Modeling Relative Energy Deficiency in Sport

Shyloh Almada, Ashley Faller, Kate Lindeman, Thawinee Thongprajiad, Ethan Wong

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Department of Bioengineering- University of California, San Diego

***Abstract*— ATP and glucose are widely accepted as forms of energy when referring to performing biological actions. In this paper, we will be exploring how these two factors relate to each other in energy production and consumption. These energy levels will be placed into a system using MATLAB's Simulink modeling system to generate simplified graphs of the levels of glucose and ATP concentrations during exercise and at rest. The results from this experiment are meant to be the simplified start to a system that can be used to fully model the ATP and glucose levels of humans during exercise. These findings can then be used in understanding diseases such as RED-S and what factors control energy levels.**

I. INTRODUCTION

Relative Energy Deficiency in Sport, or RED-S, is a common syndrome that is characterized by low energy availability in athletes, which commonly occurs in endurance sports when athletes are overtraining and not adequately fueling. RED-S can cause a decrease in bone mineral density, increase likeness of injury, as well as many other effects to the endocrine and reproductive systems. In our project, we will be analyzing the biosystem of the pathway that converts glucose into ATP, and the effects of having a low energy availability in this pathway. Understanding how glucose, through the foods that we eat, turns into usable energy will be helpful to examine how this deficiency affects subjects both in the rodents we are experimenting on and when the project relates to human subjects. Through the progression of our project, we can look at how this ATP energy changes levels when compared to muscle density and myosin fibers. The ultimate goal is to monitor the effect that RED-S has on the physicality of an athlete as the glucose intake is varied.

II. BACKGROUND

A. Defining RED-S

According to the International Olympic Committee, RED-S, or Relative Energy Deficiency in Sport, is defined as "impaired physiological function including, but not limited to, metabolic rate, menstrual function, bone health, immunity, protein synthesis, cardiovascular health caused by relative energy deficiency" [1]. The term originated from the Female Athlete Triad, which emphasized three main characteristics - menstrual function, bone health, and energy availability- that could lead to a decline in health and athletic performance of the female athlete. But it was later degendered to include male athletes, who could also be affected by low energy availability, and thus could also have reproductive health issues as a consequence [1]. Thus, RED-S is now defined as when an athlete displays high energy expenditure and low energy intake, resulting in low total energy availability [2]. Low energy availability is typically quantified as less than 30 kcal·kg−1 fat-free mass·day, whereas a normal amount of energy availability is seen as greater than or equal to 45 kcal·kg−1 fat-free mass·day [2]. This can lead to various endocrine responses, reduced bone health, and many negative psychological effects as well.

B. Current Treatments

The only current treatment methods available are to increase the athlete's energy intake, or decrease their energy expenditure, or ideally a combination of both [1]. While these are viable options for some, higher level athletes may not be able to reduce activity level during competition season, and thus further research is required to understand more about the effects of RED-S on athletes, in order to produce more flexible and individualized treatment options for patients. One way to do this is through the utilization of mice models in order to replicate the low energy availability seen in RED-S athletes.

Another way to accomplish this would be through a mathematical based model of the biosystem, in which energy expenditure can be calculated through monitoring ATP concentration as well as oxygen production at varying levels of exercise. Thus, the aim of this model is to analyze the effects of exercise on overall energy expenditure in a healthy subject, with the hopes of applying this to further research on RED-S in the future. The end goal of this study would be to utilize this model along with the mouse model to have a better understanding of the effects of RED-S on the body system. Then, biomarkers could be used in clinical settings to monitor an athlete's likelihood of developing RED-S, and preventative measures can be taken.

III. MATHEMATICAL MODEL

A. Equations:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_20 + 36ATP \quad \textbf{(1)}$$

$$\frac{dG}{dt} = \; - kCG - K_f GO^4 + k_r CO_2^6 \qquad \textbf{(2)}$$

$$\frac{dP}{dt} = BkGO_2^6 \qquad \textbf{(3)}$$

$$\frac{dO_2}{dt} = \alpha\beta - \frac{Q}{v}O_2 - 6kGO_2^6 \qquad \textbf{(4)}$$

Equation (1) is the summary of cellular respiration reaction equations, which consist of glycolysis, pyruvate oxidation, citric acid cycle, and oxidative phosphorylation [3]. Initially, nutrients in the form of glucose are broken down into carbon dioxide, and O_2 is split apart to form water, which in turn releases energy in the form of ATP [3]. The equation states that an input of a single glucose molecule with six molecules of oxygen can output six molecules of carbon dioxide, water, and 36 ATP [4]. Accordingly, the ATP produced as a function of time is the product of the amount of ATP per cellular respiration cycle, reaction rate of the cycle, glucose concentration, and oxygen concentration, as shown in Equation (3). Next, Equation (2) displays the rate of glucose concentration over time, as a function of oxygen and glucose concentration. Lastly, Equation (4) models oxygen consumption, which was derived from the initial equation for cellular respiration. This was done by subtracting the total amount of oxygen in the bloodstream by the amount of oxygen needed to be retained in the blood and the amount used in cellular respiration [3]. In this equation, αβ is the percentage of V_{O_2} max currently utilized by the person, Q is the blood flow rate, and V is the volume of the artery.

B. *Assumptions:*

Initially, it was assumed that the system was constantly in an aerobic condition, so anaerobic respiration was not taken into account. Next, it was assumed that the subject for the biosystem was a healthy adult with average concentrations of glucose, oxygen, and an average percentage of V_{O_2} max used while exercising. This therefore implies that the person's glucose levels were relatively constant with little perturbation, and thus it was also assumed that the rate of change of glucose concentration over time was zero, so Equation (2) was not used as a part of the model [5]. The resting percentage of V_{O_2} max used was 40%, or 0.4, and the exercising percentage was 90%, or 0.9 [6]. Also, in Equation (1), it was assumed that for every cycle of cellular respiration, 36 molecules of ATP were produced. In reality, it lies between 32 and 38, but 36 is typically the average value observed [3]. Finally, in Equation (4), it was assumed that the flow rate over volume ($\frac{Q}{v}$) was 1 ($\frac{1}{hr}$), and that the rate of the reaction (k) was also 1 ($\frac{mL}{kg*hr}$) [7].

IV. MODEL AND SIMULINK

A. Simulink Diagram

The Simulink software was used to model this system, as it provides a simple and efficient way to connect the various equations of the model without having to numerically linearize or solve the equations. Also, plots are able to be generated before and after integration, which expands the possibility of the data obtained. Keeping this in mind, a Simulink model of Equation (3) and Equation (4) was created to observe the concentration of oxygen and ATP at the two different percentages of V_{O_2} max: 40% and 90%. As noted, Equation (2) was eliminated as the glucose concentration was assumed to be constant, and thus was not included in the model. Similarly, Equation (1) was used to derive Equations (2) and (4), and thus was also omitted from the Simulink model.

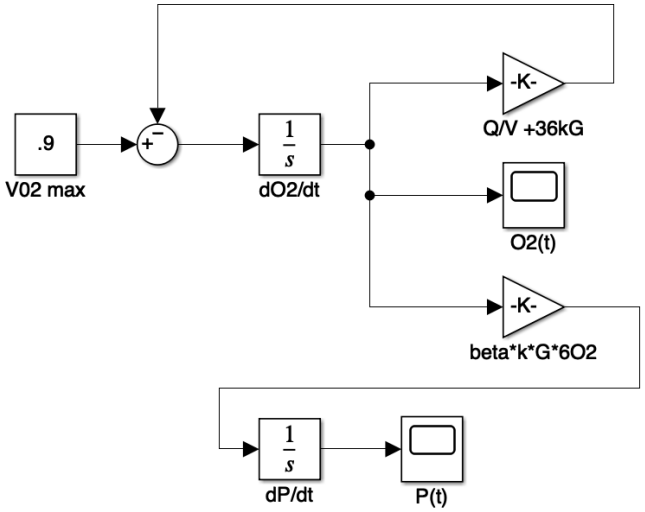
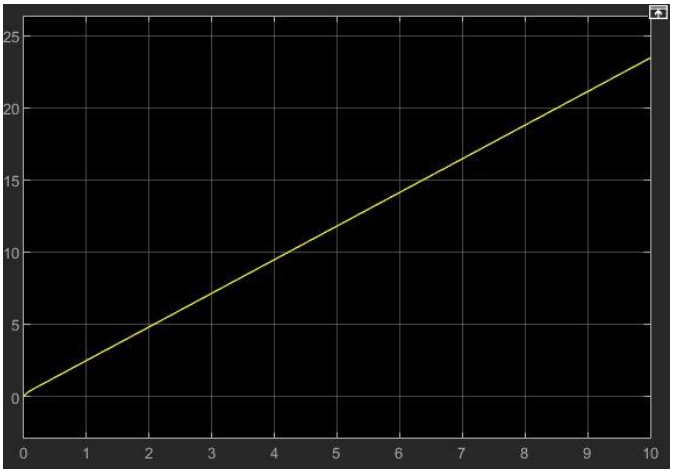


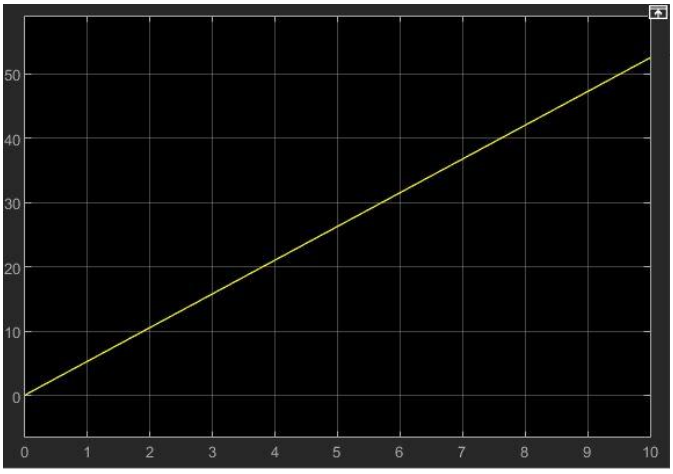
Figure 1: Figure 1 illustrates the simulink diagram that describes equations (3) and (4). From this diagram, both the oxygen concentration ($O_2(t)$) *and the concentration of ATP*($P(t)$) *were monitored over time in response to changing* V_{O_2} *max percentage. This figure displays the exercise version of the model, and thus the percentage of* V_{O_2} *max is* 90%, *or* 0.9. *In the resting model, this value is changed to* 40%, *or* 0.4.

The model was created by using an integrator block for the derivatives of ATP and oxygen with respect to time, so that the concentration of each value with respect to time could be obtained. The initial condition used for the concentration of ATP was 0, such that the total amount of ATP throughout the cellular respiration process could be observed. Additionally, the initial condition used for the concentration of oxygen was 0.04 g/L. Next, the constants were condensed into two gain blocks for each equation, which were multiplied by each concentration. Finally, the V_{O_2} max was added to the model for Equation (4), and was changed from 0.9 to 0.4 to see how the plots would change in response to variance in the constant block.

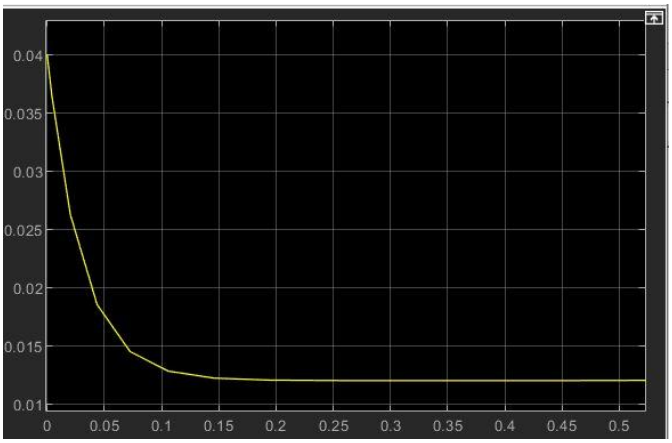
V. RESULTS



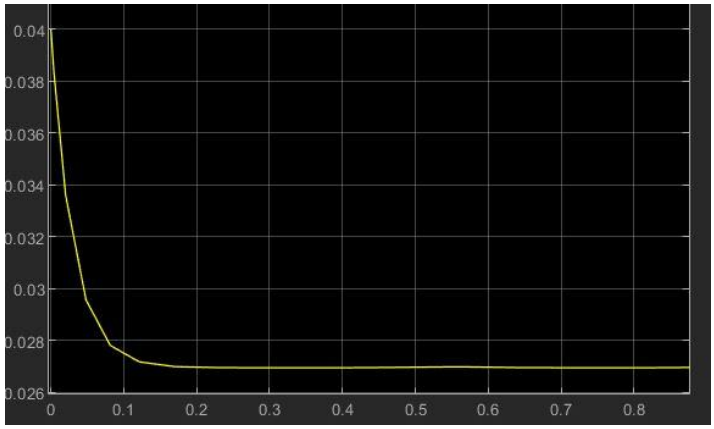
(a) *ATP concentration versus Time while at rest*



(b) ATP concentration versus Time during exercise



(c) O_2 concentration versus Time at rest



(d) O_2 concentration versus Time during exercise

Figure 2. (a) ATP concentration at rest (b) ATP concentration during exercise (c) O_2 concentration at rest and (d) O_2 concentration during exercise. For figures (a) and (b), the x axis represents time in hours, and the y axis represents concentration of ATP in the number of ATP molecules. For figures (c) and (d), the x axis still represents time in hours, but the y axis represents concentration of O_2 in g/ L.

Figure 2(a) shows a linear relationship between ATP concentration and time at a resting period with roughly 25 ATP molecules generated for a 10 hour time frame. Figure 2(b) displays the same linear relationship with ATP concentration approximately doubling to 50 ATP molecules over the same 10 hour time period. Figure 2(c) depicts the O_2 concentration change over a small period of time during rest. In viewing the graph, a decreasing slope is observed within the first 6 minutes of resting before plateauing to a constant value. The same decreasing trend is observed in figure 2(d) within the first 6 minutes during exercise. In comparing the two, the final concentration of O_2 within an exercising state is roughly doubled that of an individual during a resting state.

The original assumptions were that a larger amount of ATP would be generated during the state of exercise, as well as a larger increase in the concentration of O_2 during exercise. In analyzing the figures, the results showed the relationship that we anticipated, as both ATP and O_2 concentration during exercise was roughly double that of the concentration during resting. This aligns with our initial intuition, since it should be expected that as the percentage of V_{O_2} max increases during difficult exercise, the amount of oxygen and ATP required to maintain the activity would increase.

VI. CONCLUSIONS / FUTURE STUDY

Energy production and consumption are important processes in an athlete's performance. However, these processes are both very difficult to model. Our model is a

simplified system of ATP generation used in the understanding of the constraints placed around ATP production. This data can be used in the study of RED-S by relating ATP aerobic generation to oxygen availability. As this subject has much more depth that should be explored, some areas to examine further would be the addition of anaerobic ATP production for short durations under high intensity activities, unstable glucose levels, and the respiration rates of both aerobic and anaerobic processes. Firstly, it should be understood that there is anaerobic respiration that converts glucose to ATP at a much different rate, being less efficient but reacting at a faster rate. It should also be noted that we would want to see how glucose restricts ATP production in studying RED-S, as not having sufficient amounts of an energy source from the lack of food would affect the overall ATP system. Additionally, this study could also be utilized in the future to understand how medical conditions such as diabetes affects energy levels due to varying glucose levels. Lastly, this system would be best understood when we are able to quantify and relate the reaction rates of aerobic and anaerobic respiration as they are opposite in nature due to the differences in function. As aerobic respiration is a slow reaction, this value can vastly change the amount of ATP production and oxygen consumption in the system due to the high number of ATP produced along with the need for 6 O_2 molecules per reaction. On the other hand, anaerobic respiration is a process that has a much faster reaction rate but it only produces 2 ATP per glucose molecule. Both of the rates are needed to get a clearer model of the ATP consumption and production during the various stages of respiration during exercise. This would be able to give us a clearer understanding of the glucose consumption. Overall, this model begins to give us insight into the vastly complicated system of energy production and consumption. The future iterations of this system can help us understand RED-S and the biological effect on the ATP consumption can have on overall oxygen and glucose consumption. Both oxygen and glucose levels are important in relating to the many negative effects that RED-S has on humans and this understanding of the system along with numerical tests would be able to help explain the causes of some of these effects.

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VIII. REFERENCES

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