

Body Temperature Control via Artery Dilation

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I. Abstract

The human body has a desired resting body temperature of anywhere between 97 and 99 degrees fahrenheit, and the body has many modalities to maintain temperature homeostasis. Specifically for raising internal temperature, there are three major ways the body can raise internal temperature. The most common way is to raise the metabolic rate, burning more calories for heat production. If the body temperature is still too low, the shivering reflex is triggered. Shivering is when skeletal muscles begin to contract and loosen rapidly, causing the body to shake and creating warmth by expending energy. Beyond this point, when the body temperature is dangerously low, the body will try to mitigate heat loss to the environment through vasoconstriction, controlled through the release of norepinephrine.

Using Simulink, we have created a model for the controlled release of norepinephrine to raise internal body temperature to a target level. Assuming constant metabolic and shivering heat production, our PID controller acted as we expected in the quick and stable raising of body temperature to target levels.

II. Introduction

Norepinephrine is both a hormone and a neurotransmitter of the sympathetic nervous system and is responsible for increasing the rate of skeletal muscle contraction in the body. An operant of the body's fight-or-flight response,¹ norepinephrine is only released during episodes of acute threat to the body such as severe cases of hypothermia. During such an episode, one of the most commonly observed effects of norepinephrine release is vasoconstriction of the cutaneous blood vessels due to an increase in the force of skeletal muscle contractions. Constricting the vessel leads to a decrease in blood flow due to the increase in vascular resistance and results in a conservative thermoregulatory effect. More in detail, a decrease in skin blood flow results in a net decrease in thermal heat dissipation through the skin surface along with a decrease in heat convection from the core to the skin². Thus, heat loss due to the body's metabolism is minimized. All in all, the aim of this project is to

closely study the effects of norepinephrine increase on the total heat loss of the body during adverse, hypothermic conditions and to model this system using a PID controller.

III. Methods

A. Defining the System

The control system is modeling the regulation of body temperature in hypothermia by considering vasoconstriction as the sole method the body utilizes to minimize heat loss in the moment. For simplification of the model, norepinephrine is considered to be the main hormone responsible for vasoconstriction. The biosystem takes into account how the body produces its own heat through metabolism and other mechanisms such as shivering that occur in a hypothermic state. It also takes into account the heat lost to the surroundings based on the diameter of the vessels and how that changes as the vessels constrict. To determine the rate of heat loss at the surface of the skin, a heat transfer equation for an open ended cylinder was used. The boundary for the system was defined as the skin and for this simulation, it is assumed that there is a constant sink at that boundary.

B. Assumptions

For the system, we assumed that norepinephrine is the only hormone or neurotransmitter that is responsible for vasoconstriction. This is not accurate because there are numerous hormones that contribute to the constriction of blood vessels, but for the simplification of the model it is necessary to just focus on one. We are also assuming that the body is in an initial hypothermic condition where vasoconstriction would occur. This is an important assumption because norepinephrine would not be released unless the body was in a severe hypothermic state, about 35°C³. Another assumption being made is that the heat lost to the surroundings can be modeled as a heat exchange equation of an open ended cylinder for the simplification of the model. The diameter of the capillaries is also assumed to have a linear relation to the amount of norepinephrine in the blood. This relation can be used to model the surface area and heat loss of the system. The last assumption

for this model is that the metabolic heat and other body functions such as shivering are the sole cause for the increase in body temperature, and that these values can be scaled down to our scope of the blood vessel.

C. Governing Equations

Regulation of temperature through vasoconstriction requires comparison between the heat produced by the body through metabolism and the heat lost to the environment through heat transfer (1). Heat transfer is modeled by the equation $Rate = \frac{kA}{d}(T_1 - T_2)$, where k is the thermal conductivity of the blood vessels, A is the surface area over which the heat transfer occurs, and d is the thickness of the blood vessels. The area, A , was derived by using the equation for surface area of a cylinder, $A = 2\pi rl$, where r is the radius. The radius and the concentration of norepinephrine were related through Poiseuille's Law, $R = \frac{8\eta l}{\pi r^4}$, where R is the resistance and η is the viscosity of blood. Using data from the paper by Nette⁴, it was approximated that there was a linear relationship between the resistance, R , and the concentration of norepinephrine, $C(t)$, following the form $R = mC(t) + b$. Solving for the radius and inserting the result into the equation for area, equation (1) is derived. The constant M represents the average energy produced by the body through metabolism and other natural functions such as shivering. $T_B(t)$ represents the temperature of the body as a function of time and T_E represents the temperature of the surrounding environment.

$$\frac{dT_B}{dt} = \alpha \left(M - \frac{2\pi l k}{d} \cdot \sqrt[4]{\frac{8\eta l}{\pi(mC(t)+b)}} (T_B(t) - T_E) \right) \quad (1)$$

The governing equation for the concentration of norepinephrine (2) consists of the secretion and uptake of norepinephrine by the body. The secretion of norepinephrine, $I(t)$, is regulated by the PID controller (3) and is correlated to concentration in the blood by the proportionality constant β . The norepinephrine uptake is related to the concentration currently in the blood, $C(t)$, and the time constant τ .

$$\frac{dC}{dt} = \beta I(t) - \frac{1}{\tau} C(t) \quad (2)$$

A PID controller was chosen for this system as it provides the most accurate and efficient response to changes in the biosystem. The coefficients in equation

(3) were chosen such that the zeros produced by the controller coincide with the poles of the biosystem (1). Equation (4) describes the temperature error between the biosystem and the target. The polarity of this equation is important as a body temperature lower than the target temperature will result in the production of norepinephrine.

$$I(t) = K_p e(t) + K_i \int_{-\infty}^t e(t) dt + K_d \frac{d}{dt} e(t) \quad (3)$$

$$e(t) = T_T - T_B(t) \quad (4)$$

D. Laplace and Linearization

The model for the biosystem is nonlinear, so equation (1) had to be linearized in order to obtain the transfer function for the system, $H(s)$. The linearized form of equation (1) is as follows:

$$\frac{dT_B}{dt} = NT_B(t) + QC(t) \quad (5)$$

$$\text{Where } N = \frac{-2\alpha\pi l k}{d} \sqrt[4]{\frac{8\eta l}{\pi(mC(t)+b)}} \\ \text{and } Q = \frac{-4\alpha\pi\eta l^2 k}{d(mC(t)+b)^{5/4}} \cdot \left(\frac{8\eta l}{\pi}\right)^{-3/4} \cdot (\bar{T}_B(t) - T_E)$$

The system was linearized around the average concentration of norepinephrine for the simulation and the temperature at which the body transitions to a dangerously hypothermic state, 35°C. Using the linearized system, the transfer function $H(s)$ was obtained as seen in equation (6).

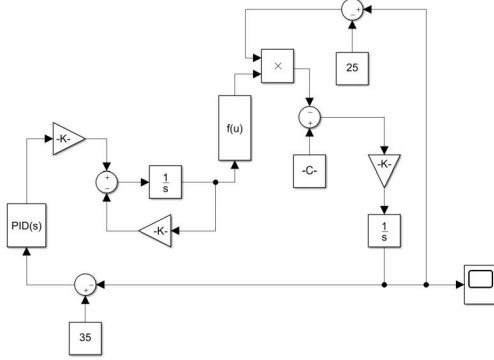
$$H(s) = \frac{T_B(s)}{I(s)} = \frac{Q\beta s}{(s-N)(s+\frac{1}{\tau})} \quad (6)$$

$$F(s) = \frac{K_d s^2 + K_p s + K_i}{s} \quad (7)$$

The open loop transfer function was then obtained using the equation $OL(s) = H(s) \cdot F(s)$, where $F(s)$ is the Laplace of the biosystem PID controller. The resulting open loop transfer function is seen in equation (8). The open loop transfer function will serve as a tool to determine the system's tendency to oscillate, and thus implication regarding stability. By looking at the phase margin of the open loop transfer function, one can analyze the degree of damping that the system will produce. Thus, the PID controller can be fine tuned to make the system achieve more desirable outputs.

$$OL(s) = \frac{QB(K_p s^2 + K_p s + K_i)}{s(s-N)(s+\frac{1}{\tau})} \quad (8)$$

E. Simulink Diagram



The system was linearized around 35°C (or 86°F), as this is what body temperature hypothermia starts to set in. Using the biosystem equation (1), the Simulink block diagram was created and can be seen above. The starting body temperature is 30°C, the environment temperature is 25°C, and the target temperature is 35°C. The secretion of norepinephrine is controlled by the PID controller block which ensures accurate levels of the hormone are released. The PID controller reads the error between the target and measured body temperatures and then signals for release of the appropriate amount of norepinephrine in an attempt to minimize the error. The results will paint a clearer picture of how this model relates norepinephrine to temperature and ensures the target body temperature is reached with minimal error or overshoot.

IV. Results

A. Simulink data

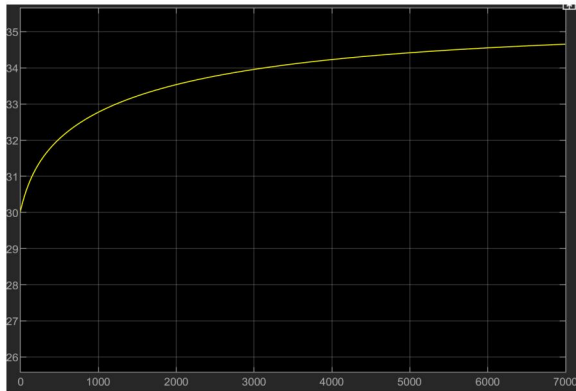


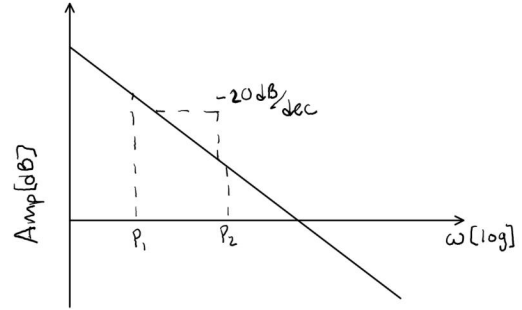
Figure 1: Simulink Simulation

The metabolic rate affects the system by changing how quickly the system reaches the steady state. With a higher metabolic rate, the system reaches steady state

quicker. α is the inverse of the specific heat of the blood, which converts the energy produced to temperature change in the area of interest. This affects the system response similarly to the metabolic rate where a higher α makes the body temperature increase faster.

B. Bode Plot

As seen in Figure 2, the phase margin of the system is greater than 90 degrees, indicating that the closed-loop dynamics of the system are overdamped and generate an approximate first-order response. This is consistent with the plot in Figure 1.



Where $P_1 = -\frac{1}{\tau}$ and $P_2 = N$

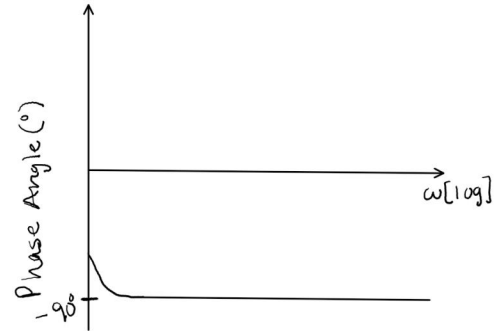


Figure 2: Bode Plot for System

V. Conclusions

A. Simulation results with physiological observations

Some major differences between our simulation and normal physiological control systems is that ours is a greatly reduced and simplified model looking more closely at extreme instances of hypothermia. Typically, when the body temperature is lower than the target, the body will start by raising the metabolic rate to produce more heat, though for the sake of simplicity, we have kept the metabolic rate constant. Getting goose bumps is a telling sign of hypothermic body temperature, after which the body will start shivering, where skeletal muscles begin to shake in small movements, creating

warmth by expending energy, which we have simplified in our simulation. These are all the first responses the body has for remediating lower body temperature, but when the body temperature drops below 86 degrees fahrenheit, the sympathetic nervous system relies on norepinephrine as a last resort to raise the body temperature⁵.

In these extreme cases, our simulated data seemed to follow what we had expected. As norepinephrine concentration increased, heat loss through the skin went down, and body temperature was able to rise. Through the PID control of the release of norepinephrine into the bloodstream, we had created an overdamped control system that resulted in the quick rise to the target temperature with no oscillations.

B. Modifying the simulation for Clinical Syndromes

Our model describes a modified version of body temperature control. Since we have omitted preliminary responses to hypothermic body temperature control, our model simulates the body's last efforts to reign in low body temperature. That said, there are some disorders that prevent the body from raising metabolism or shivering, such as hypothyroidism. An underactive thyroid gland will not produce the correct concentrations of thyroid hormones, namely triiodothyronine, that controls multiple body processes, like metabolism and shivering⁶, meaning that patients with hypothyroidism are incredibly sensitive to cold temperatures due to only having vasoconstriction to help raise their body temperature, just like our model simulates.

C. Advantages and Limitations of Simulation

An advantage to simulating the effects of controlled norepinephrine release for hypothermia remediation is two fold. First, the vasoconstriction effects of norepinephrine can be very harmful over extended periods of time, diminishing blood flow in smaller veins and capillaries, with subsequent tissue hypoxia and lactic acidosis and possible ischemic injury⁷. Second, norepinephrine is a hormone released by the body to aid in the flight or fight response when threatened. Upon release it acts to increase the force of skeletal muscle contraction and the rate and force of contraction of the heart, as well as increase the blood glucose levels⁸ to insure the body can function in strenuous situations. The culminations of these effects means that the subject with elevated norepinephrine

could feel undue stress and anxiety, as well as dangerous levels of blood pressure and hypoxia in their organs, all of which are avoided in simulation.

That said, the simulation fails to capture the big picture when it comes to temperature regulation. A healthy body has many more tools to raise the body temperature, like increasing metabolism, which for the sake of simplification we did not control in our model. Additionally, Norepinephrine is stored and released in the neurons of the sympathetic nervous system, functioning mainly as a neurotransmitter with some function as a hormone⁹. If we were to study a healthy person's recovery from hypothermia, it's unlikely there will be considerable norepinephrine in the blood unless they are in incredibly cold situations. Further muddling our simulation's accuracy is that norepinephrine affects each person differently, with its effects diminishing as people get older¹⁰.

VI. References

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