Dynamic Model for the Respiratory Response to Exercise

Daniel Acker, Tawny Bagnol, Cristina Barney, Isabella Wolf, Mingyao Xu

Abstract — **Gas exchange is a necessary process to human health in which the lungs supply the body with oxygen and dispose of unwanted carbon dioxide. During exercise, breathing rate increases because the muscles are using up more oxygen to produce the energy the body needs to work harder, while also producing more carbon dioxide as a result. This paper explores the development of a mathematical system to simulate the respiratory response to exercise using programs like Matlab and Simulink. Considering the variety of partial pressures and volumes that occur during gas exchange, this system allows for observations into what actually happens in the respiratory system during exercise. Over time, it was concluded that the venous partial pressure of oxygen drops from 40 mmHg to 20 mmHg, volume of ventilation increases to approximately 4600 mL, and breathing rate increases from a resting rate of 15 BPM to 47 BPM at the peak of exercise. These results from the simulation confirm the expectations for this biological system.**

Clinical Relevance — **Pulmonary Edema is classified by excess fluid in the lungs, specifically in the Alveoli, resulting in impared gas exchange. Physically, patients with this syndrome demonstrate extreme shortness of breath, and an increased breathing rate, BR. The fluid filling the Alveoli causes the Residual Volume, RV, of the lungs to decrease; causing the Alveolar Volume, AV, to also decrease.[1] This prevents the efficient absorption of Oxygen into the bloodstream; the partial pressure of Oxygen in the air of the Alveoli, PaO2, decreases causing the Arterial Partial Pressure of Oxygen in the blood, PbO2, leaving the lungs to decrease. This project is relevant due to its ability to simulate the above mentioned alterations with relative ease and rapid execution for immediate results.**

I. INTRODUCTION

The human body often encounters situations that cause for it to adapt. For example, when exercising the body responds by increasing heart rate and breathing rate, BR. During exercise, the muscles are working harder and the cells are using up more oxygen to produce energy while also producing carbon dioxide waste at a much faster rate.[2] With the gas levels in the body out of its ideal standard, the respiratory system would then adapt to this situation by increasing the respiratory rate to provide the body with the necessary oxygen, while removing the excess carbon dioxide that the body does not need. This is the basic concept of gas exchange that happens in the human body between the respiratory and the cardiovascular system on a daily basis.

To get a better understanding for this system, a deeper understanding of what happens during gas exchange is needed. During inhalation, the alveoli in the lungs will expand and fill with air. The oxygen that is inhaled will move from the alveoli into the bloodstream, while the carbon dioxide will move from the bloodstream, into the alveoli, and eventually out of the lungs when the person exhales. This occurs because gas exchange primarily occurs through the process of simple diffusion. This means that gas molecules will flow from areas of high concentration to areas of low concentration, so that when blood is low in oxygen concentration and high in carbon dioxide concentration, the concentration gradient will allow gas exchange to occur.[3] A key factor when analyzing gas exchange and diffusion of different elements within the same volume, and something that to consider in this system is partial pressure. Partial pressure is a measure of the concentration of a gas compared to the total mixture of gases in the surrounding air. Partial pressure is an important driving force in gas exchange between the respiratory and cardiovascular system and a visual representation of the partial pressure gas exchange process can be seen in Figure 1.

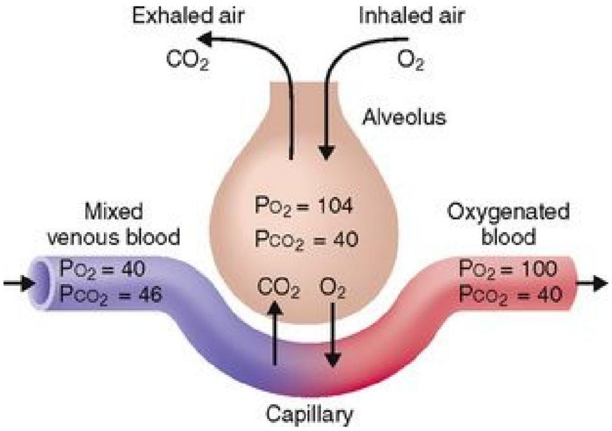

Figure 1. Gas exchange process that occurs through partial pressure[4]

In addition to these partial pressures, this system will also analyze the various volumes, such as tidal and residual volume, that occur during gas exchange, while considering the faster respiratory rate caused from physical activity. From this point forward, the team can simulate this gas exchange process through Matlab and Simulink and expect the system to have an outcome that displays an increased amount of oxygen delivery into the bloodstream due to the increased breathing and gas exchange rates caused from the respiratory response to exercise.

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[1] Mayo Clinic. 2020. Pulmonary Edema - Symptoms And Causes. [online] Available at: <https://www.mayoclinic.org/diseases-conditions/pulmonary-edema/symptoms-causes/syc-20377009#dialogId46715794> [Accessed 15 December 2020].

[2] Breathe (Sheff). "Your lungs and exercise". v.12(1): 97-100. Mar. 2016

[3] Kerr, Shana. "Oxygen and Carbon Dioxide Gas Exchange". Georgia Tech Biological Sciences: 2020

[4] Basicmedical Key. "Pulmonary diseases" Ch.4, Figure 5-6.

II. ASSUMPTIONS

A. Partial Pressures

The partial pressure of oxygen in alveolar air is simplified as P_aO_2, and is used as a constant of 104 mmHg, and is controlled by the combination of the residual air that stays in the lungs and the atmospheric air that is inhaled with every breath. The arterial partial pressure of oxygen, P_bO_2, is used in this system as a constant of 102.22 mmHg calculated with a simple diffusion equation taking into consideration the total volume of alveolar air and the flow rate of blood through the lungs. It is assumed that the body will keep these values constant throughout the process.[5]

B. Respiratory Rate

The range for an average resting respiratory rate at rest is between 12-20 breaths per minute, with an average at 15 BPM. In this system, it is assumed that the resting breathing rate, BR_r, is constant at 15 BPM for an average male at rest.[6]

C. Tidal Volume

Tidal volume is the amount of air displaced between normal inhalation and exhalation without any extra effort. It is assumed that the tidal volume, TV, in this system to be 495.5 mL, which is a normal value for the average male.[7]

D. Residual Volume

Residual volume is the amount of air that remains in the lungs after fully exhaling. It is assumed that the residual volume, RV, in this system to be 3000 mL, which is a normal volume for the average male. Figure 2[8] shows a representation of TV and RV in the lung.

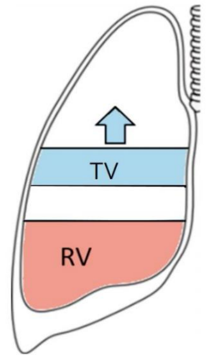

Figure 2. Difference between non-changing Residual Volume and changing Tidal Volume [8]

III. MATHEMATICAL PROCEDURE

A. Abbreviations and Units

- P_aO_2: Partial pressure of oxygen in the alveolar air (measured in mmHg). Constant at 104 mmHg.
- P_bO_2: Partial pressure of oxygen in the arteries leaving the lungs (measured in mmHg). Kept constant at 102.22 mmHg.
- $P_vO_2(t)$: Partial pressure of oxygen in the veins returning to the lungs (measured in mmHg). Initial value at steady state is at 40mmHg.
- φ: Constant flow rate of blood through the lungs of 100 mL
- TV(t): Tidal volume (measured in mL) at a point in time. Steady state at 495.5mL.
- RV: Residual volume (measured in mL) constant at 3,000 mL.
- AV(t): Alveolar ventilation at a point in time. This is defined as TV(t) + RV (measured in mL). With AV at steady state being equal to 3495.5 mL.
- $BR(t)$: Breathing rate (measured in breaths per min) at a point in time.
- BR_r: Resting breathing rate (measured in breaths per min). At an average of 15BPM.

B. Equations

The relationship between the partial pressures of oxygen within the alveolar air and the bloodstream.

$$P_bO_2 = \frac{P_aO_2 \cdot \frac{AV(t)}{} + P_vO_2(t)}{\frac{AV(t)}{} + 1} \tag{1}$$

Using equation (1) you can solve for AV(t)

$$\mathrm{AV(t)} = \frac{(P_bO_2 - P_vO_2(t))*}{P_aO_2 - P_bO_2} \tag{2}$$

To solve for Breathing Rate the following relationships are analyzed.

$$\mathrm{AV(t)} = \mathrm{RV} + \mathrm{TV(t)} \tag{3}$$

$$\mathrm{AV(t)} = \mathrm{RV} + \frac{TV(BR(t))}{BR_r} \tag{4}$$

Using the above equations, you can solve for BR(t)

$$\mathrm{BR(t)} = \frac{BR_r(AV(t) - RV)}{TV} \tag{5}$$

To analyze the rate of change of AV(t) and BR(t) you can take the derivative

$$\frac{dAV}{dt} = -\frac{}{P_aO_2 - P_bO_2} \cdot \frac{dP_vO_2}{dt} \tag{6}$$

$$\frac{dBR}{dt} = \frac{BR_r}{TV} \cdot \frac{dAV}{dt} \tag{7}$$

Using equations (6) and (7), you can solve for $\frac{dBR}{dt}$

$$\frac{dBR}{dt} = -\frac{BR_r}{TV} \cdot \frac{}{P_aO_2 - P_bO_2} \cdot \frac{dP_vO_2}{dt} \tag{8}$$

To make the system a loop with input I(t) the following equations is generated

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[5] Ortiz-Prado, Esteban; Dunn, Jeff; Vasconez, Jorge; Castillo, Diana; Viscor, Gines. "Partial Pressure of Oxygen in the Human Body: A General Overview". Am J Blood Res. v.9(1): 1-14. 2019.

[6] Whitworth, Gerhard. "What is a Normal Respiratory Rate". Medical News Today. Feb. 2019

[7] Hallett, Sasha; Toro, Fadi, Toro; Ashurst, John. "Physiology, Tidal Volume". StatPearls: 2020.

[8] Alila Medical Media. "Respiratory System Basics". May 6. 2019.

$$\frac{dAV}{dt} = -\frac{AV(t)}{P_bO_2 - I(t)} \cdot \frac{dI}{dt} \tag{9}$$

$$\frac{dBR}{dt} = -\frac{BR(t)}{AV(0)} \cdot \frac{AV(t)}{P_bO_2 - I(t)} \cdot \frac{dI}{dt} \tag{10}$$

The following graphs in Figure 3 show an expected relationship between the venous partial pressure, alveolar ventilation and breathing rate. These were generated in Matlab using equations (2) and (5). These are shown again at a bigger scale in the appendix.

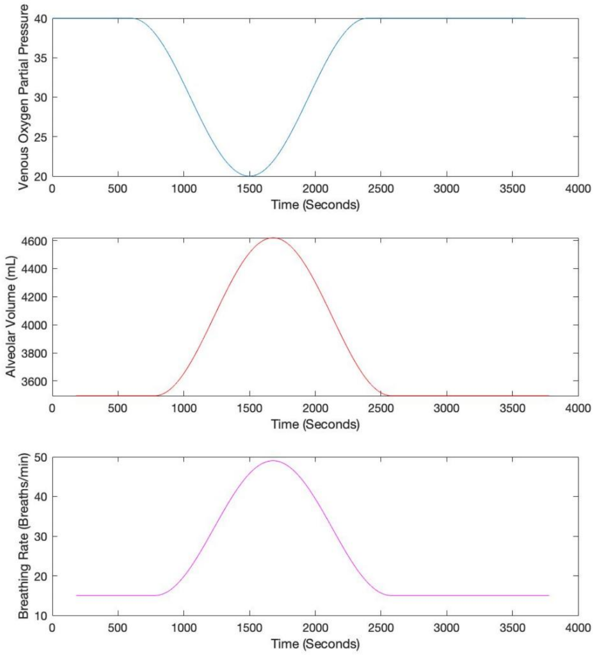

Figure 3.

IV. RESULTS

A. Block Diagram

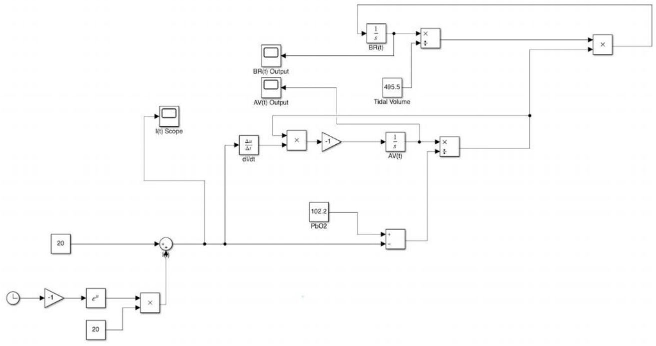

Figure 4. Respiratory Response SIMULINK Block Diagram, using equations (9) and (10). Bigger scale included in the appendix.

B. Resulting Figures

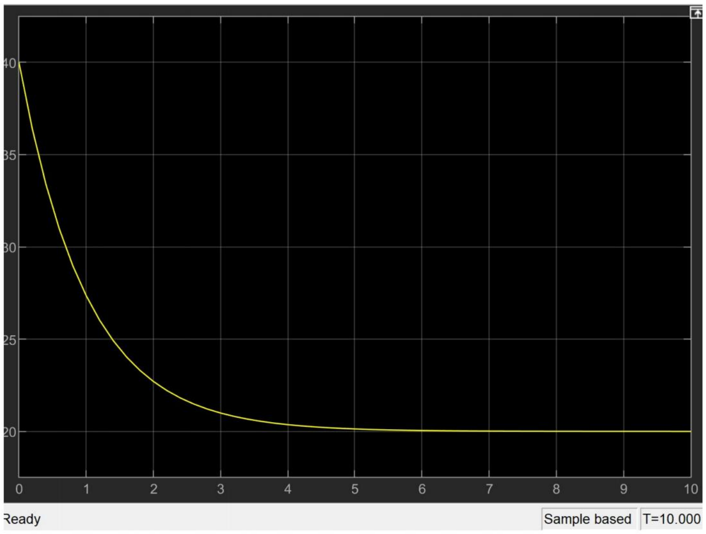

Figure 5. I(t) Venous Partial Pressure O_2 during exercise, where the horizontal axis represents time in minutes and the vertical axis represents Partial Pressure in mmHg.

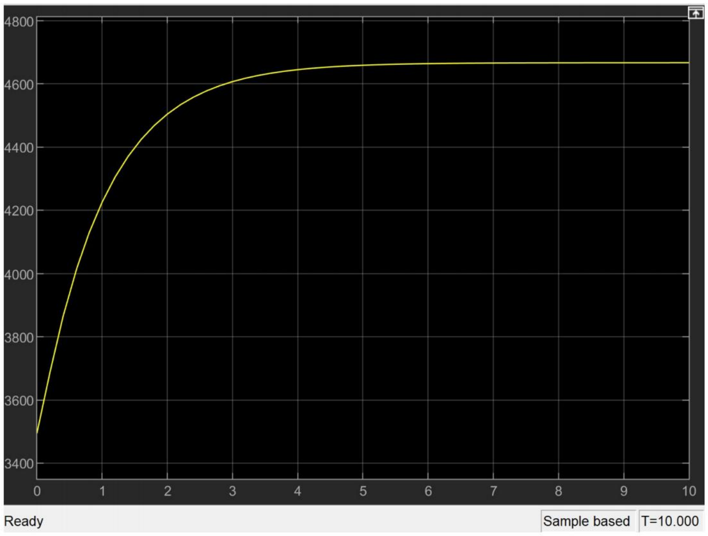

Figure 6. AV(t) Alveolar Ventilation during exercise, where the horizontal axis represents time in minutes and the vertical axis represents Volume in mL.

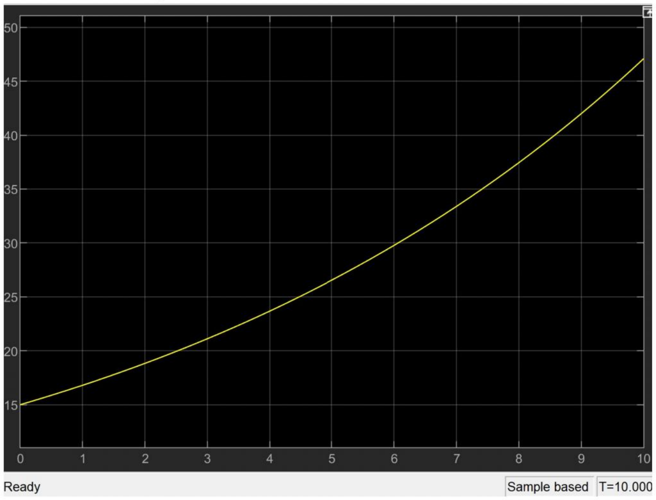

Figure 7. BR(t) Breathing Rate during exercise, where the horizontal axis represents time in minutes and the vertical axis Breathing Rate in breaths per minute.

The following graphs show the results of this system applied to a person with pulmonary edema. The disease is explained under the section titled Clinical Syndrome below.

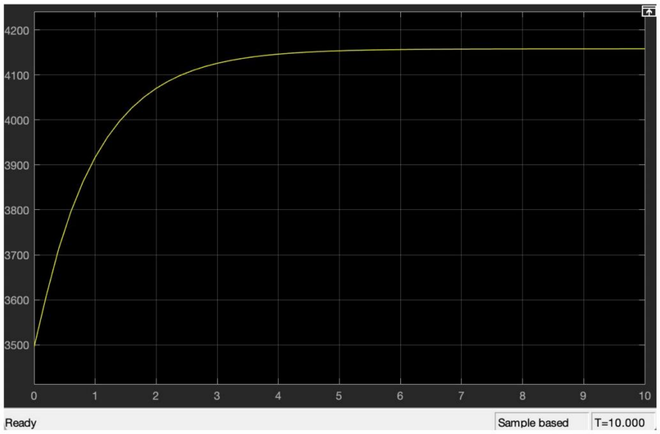

Figure 8. AV(t) with pulmonary edema, where the horizontal axis represents time in minutes and the vertical axis represents Volume in mL.

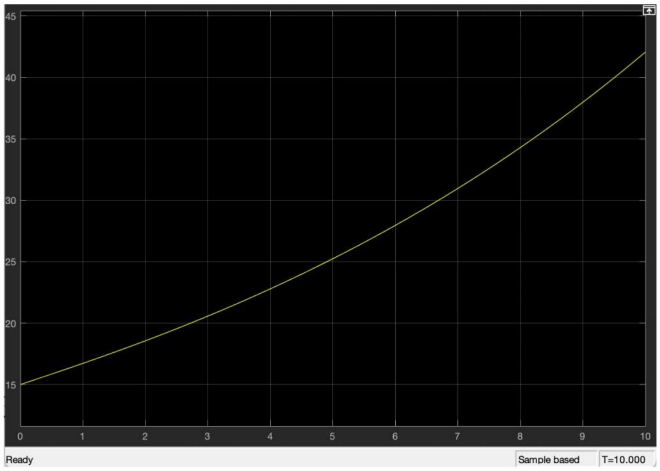

Figure 9. BR(t) with pulmonary edema, where the horizontal axis represents time in minutes and the vertical axis Breathing Rate in breaths per minute.

V. CLINICAL SYNDROME

For the modified version of the system, it is assumed that the patient is experiencing non-heart-related (noncardiogenic) Pulmonary Edema; more specifically High-Altitude Pulmonary Edema (HAPE). In this case, the vessels in the lungs constrict–due to high altitudes, usually above 2,400 meters–creating an increase in pressure, and in turn cause the blood vessels to leak fluid to the lung tissues which fill the Alveoli; reducing its volume.[9] In one particular study, a gas mixture was administered to patients to mimic the effects of HAPE on the lungs by reducing the percentage of Oxygen from 21% to 12.5%.[10] To simulate HAPE in the created system the Alveolar Volume is reduced by 40%; in other words, the Alveolar Volume input is altered to have 60% of its original volumetric capacity. The results from these adjustments are found in Figure 8 and Figure 9. From Figure 8 it is evident that the Alveolar Ventilation decreases significantly due to the decrease in Alveolar Volume. In addition, Figure 9 demonstrates a lowered Breathing Rate also due to the decrease in Alveolar Volume.

VI. DISCUSSION

The simulation of this model runs for the first 10 minutes of a change in the input I(t),m which represents the venous partial pressure of oxygen, due to exercise. It was expected the input to be an exponential decrease from 40 to 20 mmHg. This simulation matches the expectation. And for the first loop where it used the Ventilation as the first output function, it was expected to increase with similar behavior compared to the exponential function with the initial condition of 3494.5 mmL. The results also matched this expectation. The second loop of the experiment is the breathing rate, and it was expected to increase from the ideal rate of 15 to at most 60. The derivative of the breathing rate should gradually increase as the new equilibrium of oxygen supply will be reached. The simulation result meets the expectations, but it only increases to about 48 due to the time length of the simulation. This behavior makes sense because when the person first started to exercise, the lag between oxygen needed and oxygen input we could get from the air since the tidal volume and venous partial pressure need time to expand.

Physiological observation of exercising will show that the breathing rate increases, and the longer the exercise, the more intense the exercise, the faster the breathing rate is, and the larger volume of each breath that will exchange. The simulation is consistent with the observation.

The simulation was only able to include a first order function of t. If elasticity is included, a PID control system could be included to regulate the output. However, it was realized the first derivative equation is simple enough and creates no delay, and thus no control system is required. With more time a new system could be developed, taking into consideration the elasticity of the alveoli and how that affects pressure and thus partial pressure. This would result in a second order system that creates a more realistic delay. In this case, taking the partial derivatives and multiplying them by the wiggle and adding them up to linearize the equations and thus create the transfer function to develop the PID controller.

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[9] Mayo Clinic. 2020. Pulmonary Edema - Symptoms And Causes. [online] Available at: <https://www.mayoclinic.org/diseases-conditions/pulmonary-edema/symptoms-causes/syc-20377009#dialogId46715794> [Accessed 15 December 2020].

[10] Patz, M., Sá, R., Darquenne, C., Elliott, A., Asadi, A., Theilmann, R., Dubowitz, D., Swenson, E., Prisk, G. and Hopkins, S., 2017. Susceptibility to high-altitude pulmonary edema is associated with a more uniform distribution of regional specific ventilation. Journal of Applied Physiology, 122(4), pp.844-852.

An effort was made to linearize the first derivative function which is A(t). Regardless of the fact that A(t) is a function of I(t), because of the equation A(t) can be linearized and be presented in the form of t.

Below is the process of linearization and the tangent line at steady state when t = ln(1/16).

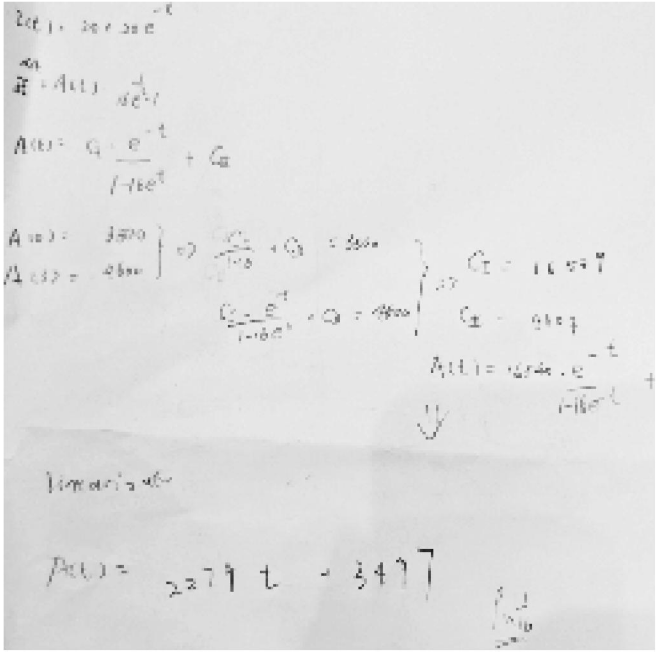

Figure 10: linearization of the equations

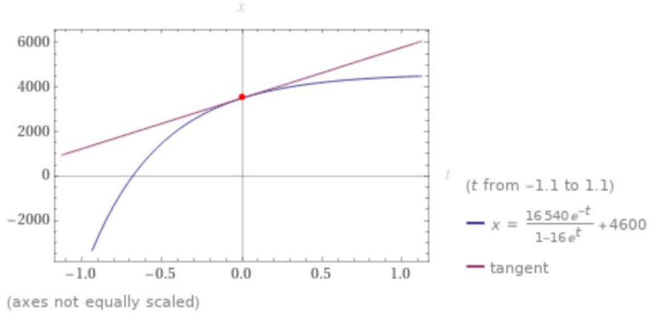

Figure 11: Graph of linearized input

It is not ideal that A(t) can be transferred into a function of t, since the lack of second control results in immediate change of the end result A(t) and B(t). However, if granted more time, the possibility of exploring the plasticity of the venous may be added, which can generate non-linear function of A(t), and as well as of B(t).

VII. SIMULATION AS AN ALTERNATIVE

The simulation can serve as an alternative to physiologic experimentation with multiple advantages including, but not limited to, an improved understanding of physiological processes, experimental design techniques, and developing research skills. The simulation would allow for students to understand the multiple physiological components needed for gas exchange to take place. Furthermore, the simulation allows for the manipulation of each of these components demonstrating their effects on the breathing rate. Both of these elements contribute to students developing their researching skills by giving way to their intellectual curiosity which is needed for finding solutions to modern scientific problems. On the other hand, this simulation is limited in comparison to physiological experimentation due to its computational methods; it may cause students to rely on a recipe-based approach to find solutions; inhibiting students' ability to approach solutions mathematically as opposed to randomly inputting values.

ACKNOWLEDGMENT

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[9] Referring to [1].

[10] Patz, M., Sá, R., Darquenne, C., Elliott, A., Asadi, A., Theilmann, R., Dubowitz, D., Swenson, E., Prisk, G. and Hopkins, S., 2017. Susceptibility to high-altitude pulmonary edema is associated with a more uniform distribution of regional specific ventilation. Journal of Applied Physiology, 122(4), pp.844-852.

APPENDIX

Enlarged Images:

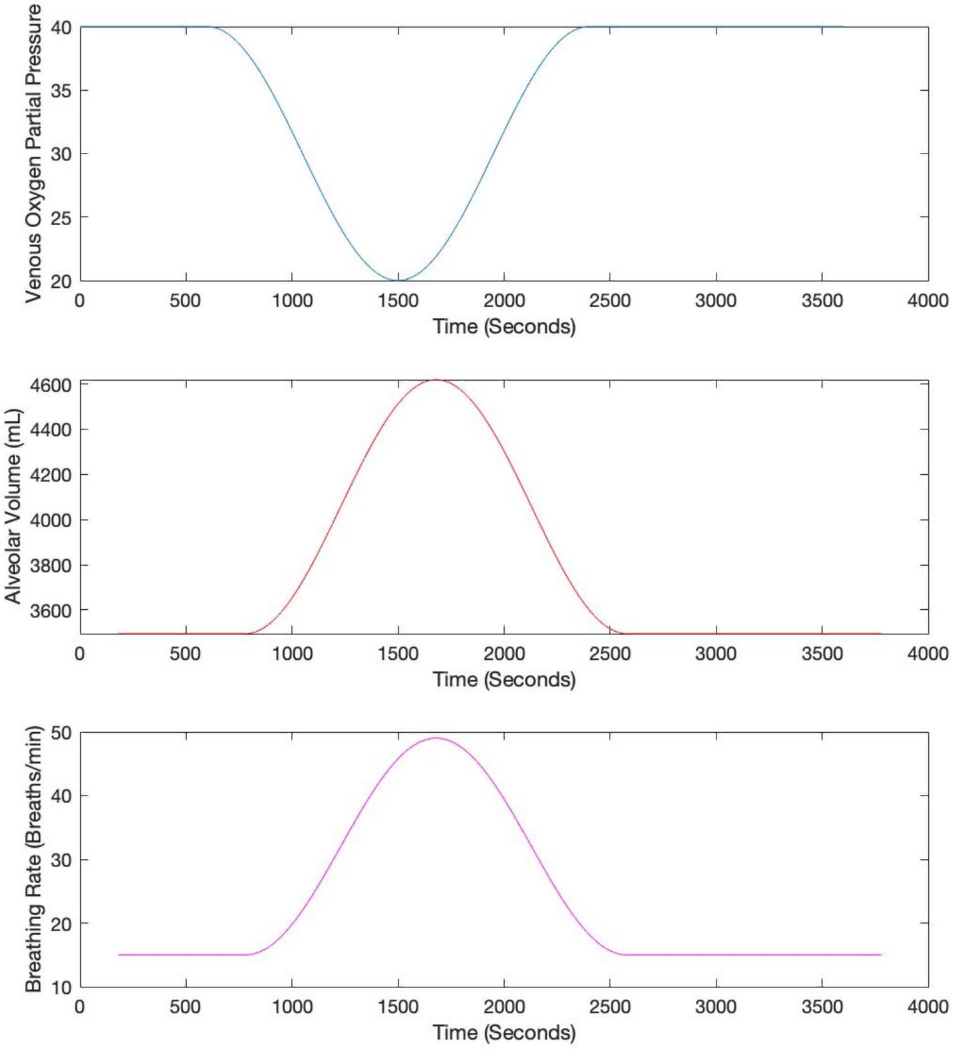


Figure 3.

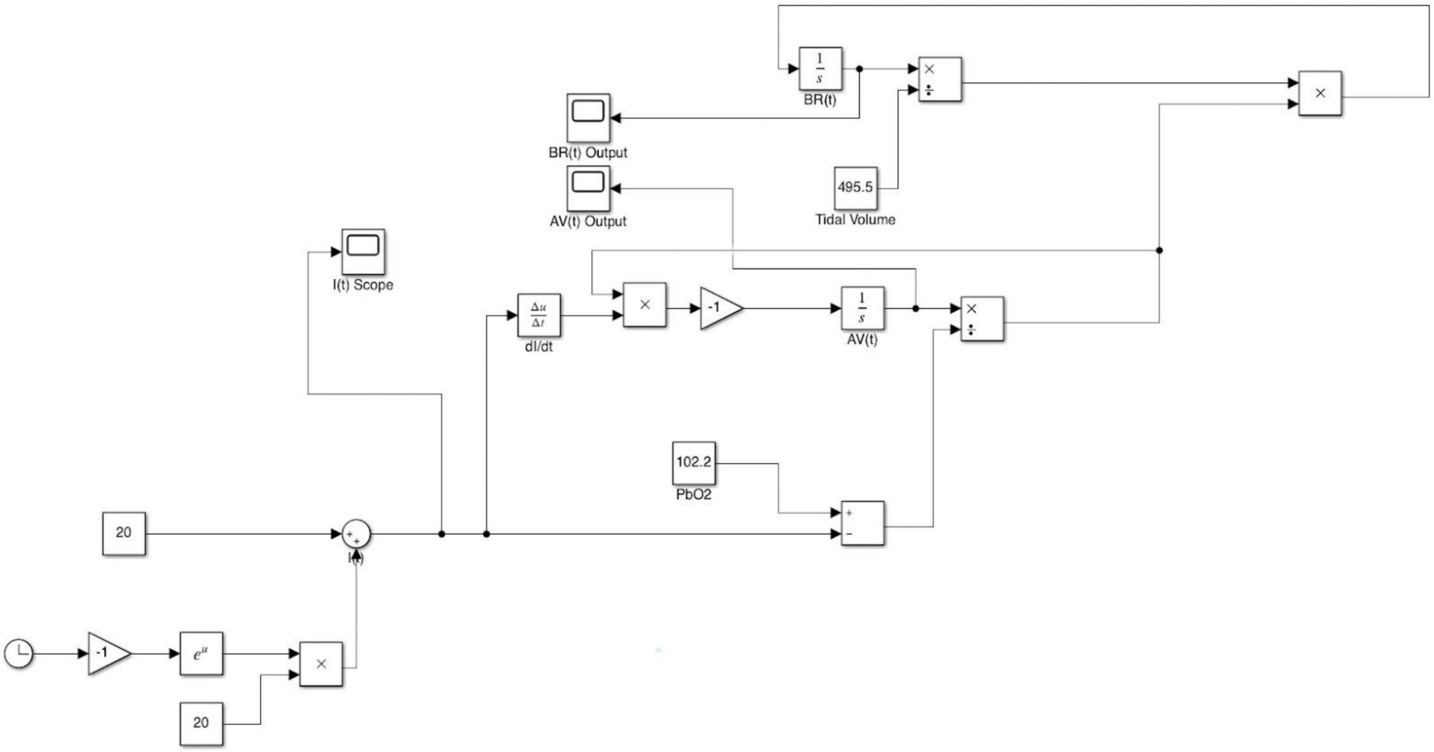


Figure 4. Respiratory Response SIMULINK Block Diagram

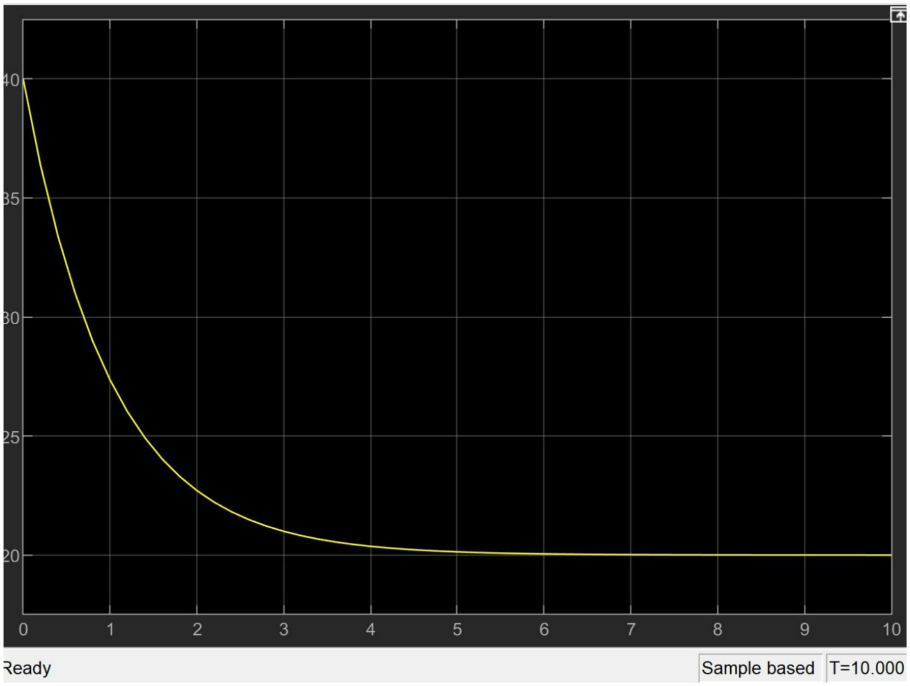


Figure 5. I(t) Venous Partial Pressure O_2 during exercise

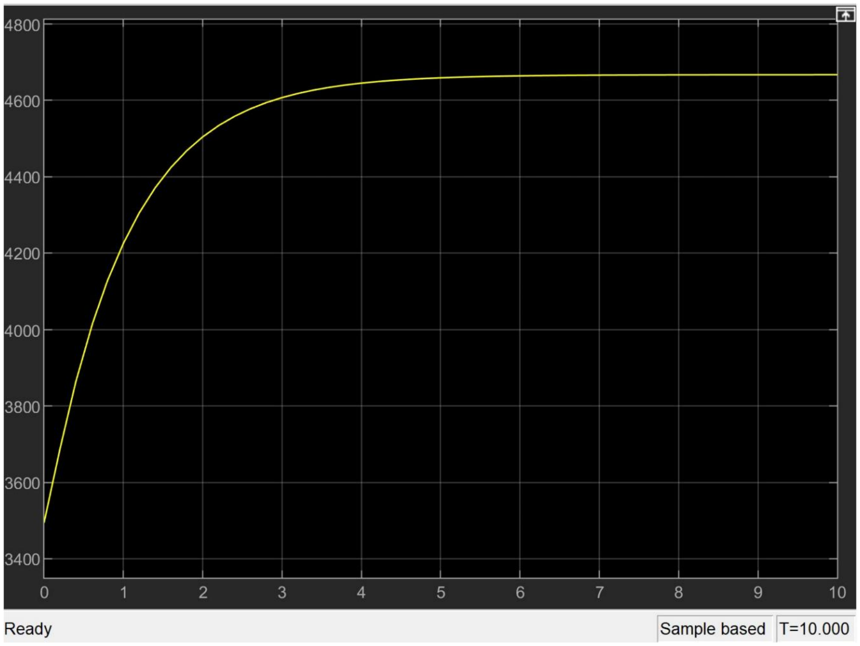


Figure 6. AV(t) Alveolar Ventilation during exercise

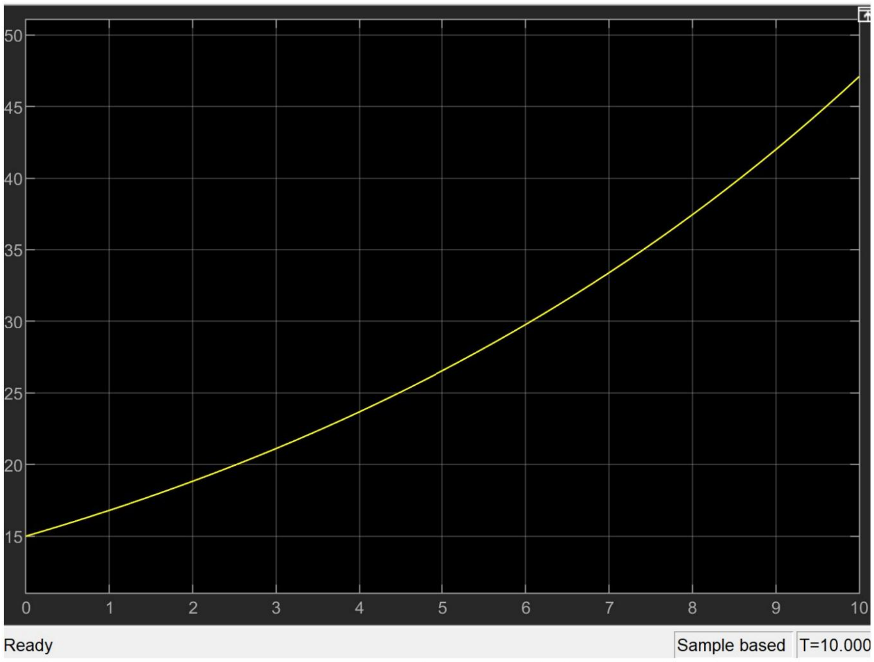


Figure 7. BR(t) Breathing Rate during exercise

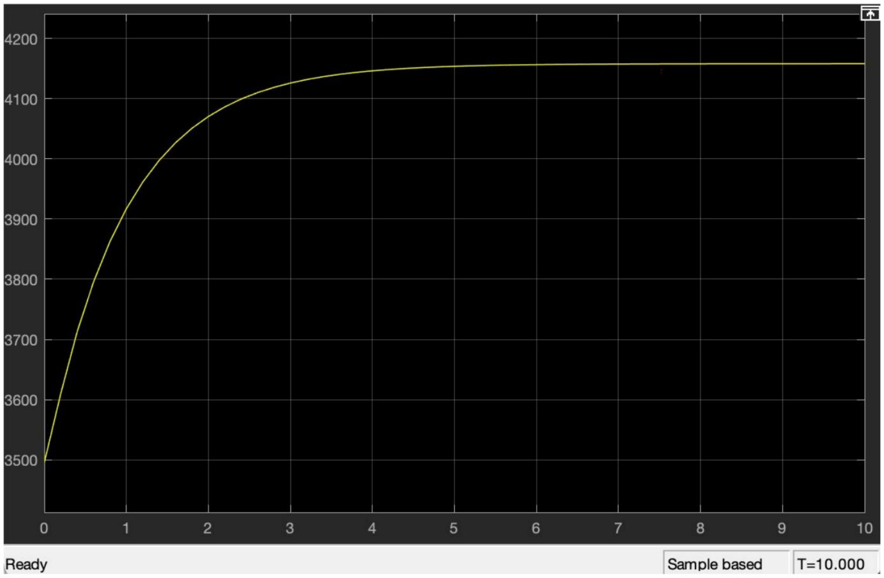
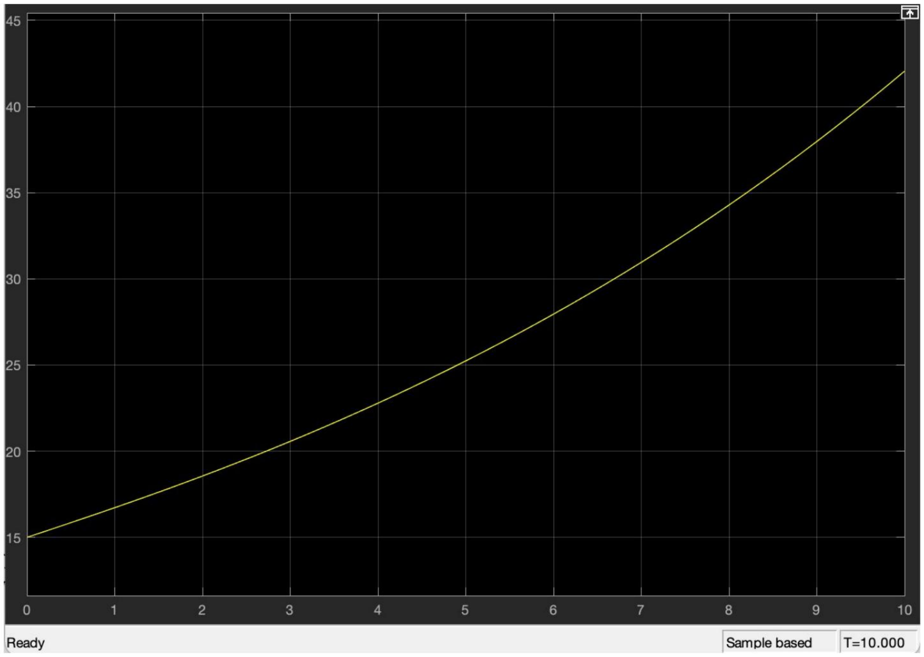


Figure 8. AV(t) with pulmonary edema



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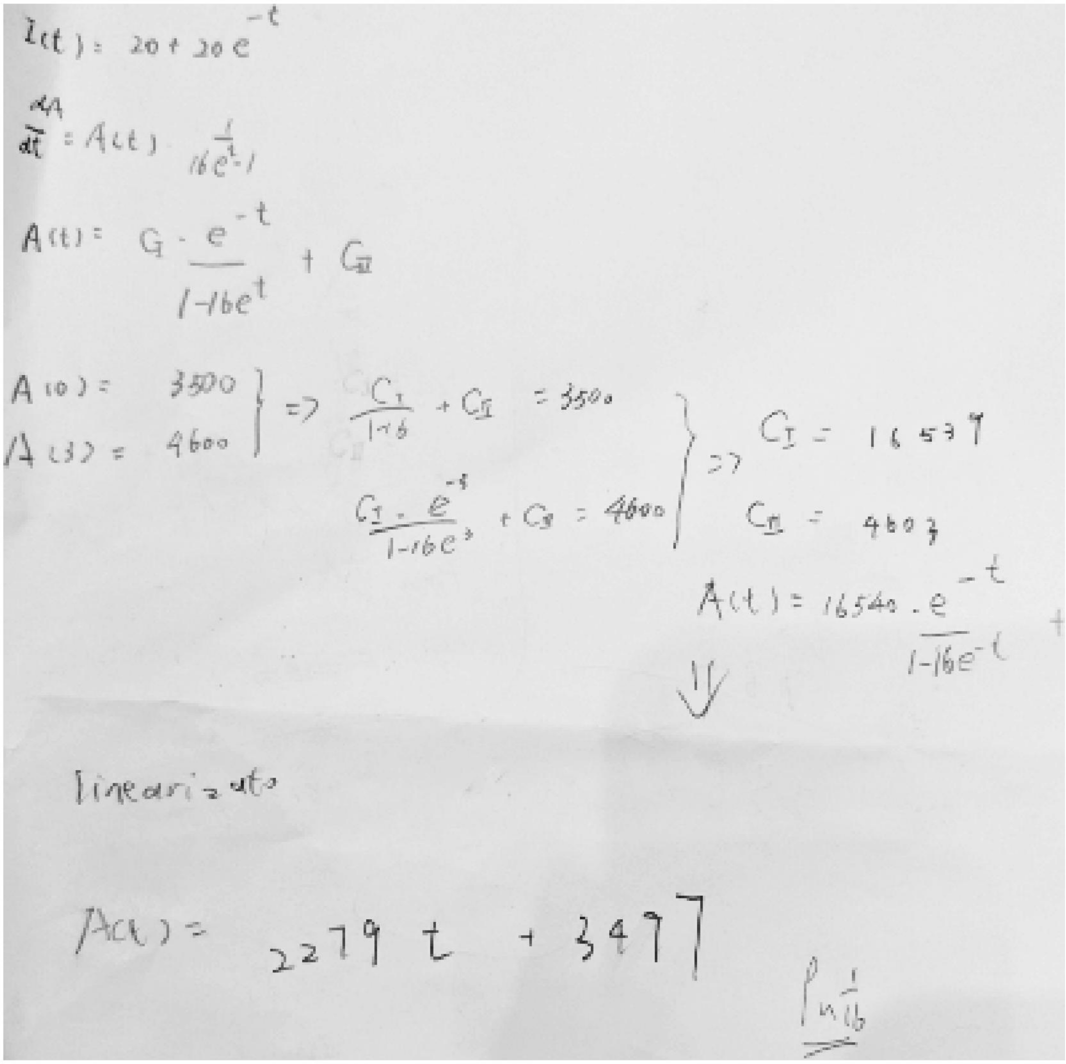

$I(t) = 20 + 20e^{-t}$

$\frac{dA}{dt} = A(t) \cdot \frac{1}{16e^{t}-1}$

$A(t) = \frac{C_I \cdot e^{-t}}{1-16e^{t}} + C_{II}$

$$\left.\begin{array}{l} A(0) = 3500 \\ A(3) = 4600 \end{array}\right\} \Rightarrow \left.\begin{array}{l} \frac{C_I}{1-16} + C_{II} = 3500 \\ \frac{C_I \cdot e^{-3}}{1-16e^{3}} + C_{II} = 4600 \end{array}\right\} \Rightarrow \begin{array}{l} C_I = 16539 \\ C_{II} = 4607 \end{array}$$

$A(t) = 16540 \cdot \frac{e^{-t}}{1-16e^{-t}} +$

$\Downarrow$

linearizato

$A(t) = 2279\,t + 3497$

$\underline{\ln \frac{1}{16}}$

Figure 10.

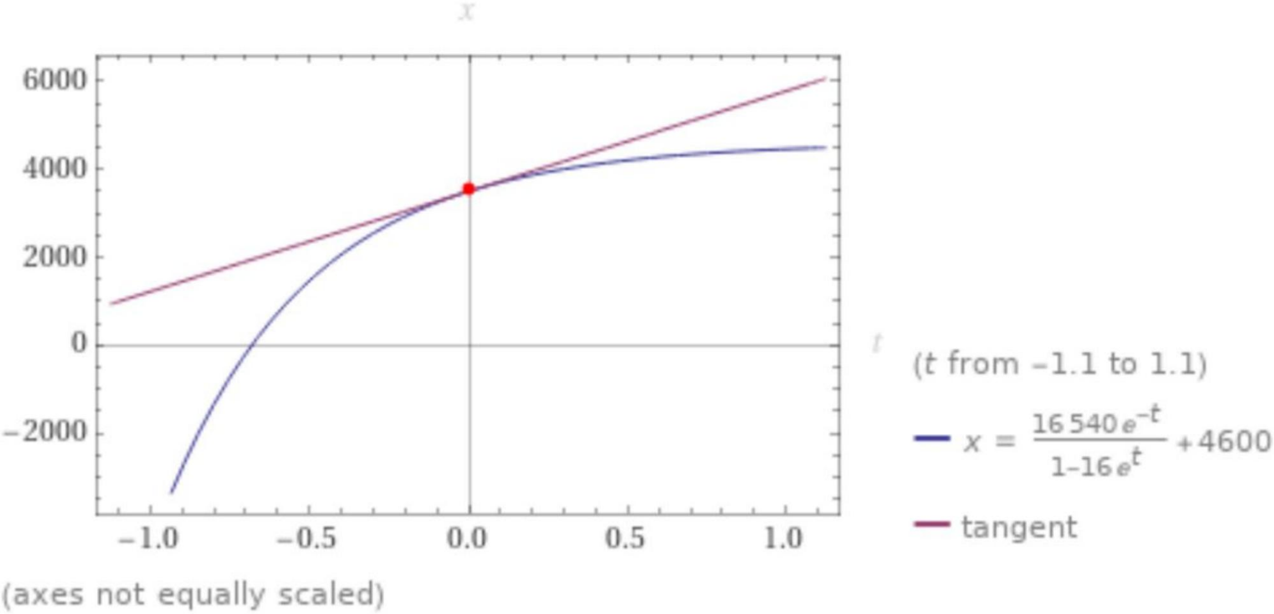

Figure 11.