Heart Rate Regulation via Metabolic Oxygen Consumption
Yasser Abdelrahman, Jessica Huberts, Alan Hurtado, Anjali Jain, Samira Sebt, Manali Shah

Abstract—The function and purpose of the cardiovascular system is well understood; many studies have been conducted to understand the behavior of the cardiovascular system in healthy and diseased patients. Studies demonstrating how the heart rate is monitored and regulated based on an individual’s metabolic oxygen need are limited. Modeling of the cardiovascular system is challenging due to the complexity of biological systems. Simulink is a promising tool to develop models of biosystems due to its easy access, friendly user interface, and built-in blocks. To understand how human heart rate (HR) is influenced by the increase in metabolic oxygen demand that arises from an increase in physical activity, we designed a simplified Simulink model of the human heart. Using step increases in oxygen consumption rate we simulated conditions for rest, walking, jogging and sprinting and observed an increase in heart rate that mirrors the magnitude of the oxygen demand increase. Our HR model can adjust to the levels of oxygen bidirectionally. Developing a refined computational model of heart function can inform the studies of heart rate during conditions that would be unethical to induce or hard to reproduce.

I. INTRODUCTION

The responsibility of the human heart extends beyond its ability to continuously beat at a steady pace. With the help of other components of the cardiovascular system, the heart must respond to changes in our environment and meet subsequent demands in our body. Controlled fluctuations in HR are key to maintaining physiological balance. A clear example is how our body’s need for oxygen varies through the day depending on the intensity of physical activity and other internal or external stimuli. Our project focuses on modeling the relationship between HR and oxygen concentration as a function of our metabolic consumption and the efficiency of oxygen diffusion. We began by identifying the essential physiology behind the cardiovascular system in order to effectively describe and constrain our biosystem. Based on the physiological behavior of the cardiovascular system we derived the governing equations that describe the response of our proposed biosystem. Using the governing equations we designed a Simulink block diagram to run our simulations. As part of the block diagram model, we designed a PID controller to regulate HR based on the measured oxygen concentration. The PID parameters were selected to improve the stability of our biosystem. This approach helped us identify the behavior of our constructed cardiovascular system under the fluctuation of varying metabolic consumption rates, which is a representation of an increase in physical activity. By monitoring HR we were able to conduct a proper analysis of our system in relation to a real physiological response. After careful analysis of our results we pin-pointed the sources of errors in our model, and identified areas where our model behaves similar to a real scenario as well as areas where the response shows discrepancies.

II. PHYSIOLOGY

A. Cardiovascular system

The cardiovascular system is composed of the heart and a complex network of blood vessels that span the entire body. Pumped by the heart, blood transports oxygen, carbon dioxide, nutrients, proteins, hormones, metabolites, and cells through the body in order to provide nourishment to the tissues, remove waste, stabilize body temperature, fight pathogens, regulate pH, and maintain homeostasis.

When the cardiovascular system functions properly, the amount of blood pumped by the heart, termed cardiac output (CO), is on average 5-6 liters per minute at rest. 3 Low CO may indicate heart malfunction, and in extreme cases, heart failure. If left untreated, a low CO can cause serious and sometimes irreversible damage to the tissues and organs. Another important parameter that helps quantify heart functionality is the stroke volume (SV), which is a measure of the volume of blood ejected from the left ventricle in a single pump of the heart. This volume is the difference between the end diastolic volume of blood in the heart when it is relaxed, and the end systolic volume of blood in the heart when it contracts. It is well documented that CO can be computed as the product of HR and SV.

HR, measured in beats per minute (bpm), can be affected by several factors, including endogenous hormones, physical activity, illnesses and pharmaceuticals. A common example is the sympathetic stimulation by epinephrine and norepinephrine, secreted when the body has a fight-or-flight response, which causes the HR to increase. Likewise, an increase in physical activity leads to a rise in the metabolic consumption of oxygen, thus requiring a higher oxygen intake and resulting in a faster HR. Different illnesses can also affect HR through dehydration and damage to cardiac
muscle or pacemaker cells depending on the nature of the condition. To reverse or prevent the effects of an illness, a person might take medication that meets their needs to regulate HR.

B. Respiratory system

The cardiovascular system functions in tandem with the respiratory system to provide a regular supply of oxygen based on the metabolic demands of the individual. Respiration is the process by which inhaled oxygen enters the lungs to be absorbed into the bloodstream and replaced by carbon dioxide, which is a cellular waste product that is then expelled from the body during exhalation. This oxygen-rich blood is pumped by the heart through the left ventricle and into the body. At the cellular level, cellular respiration consumes the available oxygen and produces carbon dioxide. In simple terms, we consider this a gas exchange process. The deoxygenated blood flows back into the heart, where it is then pumped through the right ventricle and back to the lungs. Here, the cycle starts again by exchanging carbon dioxide with the inhaled oxygen. Lastly, the carbon dioxide is expelled from the body during exhalation.

The first equation shows the relationship between cardiac output (CO), heart rate (HR) and stroke volume (SV). Stroke volume is the amount of blood that is ejected from the heart in one heartbeat.

Equation 1 depicts the change in the blood oxygen concentration ($d[O_2]/dt$) as a function of CO and $[O_2]$. The first term in this equation displays the positive contribution of the addition of $O_2$ into the cardiovascular system as a function of cardiac output. The second term describes $O_2$ consumption based on metabolic need. From the above descriptions, it becomes clear that $k_1$ describes the efficiency of oxygenation, i.e. the rate of $O_2$ transport from the lungs to the blood vessels with units of $\frac{mL}{min}$. Parameter $k_2$ in turn represents the rate at which $O_2$ is being consumed ($\frac{mL}{min}$) throughout the body. Lastly, the final term provides the rate of “decay” of $[O_2]$ in the biosystem. In other words, $\frac{d}{dt}[O_2]$ provides information on the time it takes for the oxygenated blood to circulate the entire body while gradually losing oxygen concentration and eventually leading to deoxygenated blood returning to the heart. The time constant of this circulation is given by $t = \frac{V}{k_2}$ where $V$ is the total blood volume of the cardiovascular system, which is on average 5 L. \(^1\)

Equation 2 represents the delay in the sensing of $O_2$ levels by the biosystem. Rapid changes in oxygen consumption cause rapid changes in oxygen concentration levels. However, there is a time delay in the body for the $[O_2]_{Meas}$ to reflect the true $[O_2]$ value. The time constant of this delay is shown as $t_{Meas}$ in the equation. Since the body is more sensitive to $[CO_2]$ than $[O_2]$, this time delay can also be thought of as the time it takes for the chemoreceptors to sense the changes in $[CO_2]$ levels as a byproduct of metabolism, and therefore transmit the signal-for-action accordingly.

From Eq.1 the relationship between the steady-state values of CO and $[O_2]$ was found. The equation simplifies to the following:

$$[O_2]_{ss} = \frac{k_1 CO}{k_2}$$ \hspace{1cm} Eq. 3

This equation provides significant information for the construction of the parametric constraints of our model. Taking the limit of the above equation as $CO_{ss}$ approaches infinity, gives rise to the expression seen below.

$$[O_2]_{ss at CO \rightarrow \infty} = k_1 V$$ \hspace{1cm} Eq. 4
Since it is not physiologically possible for CO to approach infinity, it can be concluded that the equation below must always hold for this model.

\[ k_1 \gg \frac{[O_2]_{\text{target}}}{I} \quad \text{Eq. 5} \]

Additionally, from Eq. 3, the following relationship between \( k_1 \) and \( k_2 \) was derived.

\[ k_1 = \frac{[O_2]_{\text{Meas}}}{I} k_2 + \frac{[O_2]_{\text{Meas}}}{I} \quad \text{Eq. 6} \]

Combining Eq. 5 and Eq. 6 provides a constraint on \( k_2 \) where \( k_2 \gg 0 \).

Please note that \([O_2]_{\text{Meas}}\) and \([O_2]_{\text{target}}\) are being used interchangeably in this model as they represent the natural “healthy” physiological baseline of \([O_2]\) in the body which is assumed to be constant.

B. Control System

As a simplified response to a decrease in \([O_2]\) in the blood due to increased metabolic consumption, the body must compensate for this drop by increasing the heart rate in order to keep the oxygen levels at the target value. Therefore, we represent this mechanism using a PID controller \( F(s) \) with the error as an input of measured \([O_2]\) and the output as HR. The relevant equations for the control system are shown below along with a schematic of the modeled cardiovascular system where \( H(s) \) represents the biosystem, and \( G(s) \) represents the measurement system.

\[ e = [O_2]_{\text{target}} - [O_2]_{\text{Meas}} \cdot G(s) \quad \text{Eq. 7} \]

\[ F(s) = k_p + k_i s + \frac{k_d}{s} \quad \text{Eq. 8} \]

\[ HR = F(s) \cdot e \quad \text{Eq. 9} \]

In the time domain:

\[ HR = k_p \cdot e(t) + k_d \frac{de(t)}{dt} + k_i \int e(t)dt \quad \text{Eq. 10} \]

Note that we are including the delay of blood oxygen sensing from Eq. 2 as part of the biosystem, leading to a measurement system of \( G(s) = 1 \).

IV. RESULTS

A. Simulink Model

The simulink model (Fig. 3) was designed based on the governing differential equations. The closed loop model utilizes a PID controller with tuned parameters in order to increase the effectiveness of the continuously modulated control. The center of the model surrounds a “step input” that represents the change in metabolic demand that ultimately induces change in HR and oxygen concentration.

Table 1: Simulink parameter values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( k_p )</td>
<td>100</td>
</tr>
<tr>
<td>( k_d )</td>
<td>0.10974</td>
</tr>
<tr>
<td>( k_i )</td>
<td>9.89025</td>
</tr>
<tr>
<td>( k_1 )</td>
<td>3.004</td>
</tr>
<tr>
<td>( k_2 )</td>
<td>900 - 1530</td>
</tr>
</tbody>
</table>
B. Transfer Functions

While Eq.1 represents the reality of the cardiovascular system behavior, its nonlinearity makes it a challenge to recreate the system. Consequently, in order to find the transfer function of the biosystem we linearized the equation. The result of this linearization can be found below.

\[
\frac{d[O_2(t)]}{dt} = (k_1 - \frac{[O_2]}{C_0})CO - (k_2 + \frac{CO}{V})[O_2] \quad \text{Eq. 11}
\]

As depicted in Fig. 2, the biosystem \(H(s)\) consists of three equations.

The first equation is simply converting the input heart rate into cardiac output.

The second equation which is the linearized version of Eq.1, shown above as Eq.11, describes the relationship between CO and \([O_2]\) which gives rise to the following transfer function:

\[
\frac{[O_2(t)]}{CO(s)} = \frac{k_1 [O_2]}{s + k_2 + \frac{CO}{V}} \quad \text{Eq. 12}
\]

The third equation implements the delay of oxygen sensing between the true and measured value of oxygen concentration in the blood as part of the biosystem, and has the following transfer function:

\[
\frac{[O_2(t)]_{\text{meas}}}{[O_2(t)]} = \frac{1}{s + \frac{1}{\tau_{\text{meas}}}} \quad \text{Eq. 13}
\]

Therefore, the transfer function of the whole biosystem \(H(s)\) can be found as the product of Eq.12 and Eq.13.

\[
\frac{[O_2(t)]}{CO(s)} \cdot \frac{[O_2(t)]_{\text{meas}}}{[O_2(t)]} = \frac{[O_2(t)]_{\text{meas}}}{CO(s)} = \frac{k_1 [O_2]}{(s + \frac{1}{\tau_{\text{meas}}})(s + k_2 + \frac{CO}{V})} \quad \text{Eq. 14}
\]

C. Bode Plots and PID Tuning

Once the equations for the biosystem transfer function were found, the PID controller was tuned accordingly. As seen in Fig. 4, \(H(s)\) has two poles. Looking at Eq.14, we can conclude that these poles are \(p_1 = -\frac{1}{\tau_{\text{meas}}}\) and \(p_2 = (k_2 + \frac{CO}{V})\).

![Image of Bode plot](image)

Figure 4. Bode plot of the biosystem transfer function

The open loop transfer function of the system, which will be denoted as \(OL(S)\), consists of the product of the PID transfer function and the biosystem transfer function as shown below.

\[
OL(S) = \frac{k_p s + k_i s^2 + k_d}{s + \frac{1}{\tau_{\text{meas}}}(k_1 - \frac{[O_2]}{C_0})} \quad \text{Eq. 15}
\]

In order to increase the accuracy of the closed loop feedback system, the low frequency open loop gain must approach infinity. To do this, the integrated control must have a “zero” at \(p_1\). Additionally, to improve the high frequency response and stability, a “zero” is placed at \(p_2\) for the derivative control. Consequently, the open loop (\(OL(S)\)) transfer function will simplify to a first order transfer function with a single pole at \(s = 0\).

\[
OL(S) = \frac{k_p}{s} \quad \text{Eq. 16}
\]

![Image of Open Loop Bode plot](image)

Figure 5. Bode plot of OL with a stable phase margin of 90°
From the open loop response, the closed loop transfer function was computed.

\[
CL(s) = \frac{OL(s)}{1+OL(s)} = \frac{k_d k_1 \left(\frac{[O_2]}{t}\right)}{M_{os} s + k_1 \left(\frac{[O_2]}{t}\right)}
\]

Eq. 17

As expected, the closed loop transfer function CL(s) has a gain of 1 (equivalently 0dB) until the cut-off frequency at \(\omega_c = \frac{k_d}{M_{os} (k_1 - \frac{[O_2]}{t})}\).

Figure 6. Bode plot of CL with cut-off frequency \(\omega_c\)

D. System Behavior

Fig. 7A and 7B are modelled under the represented Simulink diagram, Fig. 3. Governed by the change in metabolic need, the figures show how HR and \([O_2]\) change with an increase in metabolic need. At rest, we observe the heart rate stays at a constant value of 75 bpm, and an \([O_2]\) of 0.02 mol/L. As the need for metabolic consumption increases at t=10 minutes, there is an increase in settling heart rate in order to compensate. The larger the increase in metabolic need, the higher the heart rate. Conversely we notice a downward spike in the oxygen concentration at time 10 that corresponds to the increase in oxygen consumption, the more consumption the larger the spike. The oxygen concentration is returned to a constant value of 0.02 mol/L by the increase in heart rate.

Figure 7A. HR changes over time as a response to incremental steps in metabolic demand of oxygen.

Figure 7B. Display the change in oxygen concentration over time.

V. DISCUSSION

A. Comparison with Physiological Results

During an increase in physical activity a healthy heart will respond by increasing its pulse rate to meet the new oxygen demand. Figure 7A shows the HR response of our system to a step increase in oxygen demand. We observed that a 20% increase in oxygen metabolic consumption produces a 20% increase in HR magnitude, and similarly a 70% increment in oxygen consumption leads to a 70% increase in HR. Based on our observations of the system behavior we deduce that the relation of HR with oxygen consumption is linear near the endpoints. This behavior is similar to what we expect from the physiological system if HR was exclusively regulated by oxygen metabolism.

After quantifying the time response of our system we observed some discrepancies from what we would observe in a physiological system. Our results indicate that when regulated by metabolic oxygen demand, the HR response time is approximately 20 minutes while a real heart will respond within a...
minute. Although the observed HR values are within the normal physiological range, real values depend greatly on other physiological factors including one's age, size, gender, and physical health.

B. Sources of Error

Discrepancies from physiological responses are expected due to the assumptions and simplifications of the biosystem. Besides the physiological differences that lead to discrepancies of the results, we identified a list of errors that correlate with the differences in physiological and computational responses. Our model observes the cardiovascular system independently of regulatory influences of other organ systems in the body, specially the nervous and endocrine systems. Our Simulink model represents a simplification of a system that would need to be far more complex to accurately represent heart functionality. An important simplification is the ignored effects of vasodilation, which can have a significant impact in the HR response if included in the calculations. Vasodilation occurs at low oxygen levels to increase blood flow by increasing the cross sectional area of vessels. Allowing a higher volumetric flow in combination with an increased HR speeds up the tissue oxygenation and indirectly affects the heart response.

Another major simplification of our system comes from assuming that oxygen transport rate is constant during moderate and high physical activity. We know that in a physiological system, oxygen transport rate will rise because respiratory rate will increase as a response to increasing physical activity. Taking breathing rates into consideration will have a significant impact in the oxygenation of tissue.

Several errors are attributed to our measurement of heart rate where we assumed the effects of cardiac muscle during contraction were negligible. During a physiological response we would expect to observe an increase in the myocardial contractility, which will have a direct effect in cardiac output. Taking into consideration cardiac muscle contraction will also change the stroke volume, which we assumed to remain constant. In reality, stroke volume tends to decrease after physical activity due to the increase in heart rate.

C. Applications in Science

Designing a biosystem that regulates heart rate with oxygen consumption control has many potential applications. A more developed version of our system can be used to analyze dynamic responses of the heart in models of healthy and diseased systems. One strength of a simulated system, as opposed to physiological experimentation, is that it offers the ability to test conditions that are unethical to induce or difficult to reproduce. We can easily alter the base system to represent various health conditions, such as tachycardia or low blood pressure. Such a system helps us gain a better understanding of the relationship between heart rate and oxygen concentration in the tissues. Another advantage of using a computational model instead of a physiological model of heart responses is the reduced need for animal experimentation.

VI. Conclusion

Maintaining homeostasis is pivotal to the proper functioning of biological systems. Increasing the magnitude of physical activity results in a perturbation to equilibrium oxygen metabolism. The cardiovascular system must work in parallel with the respiratory system, nervous system, and endocrine system to maintain a homeostatic balance of oxygen concentration in the blood.

We have shown that it is possible to replicate physiological behavior using computational models to mimic the behavior of biosystems under physiological conditions. Even with slight variations in the computational results, our system behaves in a predictable manner. We have successfully replicated the conditional and on demand regulation of HR from a rise in oxygen metabolic consumption resulting from an increase in physical activity. Another advantage of using a computational model is that the block diagram set up makes it easy to modify parameters if necessary.

A next step is to incorporate the dynamics of other important physiological parameters in the regulation of HR. Due to the close connection between the respiratory rate and the oxygen consumption rate, as defined by Eq. 6, it would be appropriate to start by including the changes in respiratory rate during exercise.

In a future study it would be interesting to test the effects of including the influences of other organ systems on the response. The nervous system plays a critical role in the regulation of HR by influencing the many parameters of the cardiovascular system. Thanks to the ease of implementation of Simulink it is possible to create and connect multiple subsystems representing other biological systems. Running simulations of pathophysiological conditions can increase the understanding of disease progression and its effect on the human biosystems. In addition, it can inform the production of more specialized treatments and therapies for the diseases under study.

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REFERENCES


