Modeling Baroreflex Feedback Control for Blood Pressure Regulation

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Background

- Blood pressure regulation is a homeostatic process
  - Parasympathetic responses correspond to positive feedback loops
  - Sympathetic responses correspond to negative feedback loops

- Baroreceptors are located in arterial walls
  - By measuring pressure, the baroreflex affects the firing rate of the associated neurons, which will increase/decrease the systemic arterial pressure

- Investigate how a change in carotid sinus pressure relates to the feedback adjustment of systemic arterial pressure due to the relationship between baroreceptors and peripheral nervous system
Goals

1. Model a human sympathetic baroreflex response through mathematical governing equations and simulink/MATLAB

2. Introduce closed- and open-loop transfer functions that relate input carotid sinus pressure to output arterial pressure

3. Conduct a Bode plot analysis and evaluate the feasibility of our model in human model application

4. Investigate medical conditions such as multiple sclerosis (MS) and their effects on blood pressure regulation through model
Defining Our System: Assumptions

1. We assume that all governing equations, transfer functions, and datasets from literature apply to normal human physiological conditions.

2. For our governing equations, we assume that the efferent sympathetic nerve firing rate, modeled as $f$, is determined through a linear amplifier model.

3. In literature, rabbit experimental data assumed that the influence of muscular activity is eliminated through anesthetization. For consistency, we assume that human muscular activity does not affect our model.

4. We assume that arterial and carotid sinus pressure are similar to the point of being interchangeable.

5. We assume that stroke volume and total peripheral resistance are constant gain values in calculating the carotid sinus pressure as a function of resting heart rate.
Methods

- The blood pressure was related to the baroreceptor firing rate (efferent sympathetic nerve activity) through arterial wall deformation, modelled through artery wall strain, and mechanoreceptor stimulation, modelled through end nerve strain.
- Governing equations relating these terms together were modelled in simulink.
Baroreceptor Nerve Firing Equations and Values

\[ p(t) = p_0 + 2.5 \sin(p_2 - p_1 t) \]  \hspace{0.5cm} (1)

\[ \varepsilon_w = \frac{r - r_0}{r} = K_{wall} \cdot p \]  \hspace{0.5cm} (2)

\[ \varepsilon_{ne} = \varepsilon_w - \varepsilon_1 \]  \hspace{0.5cm} (3)

\[ \frac{d\varepsilon_1}{dt} = -(\alpha_1 + \alpha_2 + \beta_1)\varepsilon_1 + (\beta_1 - \beta_2)\varepsilon_2 + (\alpha_1 + \alpha_2)\varepsilon_w \]  \hspace{0.5cm} (4)

\[ \frac{d\varepsilon_2}{dt} = -\alpha_2 \varepsilon_1 - \beta_2 \varepsilon_2 + \alpha_2 \varepsilon_w \]  \hspace{0.5cm} (5)

\[ f = s_1 \cdot \varepsilon_{ne} - s_2 \]  \hspace{0.5cm} (6)

<table>
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<tr>
<th>Parameter</th>
<th>Definition</th>
<th>Value</th>
<th>Units</th>
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<tr>
<td>(r_0)</td>
<td>zero pressure radius</td>
<td>1.13</td>
<td>mm</td>
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<tr>
<td>(h)</td>
<td>wall thickness</td>
<td>0.17</td>
<td>mm</td>
</tr>
<tr>
<td>(E)</td>
<td>elastic modulus</td>
<td>1050</td>
<td>mmHg</td>
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<tr>
<td>(K_{wall})</td>
<td>aortic distensibility</td>
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<td>mmHg</td>
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<td>elastic nerve constant</td>
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<td>mmHg</td>
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<td>elastic nerve constant</td>
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<td>mmHg</td>
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<tr>
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<td>2</td>
<td>mmHg(\cdot)s</td>
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<td>(\alpha_1)</td>
<td>nerve ending constant</td>
<td>(\frac{E_0}{\eta_1})</td>
<td>s(^{-1})</td>
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<tr>
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<td>s(^{-1})</td>
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Efferent Baroreceptor Sympathetic Nerve Firing Rate as a Function of Carotid Sinus Pressure
- The output nerve firing rate shown in green is modelled sinusoidally, even though governing equations are linear.
- Attributed to mismatched sampling rate.
- Light blue line represents an estimated corrected curve with proper sampling rate used.
The carotid sinus pressure in our model was represented as a linear function of resting heart rate, and related through the above physiological values. The values are taken from average human physiological conditions.
Transfer Functions

Sympathetic Baroreflex

Transfer functions based on anesthetized rabbits were found from literature. Models were adjusted to humans through modelling carotid sinus pressure as a function of resting heart rate.
System Block Diagram in Simulink

Carotid Sinus Pressure

Sympathetic Baroreflex

Systemic Arterial Pressure
- For an input resting heart rate of 75 bpm, or ~1.25 beats per second.
- Negative feedback is apparent, with steady-state settling at around 50 mmHg
Neural Arc & Peripheral Arc Bode Plots

Bode Diagram

Magnitude (dB)

Phase (deg)

Frequency (rad/s)

Bode Diagram

Magnitude (dB)

Phase (deg)

Frequency (rad/s)
Closed Loop System Bode Plot

Bode Diagram

Magnitude (dB)

Phase (deg)

Frequency (rad/s)
Sensitivity Analysis

Normal resting heart rate: ~75 bpm (1.25bps)

Women: 77, men 72

Assuming 95mL stroke volume and .83 mmHg/s/mL TPR [9]

Sensitivity=1/[1+P(s)*H(s)]

\[
\begin{align*}
  s^4 + 6.859 s^3 + 14.36 s^2 + 10.01 s + 1.447 \\
  s^4 + 7.123 s^3 + 13.07 s^2 + 10.81 s + 2.895
\end{align*}
\]

Maximum sensitivity at \( w=0.836 \) (rad/s) at original parameter values (\( 10^{(5/20)}=1.77 \))
### Sensitivity Stability

- **fc1** = 0.035
- 50% of fc1
- 200% of fc1

- **fc2** = 0.6
- 50% of fc2
- 200% of fc2

- **fn** = 0.49
- 50% of fn
- 150% of fn

- **Zeta** = 0.92
- 50% of Zeta
- 200% of Zeta

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<tr>
<td>CSP</td>
<td>1</td>
<td>60-160 mmHg</td>
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<tr>
<td>fc1</td>
<td>&lt;=1</td>
<td>&gt;=0.026 (75%)</td>
</tr>
<tr>
<td>fc2</td>
<td>&lt;=1</td>
<td>&gt;=0.3 (50%)</td>
</tr>
<tr>
<td>fn</td>
<td>&lt;=1</td>
<td>&lt;=0.6125 (125%)</td>
</tr>
<tr>
<td>zeta</td>
<td>&lt;=1</td>
<td>1 &gt; Z &gt;= 0.46 (50%)</td>
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Discussion + Future Directions

- Our model was able to show the behavior of a human sympathetic baroreflex response, relating carotid pressure to output arterial pressure.

In the future:
- Use the model to look at other conditions such as multiple sclerosis, which is a disease in which the immune system eats away the myelin sheaths of the nervous system.
- Further investigate the relationship between baroreflex efferent nerve firing rate input and peripheral arc response, and model in simulink.
- Expand upon linear action potential model and look into other non-linear models such as the leaky integrate-and-fire model.
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References


Thank you for listening!