear model with one time constant. Therefore, $\nu_L$ could possibly incorporate two time constants instead of one. Since $\nu_L$ in our model level out at higher workloads, it’s difficult to compare $\nu_L$ with the 2nd order linear model. However, at low intensities it’s possible that an additional time constant could improve the fit.
To investigate the computed $\tau_L$-values further, we can look at the results of outdoor tests in section 11.3. For both subjects (S1 and S2), there are remarkably similar predictions of $\tau_L$ for the different outdoor tests within the same subject. Even though the last test (T3) for S1 was completely different the two first outdoor tests (T1 and T2), the estimated value of $\tau_L$ was almost the same but with larger uncertainty in the estimate. Figure 12.2 illustrates the uncertainty in the estimated values of $\tau_L$, where a sharper curve indicates lower standard deviation (better precision). From Figure 12.2 it’s obvious that the model is sensitive to $\tau_L$, but the precision in $\tau_L$ may vary a bit within and between subjects.

If we then look at the $\tau_L$-values from the figures in section 11.3, the estimated values between S1 and S2 are barely overlapping within the standard deviation. It’s unlikely that the computed $\tau_L$ are so consistent in each subject for all outdoor tests if there isn’t any differences in $\tau_L$ in the two subjects. We should note that all outdoor tests were performed within a short period of time and fully recovered, so there should be little changes is physical condition in the outdoor tests. This support the theory that our model is able to extract a time constant connected to the speed in HR dynamics.

It’s also interesting that even though $\tau_L$ cannot directly say anything about the cardiovascular fitness of a subject, subject S1 with better cardiovascular fitness (5.14 watt/kg) than S2 (4.87 watt/kg), also seems to consistently have lower values of $\tau_L$.

### 13.1.2 Parameter $\bar{p}_T$

Our slower component ($\nu_G$) connected to lactate production, was developed to contribute to the model at somewhat higher intensities than $\nu_L$, with a $G$-value holding many of the same properties as lactate dynamics as input. Since $G$ can diverge, $\nu_G$ works as a limiter for how much HR can increase for high concentrations of lactate.

$p_T$ is a parameter in $G$ that determines at which workload the values of $G$ start to diverge. This workload was defined to coincide with the lactate threshold, and results in this thesis suggest this workload to occur at $0.8 \times$ MAP. In many ways, our way to predict the lactate threshold with reading of $SmO_2$ is more convenient than the standard procedure described in Figure 3.7, since our procedure is consistent and noninvasive. The accuracy also seems to be good according to results from the Depletion-test where all subjects had almost the same duration on the last step at $0.9 \times$ MAP, and according to Threshold-tests where we could see how $SmO_2$ dropped at $0.9 \times$ MAP and increased at $0.7 \times$ MAP.

If we go back to the $G$-model again, workloads above $\bar{p}_T$ makes $G$ diverge. Results from the Depletion-test also suggested that HR doesn’t stabilize below $HR_{max}$ for workloads above $p_T$ in some subjects. We didn’t get the same results in all subjects, although the lactate concentrations measured after the Depletion-
test were far above normal threshold lactate concentration in all subjects. Hence, it’s difficult to evaluate if the non diverging response is genetically determined or caused by the experimental setup. Regardless, we assumed that HR diverges above $\bar{p}_T$, and tuned $\nu_G$ and the $G$-model such that our model is believed to detect at which workload HR starts to diverge. Hence, we take advantage of the diverging behaviour in HR above the lactate threshold to detect $p_T$.

When MAP is known and supplied as input to the model, our model should predict $\bar{p}_T \approx \kappa$. The results from optimization of Threshold-tests for five different subjects are shown in Table 12.1. The results are very promising, where all estimates of $\bar{p}_T$ are close to $\kappa$ (0.8) when MAP is known. From Figure 12.3 we also illustrated that the model is highly sensitive to changes in $\bar{p}_T$. This supports the theory that our model detects $p_T$ in different subjects for large variations in cardiovascular fitness when MAP is known\(^1\).

In section 12.3 we saw that even when MAP is unknown, our model is still able to detect almost the same threshold regardless of input MAP. A guess 100 watt off the correct MAP-value, only gave 5-10 watt difference in estimated $p_T$ for both S1 and S2. However, I have no good explanation why the estimates of $p_T$ get a downward drift for higher guesses of input MAP, and a stricter error tolerance in the optimization didn’t seem to affect the downward drift. It seems like the optimizer systematically ends in the wrong minimum for higher and lower values of MAP.

Subjects tested in this project had a MAP-value between 250 watt and 411 watt, which gives a difference of 161 watt. A guess of MAP withing 100 watt off the correct value of MAP should therefore be manageable. However, there are still some variations in $p_T$ in subjects in short term, as we saw in section 11.3 in the outdoor tests. S1 had a variation of 29 watt in $p_T$ between T1 and T3. S2 had a variation of 16 watt between T1 and T2. If the variation in $p_T$ is correct is impossible to evaluate from our results, but we expect small variations in $p_T$ in short term for a subject. A variation of 29 watt in $p_T$ for S2 seems a little to high in short term. A further validation is necessary to evaluate if estimated $p_T$ can be used to distinguish between ”good“ and ”bad“ days for a subject. However, there is no doubt that our model is able to distinguish between an untrained subject and a world class cyclist, under the assumption that fair\(^2\) input value of MAP are supplied into our model.

### 13.1.3 Parameter $\nu_{min}$

The last parameter that I chose to optimize, $\nu_{min}$, turned out to be very important. It can be difficult to find the correct baseline HR due to ”noisy“ HR

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\(^1\)MAP-values ranged from 250 watt to 400 watt for the five subjects that completed the Threshold-test.

\(^2\)A fair guess would generally be around 300 watt.
behaviour at rest. As we saw in Figure 12.4, the solution is very sensitive to $v_{\text{min}}$, such that only a small change will give low values for $R^2$. This made $v_{\text{min}}$ a parameter we wanted to avoid as input to our model. In addition, $v_{\text{min}}$ is a parameter that may change on a daily basis in subjects, and is therefore of interest to predict physical condition. An elevated value of $v_{\text{min}}$ is supposed to indicate over training or illness. It was therefore natural to set $v_{\text{min}}$ as a free parameter.

### 13.1.4 Subject dependent parameter HR$_{\text{max}}$

The only input parameter needed to know a priori in our model is HR$_{\text{max}}$, but a proper choice of MAP seems to improve the estimate slightly, as discussed above. Optimally, there shouldn’t be any parameters that need to be known a priori. We can use simple formulas based on age to predict HR$_{\text{max}}$, as mentioned in section 3.1. Due to large individual difference, this might give values way off the correct value, but we could also be lucky and get the correct value of HR$_{\text{max}}$. We consider HR$_{\text{max}}$ to be a value that is quite easy to find, and when the subject knows its value of HR$_{\text{max}}$, HR$_{\text{max}}$ can successfully be considered as a constant over several months, since HR$_{\text{max}}$ only is reduced by 0.64 on average per year [52]. It’s possible to set HR$_{\text{max}}$ as a free parameter to optimize, which would make the model completely free for subject dependent parameters needed to know a priori. This has not been tested in this thesis.

### 13.2 Evaluation of experimental setup

During the experiments we tried to make conditions as similar as possible, with comfortable temperatures. Subjects had to keep track of the workload they were demanded to keep, and we had little control of the cadence the subjects selected to use at different intensities. This might introduce some noise in predefined experimental protocols, but could be avoided if we used a magnetic brake bicycle with remote and fixed cadence instead of a normal bicycle. However, we saw in Figure 8.3b that most subjects selected to use almost the same cadence at the same relative power, and close to what’s considered optimal by some researchers [44].

With our experimental protocol, the subjects got almost the same feeling as they do outdoors, which is where we want the model to work. In fact, our free protocol where the subjects control power and cadence freely, could therefore be a strength rather than a weakness, under the assumption that the subjects do their best to keep the demanded workload and use the cadence that feels most comfortable at different workloads. However, in a future model cadence should be an input parameter as well, to account for varying choices of cadence, in accordance to Mazzoleni et al. [46] (2016), who argued that cadence and power as input gave a better estimate than when power was the only input.
All participants in our study were trained and healthy males without known heart disease. This was to prevent recruited subjects from not being able to complete different tests, but also to avoid possible complications in subjects during strenuous exercise. By choosing subjects that are used to do high intensity training, there was a minimal risk for something unwanted to happen during experiments. Since we only chose trained and healthy males, the homogeneity of the participants may affect our model. It’s possible that our model works differently or has less consistent results on females and untrained subjects. However, this can easily be tested in future research.

13.3 Evaluation of equipment and sources of errors

We used several Garmin premium chest straps, and all straps gave stable readings of HR. We applied water on the electrodes on the chest strap to prevent noisy reading of HR in the beginning of tests. HR chest straps use well documented technology and the accuracy should be sufficient for our purposes. We note that HR readings are averages of a selected number of subsequent R-R intervals. Since Garmin’s formula to calculate HR is proprietary, we don’t know how smoothed the measured HR is. This might affect the estimate of $\tau_L$ with a quite short time constant ($\approx 20 – 50$ s). In future research we should consider to calculate HR from own readings of R-R intervals to have control of the smoothing.

The Garmin Vector pedals we used to measure power and cadence had a specified uncertainty of $\pm 2\%$. Since we installed the pedals as described in the manual, and calibrated\(^3\) the pedals before each test, our reading of power and cadence seemed stable and accurate in all experiments. We have therefore no reason to believe that the accuracy was beyond specified uncertainty of $\pm 2\%$.

Moxy gave us various results, and the noise in readings of $SmO_2$ varied a lot. Some subjects tended to have more consistent $SmO_2$-readings with less noise than others. However, there could also be variations within subjects. Readings of $SmO_2$ could be very noisy in one experiment in a subject, but less noisy in another experiment. This indicates that there can be physiological differences, but also that readings of $SmO_2$ can be very sensitive to the placement of Moxy. We tried as good as possible to place Moxy at the same location on the calf in all experiments. However, the calf is divided into several groups of muscles, and it’s hard to place it accurately at the same location each time. More knowledge about placement of Moxy and a better procedure for placement will be beneficial in future research.

Lactate Pro 2 was (as mentioned earlier) used to verify that subjects were above $p_T$ at the last step on the Threshold-test. The accuracy of Lactate Pro 2

\(^3\)Calibration was done with Garmin Edge 1000.
has been validated to about $\pm 3.3\%$ [30], and the lactate measured after the Threshold-tests was always way above the typical lactate concentration of 4 mmol/l at the threshold, ref. subsection 8.2.2. There is therefore no doubt that all subjects were above $p_T$ during the Depletion-test.

We used *Braun ThermoScan 5* to measure temperature during some experiments. These measurements were used as an indication of how much the body core temperature rises during heavy exercise. However, since measurements were done during activity with movements and in fresh air from the window in front of the subjects, it’s reasonable to believe that the uncertainty in some cases is somewhat higher than specified by *Braun* ($\pm 0.2^\circ C$).

### 13.4 Prospects

There are many possibilities in a future model. I have mentioned cadence as input to improve the model. It’s also possible that other parameters could be obtained in an optimization. HR$_{\text{max}}$ has been suggested, but also different parameters related to $\nu_G$ and $\nu_M$ could be of interest, both for extracting information from the data, but also for getting rid of the need to guess the value of so many parameters. We connected the component distribution of $\nu_L$ and $\nu_G$ to the 50/50 distribution of slow- and fast-twitch muscle fibres. Hence, we could possibly optimize $\nu_{L_{\text{max}}}$ or $\nu_{G_{\text{max}}}$ since the distribution of slow- and fast-twitch muscle fibres may vary a lot among subjects. This also opens the possibility of predicting the distribution of slow- and fast-twitch muscle fibres in subjects.

However, we have to be aware that too many free parameters may corrupt the desired behaviour of other important free parameters, since it becomes harder for the optimizer to find the correct minimum. Even when using only three free parameters it looked like the optimizer wasn’t able to find the same minimum for different input values of MAP. An improved model could also include more components, since we saw that our model had problems fitting the noisy impulses in Figure 12.1. On the other hand, more components would increase the complexity of the model further, and more thoughtful guesses of parameters would likely be necessary.

I have not validated the parameters in our model, since that wasn’t the task for this thesis. However, it would be interesting to see if there is a systematic connection between the values of $\tau_L$ and $\nu_{\text{min}}$ since both are assumed to be predictors of physical conditions. In would also be interesting to test the model on several outdoor tests for many subjects, to investigate if $\tau_L$ and $\nu_{\text{min}}$ are so consistent as they were for S1 and S2 in the outdoor test. The tests should be performed over a short period of time, with subjects fully recovered before each test. After this, the same subjects could perform an outdoor test when sick or very tired, to see if the values of $\tau_L$ and $\nu_{\text{min}}$ change as expected.

To validate $p_T$, we could let untrained subjects do a MAP-test to find their
MAP-value, and then do a road test to check if the model predicts $\bar{p}_T = 0.8$. After this, the subjects could exercise regularly for a couple of months such that the MAP-value should be significantly higher. The subjects could then do a new road test, and fit the data with the old MAP-value as input to predict the new value of $p_T$. A MAP-test should shortly after this be performed to measure $p_T$, and be compared with the modelled $p_T$ from the last road test.

In addition, our model should be tested on light exercise and exercise with small variations in HR to investigate if the model is able to get consistent readings when there are less variations in the HR data. Our model should also be tested on females and untrained subjects to verify that the model behaves consistent in completely different subjects.
Chapter 14

Conclusion

Our model for simulating HR during bicycle exercise has shown promising results. In most cases, our model seems to fit HR data pretty good, even for outdoor tests with large and fast variations in HR. However, since HR responses might have individual variations, the model should be tested on more subjects. Since $HR_{\text{max}}$ is the only subject dependent parameter that must be known a priori, the model can easily be applied on new subjects. All of the free parameters have a clear physiological interpretation and are successfully connected to properties of HR. The free parameters, especially $\tau_L$ and $\nu_{\text{min}}$, seem to be almost consistent in subjects when the model is applied on exercises with short time in between, with subjects fully recovered. However, further research is necessary to conclude if our model actually discovers variations in HR properties. I believe that $\tau_L$ and $\nu_{\text{min}}$ might indicate physical condition of a subject, while $\bar{p}_T$ estimates cardiovascular fitness.

The superior goal in this thesis was to investigate if it’s possible to model heart rate and extract physiologically interpreted parameters that might discover differences in heart rate properties in different datasets. From the discussion in this thesis, I believe that this is achievable. If the values of $\tau_L$, $\nu_{\text{min}}$ and $\bar{p}_T$ are validated and shown to work as expected, our model can be used as a supplement to analysis of heart rate data, and to give greater insight of the current health of a subject.
Appendix A

Experimental data

A.1 $SmO_2$ data from Threshold-tests

![Graph showing smoothed and normalized $SmO_2$ data for all five subjects during the Threshold-test.](image)

**Figure A.1:** Smoothed and normalized $SmO_2$ data for all five subjects during the Threshold-test.
A.2 Comparison of MAP-test and Depletion-test
Figure A.2: Comparison of MAP-test and Depletion-test HR data for different subjects. The green stippled line indicates where the equal procedure ends, while the black stippled line indicates the "expected" steady-state HR at 0.9×MAP.
A.3 MAP-tests for the same subject

![Graphs of MAP-tests for the same subject](image)

**Figure A.3:** Comparison of MAP-tests for subjects that completed two MAP-tests. HR is normalized, and the legends in the figures show the obtained MAP-value for each MAP-test. MAP-tests were performed with several months in between for each subject. The box in the upper left of each figure shows the candidate identification number.
A.4 Selected dataset

Figure A.4: Raw data from selected dataset with comparison of HR and $SmO_2$ for the same subject as in Figure 8.1a, Figure 8.4a and Figure 8.7a. Grey lines show normalized power, red lines show normalized HR and blue lines show relative $SmO_2$. 
Appendix B

Selected code

B.1 Initialize parameters

```matlab
function Parameters = SetParameters(Data, HR_max)

  % Set solver step-size
  Parameters.dt = 1;

  % Set initial conditions
  Parameters.G0 = 0.25;
  Parameters.M0 = 0;
  Parameters.HR_L_0 = 0;

  Parameters.t_span = [Data.time(1) Data.time(end)];
  Parameters.InitialConditions = [Parameters.G0, Parameters.M0, Parameters.HR_L_0];

  % Set model parameters
  Parameters.HR_min = min(Data.HR)/HR_max;
  Parameters.HR_max = HR_max/HR_max;

  Parameters.GT = 1;
  Parameters.tau_M = 1500; % [s]
  Parameters.Beta = 2;

  Parameters.MaxComponentDistribution = [0.5, 0.5, 0.1];

  Parameters.alpha_L = 0.2;
  Parameters.alpha_G = 0.82;

  Parameters.M_displacement = 0.6;
end
```

B.2 Load data from dataset and collect in struct

```matlab
function DataStruct = LoadData(Dataset, ImportPath, smoothing, smoothingParameter, smoothType, DataStart, DataStop)
```

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% Import and smooth the data
DataMatrix = csvread(strcat(ImportPath, Dataset), 1, 0);
time = DataMatrix(:, 1);
HR = DataMatrix(:, 2);
power = DataMatrix(:, 3);
cadence = DataMatrix(:, 4);
SmO2 = DataMatrix(:, 5);
THb = DataMatrix(:, 6);
if DataStop > length(time)
    DataStop = length(time);
end
% Resize data
time = time(DataStart:DataStop);
HR = HR(DataStart:DataStop);
power = power(DataStart:DataStop);
cadence = cadence(DataStart:DataStop);
SmO2 = SmO2(DataStart:DataStop);
THb = THb(DataStart:DataStop);
% Smoothing of data
if strcmp(smoothing, 'yes')
    time = filter_test(time, smoothingParameter, 1, smoothType);
    HR = filter_test(HR, smoothingParameter, 1, smoothType);
    power = filter_test(power, smoothingParameter, 1, smoothType);
    cadence = filter_test(cadence, smoothingParameter, 1, smoothType);
    SmO2 = filter_test(SmO2, smoothingParameter, 1, smoothType);
    THb = filter_test(THb, smoothingParameter, 1, smoothType);
end
% Make struct of data
DataStruct.time = time;
DataStruct.HR = HR;
DataStruct.power = power;
DataStruct.cadence = cadence;
DataStruct.SmO2 = SmO2;
DataStruct.THb = THb;

B.3 Call optimization routine

DataStart = 1; DataStop = inf;
Data = LoadData(Dataset, ImportPath, smoothing, smoothingParameter, smoothType, DataStart, DataStop);
Parameters = SetParameters(Data, HR_max);
Data.HR = Data.HR/HR_max;
Data.power = Data.power/MAP;
[OptimizedParameters, gradients, hessian, model] = fitmydata(Data, Parameters);
[RMS, GOF, estimates] = model(OptimizedParameters);
B.4 Optimization routine

```matlab
function [OptimizedParameters, gradients, hessian, model] = fitmydata(Data, Parameters)
model = @NewModel;

params0 = [20, 0.8, 0.4];
A = []; b = [];
Aeq = [] ; beq = [];
nonlcon = [];
lb = [0, 0.4, 0.1];
ub = [120, 1.5, 0.7];
options = optimoptions('fmincon', 'UseParallel', true, 'TolFun', 1e-16);
[OptimizedParameters, fval, exitflag, output, lambda, gradients, hessian] = fmincon(model, params0, A, b, Aeq, beq, lb, ub, nonlcon, options);

% New model
function [RMS, GOF, estimates] = NewModel(params)
    Parameters.tau_L = params(1);
    Parameters.PT = params(2);
    Parameters.HR_min = params(3);

    RHS = @(t, X) RHS_NewModel(t, X, Data, Parameters);
    [Time, estimates] = odeGill(RHS, Parameters.t_span, Parameters.InitialConditions, Parameters.dt);

    estimates = interp1(Time, estimates, Data.time);
    % make dimensions agree between estimates and data
    G = estimates(:, 1);
    M = estimates(:, 2);
    HR_L = estimates(:, 3);
    HR_G = HR_G_Model(G, M, Parameters);
    HR_M = HR_M_Model(M, Parameters);
    HR_estimate = Parameters.HR_min + HR_L + HR_G + HR_M;
    estimates(:, 4) = HR_G;
    estimates(:, 5) = HR_M;
    estimates(:, 6) = HR_estimate;
    RMS = sum((Data.HR - HR_estimate).^2);
    SS_res = sum((Data.HR - HR_estimate).^2);
    SS_tot = sum((Data.HR - mean(Data.HR)).^2);
    GOF = (SS_res/SS_tot);
    % R2 = 1 - GOF;
end
```

B.5 Own numerical ODE-solver implementing Gill’s method
Selected code Chapter B

function [t, y] = odeGill(dydt, t_span, y0, dt)

% INPUT: dydt = userFunc(t, y)

n = (t_span(2) - t_span(1))/dt;
t = linspace(t_span(1), t_span(2), n+1);

nTime = length(t);

nSystem = length(y0);
y = zeros(nSystem, nTime);
y(:, 1) = y0;

for i=1:(nTime-1)
    k1 = dydt(t(i), y(:, i));
    k2 = dydt(t(i) + 0.5*dt, y(:, i) + 0.5*dt*k1);
    k3 = dydt(t(i) + 0.5*dt, y(:, i) + dt*(0.5*(-1 + sqrt(2))*k1 + (1 - 0.5*sqrt(2))*k2));
    k4 = dydt(t(i) + dt, y(:, i) + dt*(-0.5*sqrt(2)*k2 + (1 + 0.5*sqrt(2))*k3));
    y(:, i+1) = y(:, i) + (dt/6)*(k1 + (2 - sqrt(2))*k2 + (2 + sqrt(2))*k3 + k4);
end

y = y';

end

B.6 RHS of mathematical model

function RHS = RHS_NewModel(t, X, Data, Parameters)

power = interp1(Data.time, Data.power, t);

dG = G_Model(X(1), power, Parameters);
dM = M_Model(X(2), power, Parameters);
dHR_L = HR_L_Model(X(3), X(2), power, Parameters);

RHS = zeros(3, 1);
RHS(1) = dG;
RHS(2) = dM;
RHS(3) = dHR_L;

end

B.7 $\nu_L$-function

function dHR_L = HR_L_Model(HR_L, M, power, Parameters)

HRR = Parameters.HR_max - Parameters.HR_min;
HR_M = Parameters.MaxComponentDistribution(3).*((1 - exp((-M(:) + Parameters.M_displacement)/Parameters.alpha_M)));

HR_Lmax = (Parameters.MaxComponentDistribution(1) - HR_M/2);
D_L = HR_Lmax*(1/(1 + exp(-power(:)/Parameters.alpha_L)) - 0.5)*HRR;
dHR_L = (1/(Parameters.tau_L))*(D_L - HR_L);

end
B.8 \( \nu_G \)-function

```matlab
function HR_G = HR_G_Model(G, M, Parameters)
    HRR = Parameters.HR_max - Parameters.HR_min;
    HR_M = Parameters.MaxComponentDistribution(3).*(1./(1 + exp((-M(:) + Parameters.M_displacement)/Parameters.alpha_M)));
    HR_Gmax = (Parameters.MaxComponentDistribution(2) - HR_M/2);
    HR_G = HR_Gmax.*(1 - exp(-(G(:) - Parameters.G0) / Parameters.alpha_G ))*HRR;
end
```

B.9 \( \nu_M \)-function

```matlab
function HR_M = HR_M_Model(M, Parameters)
    HRR = Parameters.HR_max - Parameters.HR_min;
    HR_M = Parameters.MaxComponentDistribution(3).*(1./(1 + exp(-(M(:) - Parameters.M_displacement)/Parameters.alpha_M))).*HRR;
end
```

B.10 \( G \)-function

```matlab
function [dG] = G_Model(G, power, Parameters)
    PT = Parameters.PT;
    \% Production of La
    p0 = 0.0025*Parameters.GT;
    fP_Prod = @(P) exp(P./(PT)) - 1;
    \% Removal of La
    r0 = 0.17;
    alpha(3) = 0.3*Parameters.GT;
    fP_Rem = @(P) r0 + 1 - exp(-P./(PT));
    fG_Rem = @(G) 1 - exp(-G./alpha(3));
    \% Balanced parameters
    alpha(2) = p0./(fG_Rem(Parameters.GO).*fP_Rem(0));
    alpha(1) = (1./fP_Prod(PT)).*(alpha(2).*fP_Rem(PT).*fG_Rem(Parameters.GT) - p0);
    \% RHS of lactate model
    dG = p0 + alpha(1).*fP_Prod(power) - alpha(2).*fP_Rem(G).*fP_Rem(power);
end
```

B.11 \( M \)-function
B.12 Program to convert Garmin fit-files to CSV-files

```matlab
function CSVFullFileName = FitToCSV(varargin)
    filepath= varargin{1};
    filename = varargin{2};
    CSVpath = varargin{3};
    JAVApath = varargin{4};
    myJavaPath = JAVApath;
    CSVExportDir = CSVpath;
    CSVFullFileName = [CSVExportDir name(1:end-3) 'csv'];

    % FIT CSV Tool 1.0.1.0
    % Usage: java -jar FitCSVTool.jar -b|-c <INPUT FILE> <OUTPUT FILE>
    % -b <FIT FILE> <CSV FILE> FIT binary to CSV.
    % -c <CSV FILE> <FIT FILE> CSV to FIT binary.
    % -t Enable file verification tests.
    % -d Enable debug output (also enables file verification tests).
    %run fitCSVTool:
    if exist(strcat(myJavaPath,'FitCSVTool.jar'))==2
        RunFitCSV = ['java -jar ' myJavaPath 'FitCSVTool.jar -b ' fullfile(filepath,filename) ' ' ...
        CSVFullFileName ' --data record'];
        system(RunFitCSV);
    else
        error('Cant_Find_FitCSVTool','Cannot find java-program FitCSVTool')
    end
    CSVFullFileName = [CSVFullFileName(1:end-4) '_data.csv']; %we want the "_data"-file
end
```

B.13 Program to make dataset of Peripedal CSV-files or Garmin CSV-files combined with Moxy CSV-files

```matlab
prompt1 = 'Give filename of Data: ';
prompt2 = 'Peripedal? (y/n): ';
filename = input(prompt1, 's');
peripedal = input(prompt2, 's');
```
if strcmp(peripedal, 'y')
    prompt3 = 'Start time in Peripedal (default 0): ';
    PeriStart = input(prompt3);
else
    prompt4 = 'Moxy? (y/n): ';
    Moxy = input(prompt4, 's');
    if strcmp(Moxy, 'y')
        prompt5 = 'Give startrow of MoxyData: ';
        startRowMoxy = input(prompt5);
    end
endif

if isempty(filename)
    disp('Usage error, give filename of MoxyData as a string without ".csv"');
else
endif

%########################################################################
% Set path to location where fit-files is stored
% Set path to location where CSV-files is located or exported to
% Set path to Java program
% Set path to where you want to store new dataset
% ### STIAN ###
FITpath = 'C:\Users\Stian\Dropbox\Master_UiO\data\Fit-files\';
CSVpath = 'C:\Users\Stian\Dropbox\Master_UiO\data\CSV-files\';
JAVApath = 'C:\Users\Stian\Dropbox\Master_UiO\data\java\';
ExportPath1 = 'C:\Users\Stian\Dropbox\Master_UiO\data\Datasets\';
ExportPath2 = 'C:\Users\Stian\OneDrive\Pulsrespons_Felles\Datasets\';
%########################################################################

if strcmp(peripedal, 'y')
    PeripedalData = strcat(filename, '_peripedal.csv');
    [time, HR, power, cadence, SmO2, THb, dataLength] = ImportPeripedalData(PeripedalData, CSVpath, PeriStart);
else
    if strcmp(Moxy, 'y')
        MoxyData = strcat(filename, '.csv');
        GarminData = strcat(filename, '_garmin.fit');
        ConvertData = 'yes';
        % Collecting data
        [time, HR, power, cadence, SmO2, THb, dataLength] = ImportData(FITpath, CSVpath, JAVApath, GarminData, MoxyData, ConvertData, startRowMoxy);
    else
        GarminData = strcat(filename, '_garmin.fit');
        ConvertData = 'yes';
        % Import Data from Garmin Edge 1000
        [HR, power, cadence] = ImportGarminData(GarminData, ConvertData, FITpath, CSVpath, JAVApath);
        % Get size of data
        [nRowsGarmin, nColsGarmin] = size(HR);
        dataLength = nRowsGarmin;
        % Define a corresponding time-vector
        time = linspace(0, dataLength, dataLength+1);
        time = time(1: end-1);
        % Resize data vectors
        HR = HR(1: dataLength);
        power = power(1: dataLength);
```matlab
% Make matrix for writing to csv-file
DataMatrix = zeros(dataLength, 6);
DataMatrix(:, 1) = time;
DataMatrix(:, 2) = HR;
DataMatrix(:, 3) = power;
DataMatrix(:, 4) = cadence;
DataMatrix(:, 5) = SmO2;
DataMatrix(:, 6) = THb;

% Write dataset to directories
headers = {'time', 'HR', 'power', 'cadence', 'SmO2', 'THb'};
filename1 = strcat(ExportPath1, filename, '_Dataset.csv');
fileID1 = fopen(filename1, 'wt');
csvwrite_with_headers(filename1, DataMatrix, headers);
disp('Data successfully written to: ');
disp(filename1);

filename2 = strcat(ExportPath2, filename, '_Dataset.csv');
fileID2 = fopen(filename2, 'wt');
csvwrite_with_headers(filename2, DataMatrix, headers);
disp('Data successfully written to: ');
disp(filename2);
```

**B.14 Program to import data from Peripedal CSV-file**

```matlab
function [time, HR, power, cadence, SmO2, THb, dataLength] = ImportPeripedalData(varargin)
filename = varargin{1};
CSVpath = varargin{2};
PeriStart = varargin{3};

CSVFullFileName = strcat(CSVpath, filename, '.csv');
nCols = 10;
fileID = fopen(CSVFullFileName, 'r');
headerData = textscan(fileID, '%s', nCols, 'Delimiter', ' | ');
headerData = headerData{1};
formatSpec = '%s%s%s%s%s%s%s%s%s%[\n\r];
readData = textscan(fileID, formatSpec, 'Delimiter', ' | ', 'ReturnOnError', false);
dataArray = [];
for k = 1:nCols
    dataArray = [dataArray str2double(readData(k))];
end
close(fileID);
ColNames = {'SmO2 Averaged', 'THb', 'Heart Rate', 'Power', 'Cadence'};
Cols = nan(length(ColNames), 1);
```
Section B.15 Program to import Garmin data from Garmin Edge 1000 CSV-file

```matlab
function [HR, power, cadence] = ImportGarminData(varargin)
filename = varargin{1};
ConvertData = varargin{2};
FITpath = varargin{3};
CSVpath = varargin{4};
JAVApath = varargin{5};

if strcmp(ConvertData, 'yes')
    CSVFullFileName = FitToCSV(FITpath,filename, CSVpath, JAVApath);
else
    CSVFullFileName = strcat(CSVpath, filename(1:end-4), '_data.csv');
end

nCols = 18;
fileID = fopen(CSVFullFileName,'r');
headerData = textscan(fileID,'%s',nCols,'Delimiter',',');
headerData = headerData{1};

formatSpec = '%s%s%s%s%s%s%s%s%s%s%s%s%s%s%s%s%s%s%[^
\]';
readData = textscan(fileID, formatSpec, 'Delimiter', ',', 'ReturnUnError', false);

dataArray = [];
for k = 1:nCols
    dataArray = [dataArray str2double(readData{k})];
end
fclose(fileID);

ColNames = {'record.timestamp[s]','record.heart_rate[bpm]','record.power[watts]',
            'record.cadence[rpm]'};
Cols = nan(length(ColNames),1);
for i=1:length(ColNames)
    Cols(i) = find(ismember(headerData,ColNames{i}));
end
dataArray(isnan(dataArray)) = 0;

% Get the data of interest with sampling frequency 1 sec
SmO2 = dataArray(PeriStart+1:end,Cols(1));
THb = dataArray(PeriStart+1:end,Cols(2));
HR = dataArray(PeriStart+1:end,Cols(3));
power = dataArray(PeriStart+1:end,Cols(4));
cadence = dataArray(PeriStart+1:end,Cols(5));
time = linspace(0, length(HR), length(HR)+1);
time = time(1:end-1);
dataLength = length(time);
```

B.15 Program to import Garmin data from Garmin Edge 1000 CSV-file

```matlab
for i=1:length(ColNames)
    Cols(i) = find(ismember(headerData,ColNames{i}));
end
dataArray(isnan(dataArray)) = 0;

% Get the data of interest with sampling frequency 1 sec
SmO2 = dataArray(PeriStart+1:end,Cols(1));
THb = dataArray(PeriStart+1:end,Cols(2));
HR = dataArray(PeriStart+1:end,Cols(3));
power = dataArray(PeriStart+1:end,Cols(4));
cadence = dataArray(PeriStart+1:end,Cols(5));
time = linspace(0, length(HR), length(HR)+1);
time = time(1:end-1);
dataLength = length(time);
```
%time = dataArray(:,Cols(1)) - dataArray(1,Cols(1));
HR = dataArray(:,Cols(2));
power = dataArray(:,Cols(3));
cadence = dataArray(:,Cols(4));
end

B.16 Program to import data from *Moxy* CSV-file

```matlab
function [SmO2, THb] = ImportMoxyData(varargin)
filename = varargin{1};
CSVpath = varargin{2};
startRow = varargin{3};

CSVFullFileName = strcat(CSVpath, filename);

nCols = 7;
fileID = fopen(CSVFullFileName,'r');
formatSpec = '%s%s%s%s%s%s%s\n\r';
readData = textscan(fileID, formatSpec, 'Delimiter', ',', 'headerlines', 5,'ReturnOnError', false);
dataArray = [];
for k = 1:nCols
    dataArray = [dataArray str2double(readData{k})];
end
fclose(fileID);
dataArray(isnan(dataArray)) = 0;
SmO2 = dataArray(startRow:2:end, 3);
THb = dataArray(startRow:2:end, 5);
end
```

B.17 Filtering of data

```matlab
function [filtered_signal] = filter_test(raw_data,fc,fs,type)
%filtrerer data med et 2. ordens butterworth filter.
%input: signal, cutoff, samplingsfrekvens,type('low'/'high')

N=2; %filter order
fs = 1e3; % [Hz] samplerate
if strcmp(type,'highpass')||strcmp(type,'high'))
    type = 'high';
elseif strcmp(type,'lowpass')||strcmp(type,'low'))
    type = 'low';
else
disp('Feil filtertype: bruk highpass eller lowpass');
end
```
Section B.19  Program to fit data with linear functions of 1\textsuperscript{st} or 2\textsuperscript{nd} order

17 \texttt{Wn = 2*fc/fs; %normalized cutoff}
18 \texttt{[b,a]=butter(N,Wn,type);}
19 \texttt{filtered_signal = filtfilt(b,a,raw_data);}
20 \texttt{end}

B.18  Program to fit data with linear functions of 1\textsuperscript{st} or 2\textsuperscript{nd} order

\begin{verbatim}
function [beta, beta_confidence, residuals, fitted_response, fitted_h] = nonlinFitter(order, b, t, e, r)
    % Get h function guess
    r_h = @(b, t) n_order_response(order, b, t, e);
    % Compute optimal parameters with nonlinear least square solver
    [beta, residuals, J] = nlinfit(t, r, r_h, b);
    % Obtain 95\% confidence interval for each optimized parameter
    beta_confidence = nlpredci(beta, residuals, 'Jacobian', J);
    % Obtain 95\% confidence interval for all parameters together
    [r_pred, delta] = nlpredci(r_h, mean(t), beta, residuals,'Jacobian', J);
    r_pred_lower = r_pred - delta;
    r_pred_upper = r_pred + delta;
    % Compute the optimal fit with the optimal parameters
    [fitted_response, fitted_h] = n_order_response(order, beta, t, e);
end
\end{verbatim}

B.19  Linear functions of 1\textsuperscript{st} and 2\textsuperscript{nd} order

\begin{verbatim}
function [response, h] =n_order_response(order, b, t, e)
    %b(1)=pulse height
    %b(2)=tau (time constant)
    %b(3)=tau (time constant)
    %b(4)=tau (time constant)
    % Choose transfer function guess
    if order==1
        h = b(1).*exp(-t./b(2));
    else
        h = b(1).*exp(-t./b(2)) - exp(-t./b(3));
    end
    response = conv(e, h);
    % Remove possible nan and inf from solution
    response(isnan(response)) = 0;
    response(isinf(response)) = 0;
    % Give response same length as input to prevent solver issue
    response = response(1:length(t));
end
\end{verbatim}
Appendix C

Consent form
Request for participation in the research project

”Modelling heart rate response”

Background and purpose
The heart supply the body with oxygenated blood, which the cells utilize to execute physical work. The ability to sustain intense physical exercise is therefore dependent on the hearts ability to increase the supply of blood to the working muscles. The increase in blood flow is in part facilitated by an increase in the heart rate, but the details as to how the heart rate responds to changes in exercise intensity is still not completely understood. The purpose of this project is to develop and test mathematical models for how the heart, and possibly other physiological parameters, respond to changes in exercise intensity. To this end we need to collect experimental data to be used in the development and testing of these models.

What does participation in the study entail?
The data collection is conducted in a laboratory at the Physics building, University of Oslo. We will schedule the time for data collections with you directly. We would like you to complete different test protocols on a bicycle ergometer, hence we will need you to be available for testing on several days. The duration of a typical test will be about one hour, and we would like you to avoid consuming food for a period of one hour before the test starts. The first test you will do is an incremental test to voluntary exertion. Before the test we will measure your body mass and body height, and we will need to know you age and your current and previous activity level. On later tests we will ask you to complete a given intensity profile adjusted to your physical capacity. During the data collections we will continuously measure your heart rate using a chest strap, and the oxygen saturation in a muscle using a small sensor positioned on your leg. Both sensors are non-invasive, and are based on either measurements of electric signals or light absorption.

By volunteering to participate in this study you will be given the ability to test your physiological capacity on standardized tests, which will give you a good indication of your physical shape. You will also contribute to aiding our understanding of how the heart responds to exercise. The risks of injury or other complications while cycling on a bicycle ergometer are small, but accidents might still occur.
Appendix D

Scheme filled out by participants in the study
### Spørreskjema: Modellering av pulsrespons

<table>
<thead>
<tr>
<th>Fylles ut av forsøksperson:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fødselsår</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trening siste 6 mnd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gjennomsnittlig antall økter per uke</td>
</tr>
<tr>
<td>Typisk aktivitetstype (inntil 3 typer)</td>
</tr>
<tr>
<td>Gjennomsnittlig intensitet på øktene (1-3)</td>
</tr>
<tr>
<td>1: meget lett (f.eks. gåtur, yoga)</td>
</tr>
<tr>
<td>2: middels (f.eks. joggetur, lek med ball, styrke)</td>
</tr>
<tr>
<td>3: hardt (f.eks. konkurranser, intensive utholdenhetsøkter)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trening siste 5 år</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gjennomsnittlig antall økter per uke</td>
</tr>
<tr>
<td>Typisk aktivitetstype (inntil 3 typer)</td>
</tr>
<tr>
<td>Gjennomsnittlig intensitet på øktene (1-3)</td>
</tr>
</tbody>
</table>

### Anslag på fysisk form

<table>
<thead>
<tr>
<th>Estimat på egen form (0-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: Meget dårlig</td>
</tr>
<tr>
<td>3: Under gjennomsnittet</td>
</tr>
<tr>
<td>5: Gjennomsnittlig</td>
</tr>
<tr>
<td>7: Godt mosjonsnivå</td>
</tr>
<tr>
<td>10: Verdensklasse</td>
</tr>
<tr>
<td>Hvor hurtig anser du deg? (1-3)</td>
</tr>
<tr>
<td>1: under gjennomsnittet</td>
</tr>
<tr>
<td>2: gjennomsnittlig</td>
</tr>
<tr>
<td>3: over gjennomsnittet</td>
</tr>
</tbody>
</table>

### Fylles ut av testpersonell:

| ID | Ikke skriv her! |
Bibliography


