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JACOBS SCHOOL OF ENGINEERING
Bioengineering

Modeling Baroreflex Feedback Control for Blood Pressure Regulation

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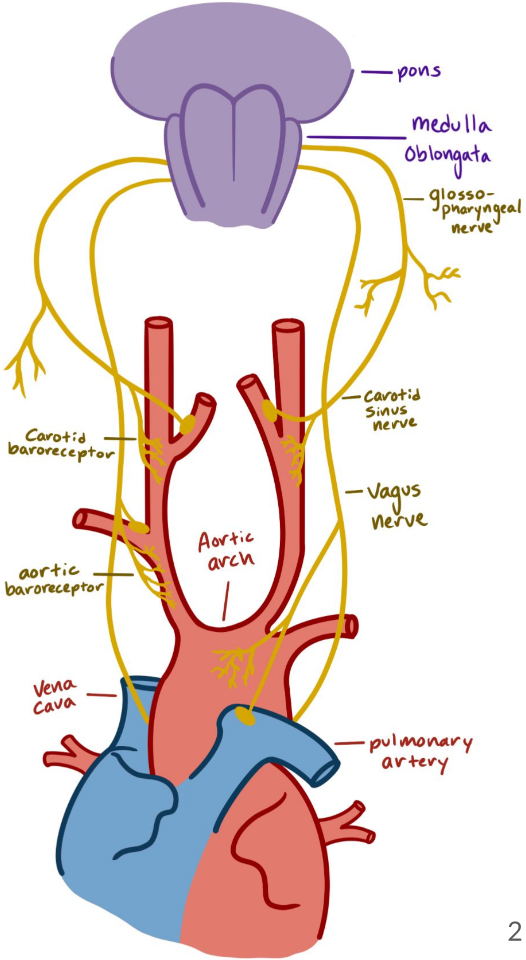
Background

- 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.

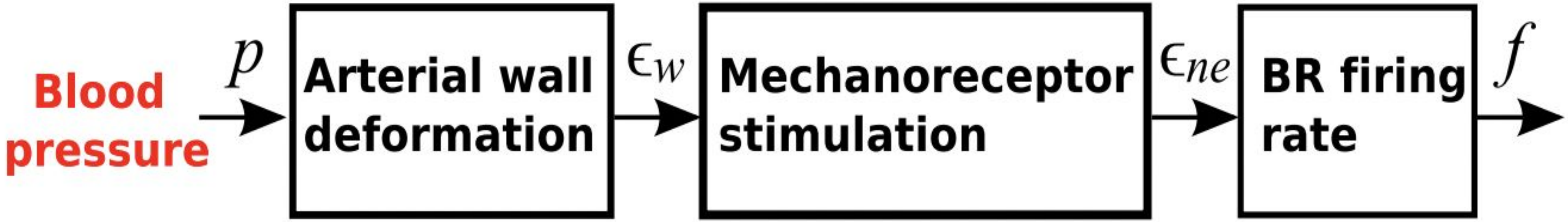
2. For our governing equations, we assume that the efferent sympathetic nerve firing rate, modeled as f, is determined through a linear amplifier model.

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

$$p(t) = p_0 + 2.5sin(p_2 - p_1 t) \quad (1)$$

$$\epsilon_w = \frac{r - r_0}{r} = K_{wall} * p \quad (2)$$

$$\epsilon_{ne} = \epsilon_w - \epsilon_1 \quad (3)$$

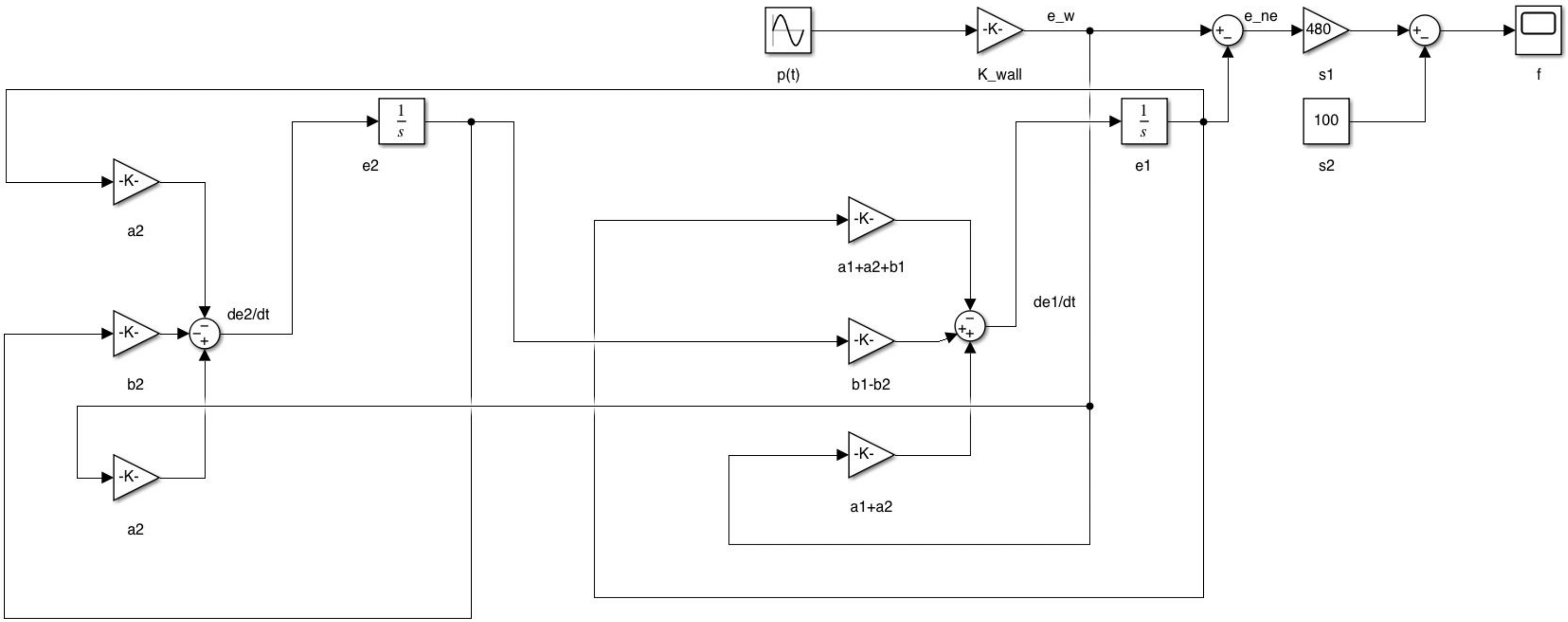
$$\frac{d\epsilon_1}{dt} = -\left(\alpha_1 + \alpha_2 + \beta_1\right)\epsilon_1 + \left(\beta_1 - \beta_2\right)\epsilon_2 + (\alpha_1 + \alpha_2)\epsilon_w \quad (4)$$

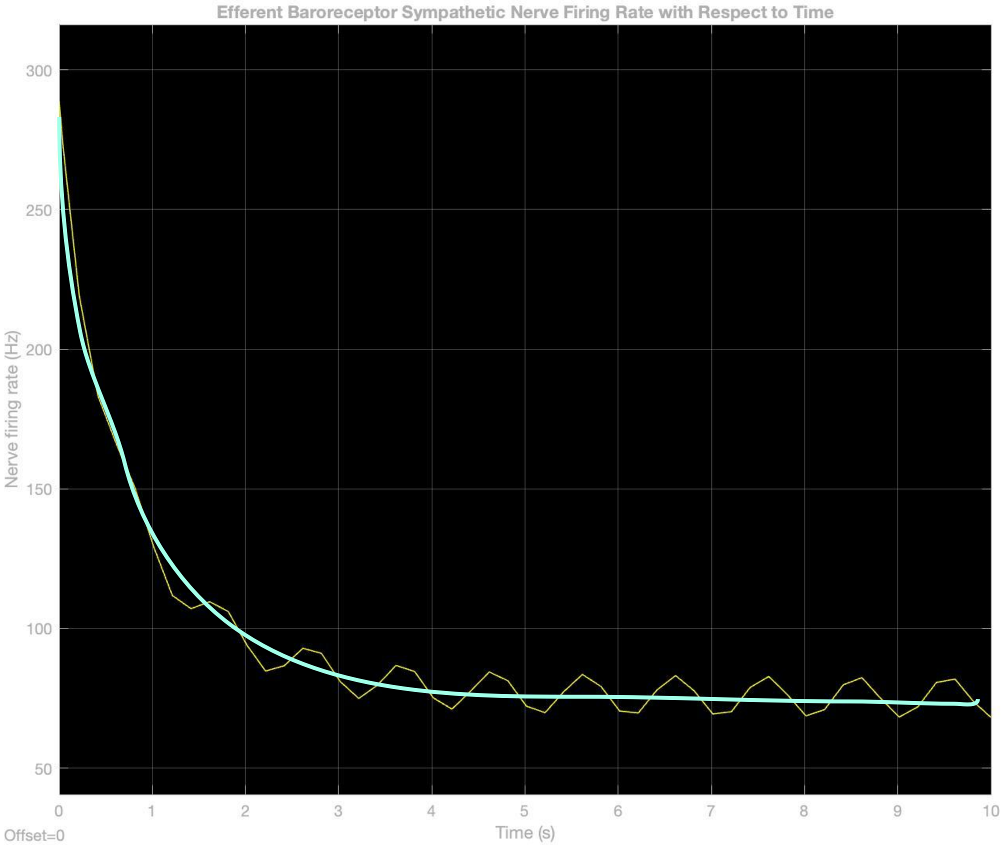
$$\frac{d\epsilon_2}{dt} = -\alpha_2\epsilon_1 - \beta_2\epsilon_2 + \alpha_2\epsilon_w \quad (5)$$

$$f = s_1 * \epsilon_{ne} - s_2 \quad (6)$$

Parameter	Definition	Value	Units
r_0	zero pressure radius	1.13	mm
h	wall thickness	0.17	mm
E	elastic modulus	1050	mmHg
K_{wall}	aortic distensibility	r_0 / (Eh)	$mmHg^{-1}$
E_0	elastic nerve constant	1	mmHg
E_1		1	mmHg
E_2		5	mmHg
E_3		10	mmHg
η_1	viscous nerve coupling constant	2	mmHg*s
η_2		2.5	mmHg*s
η_3		1	mmHg*s
α_1	nerve ending constant	E_0 / η_1	s^{-1}
α_2		E_0 / η_2	s^{-1}
α_3		E_0 / η_3	s^{-1}
β_1	nerve ending relaxation rate	E_1 / η_1	s^{-1}
β_2		E_2 / η_2	s^{-1}
β_3		E_3 / η_3	s^{-1}
s_1	firing constant	480	s^{-1}
s_2	firing constant	100	s^{-1}

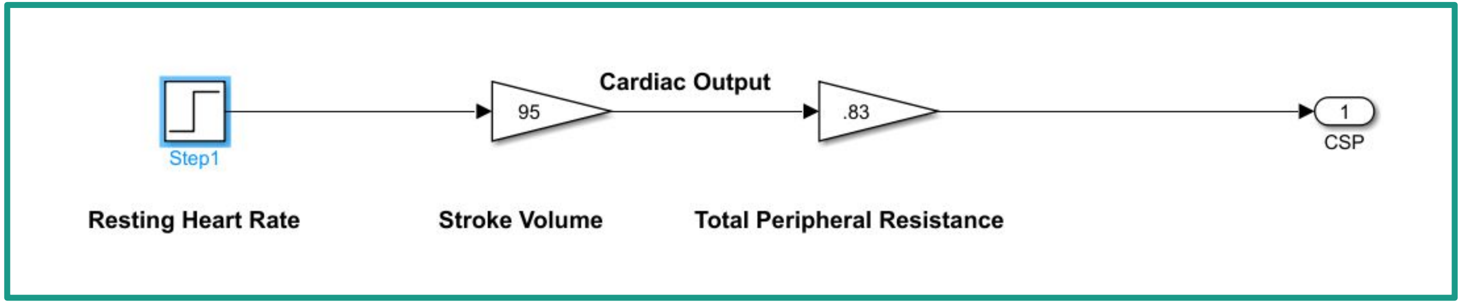
Efferent Baroreceptor Sympathetic Nerve Firing Rate as a Function of Carotid Sinus Pressure





- 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.

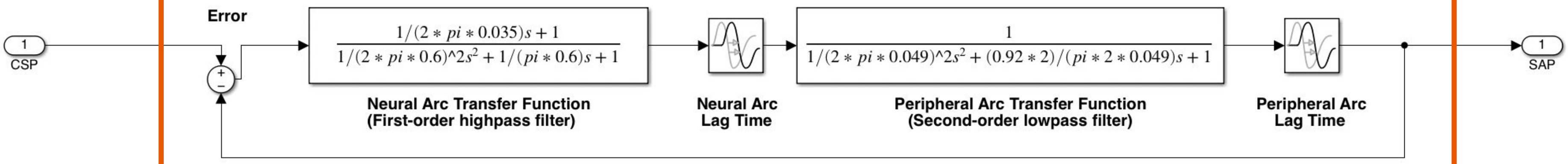
Carotid Sinus Pressure



- 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

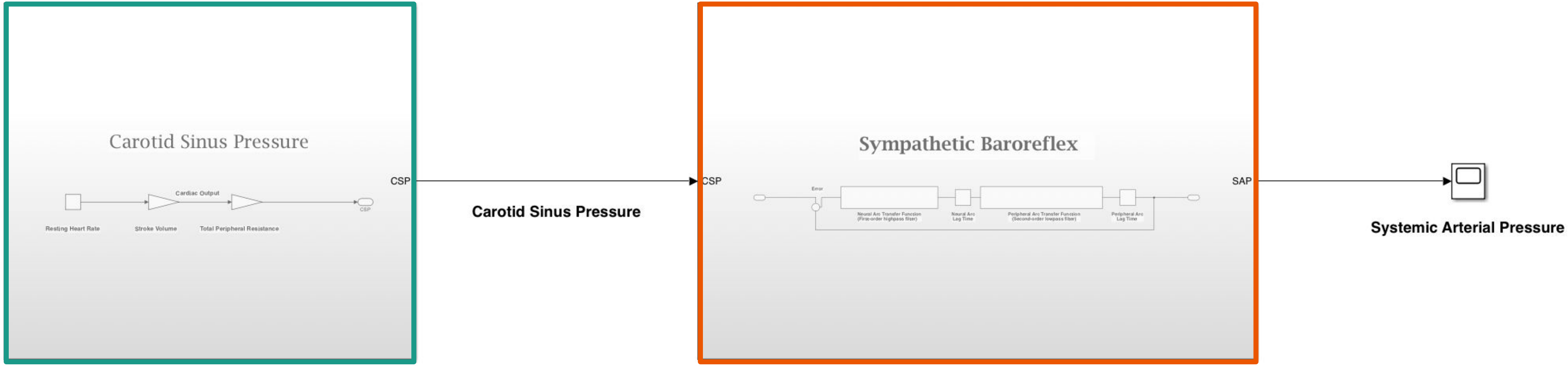
Sympathetic Baroreflex

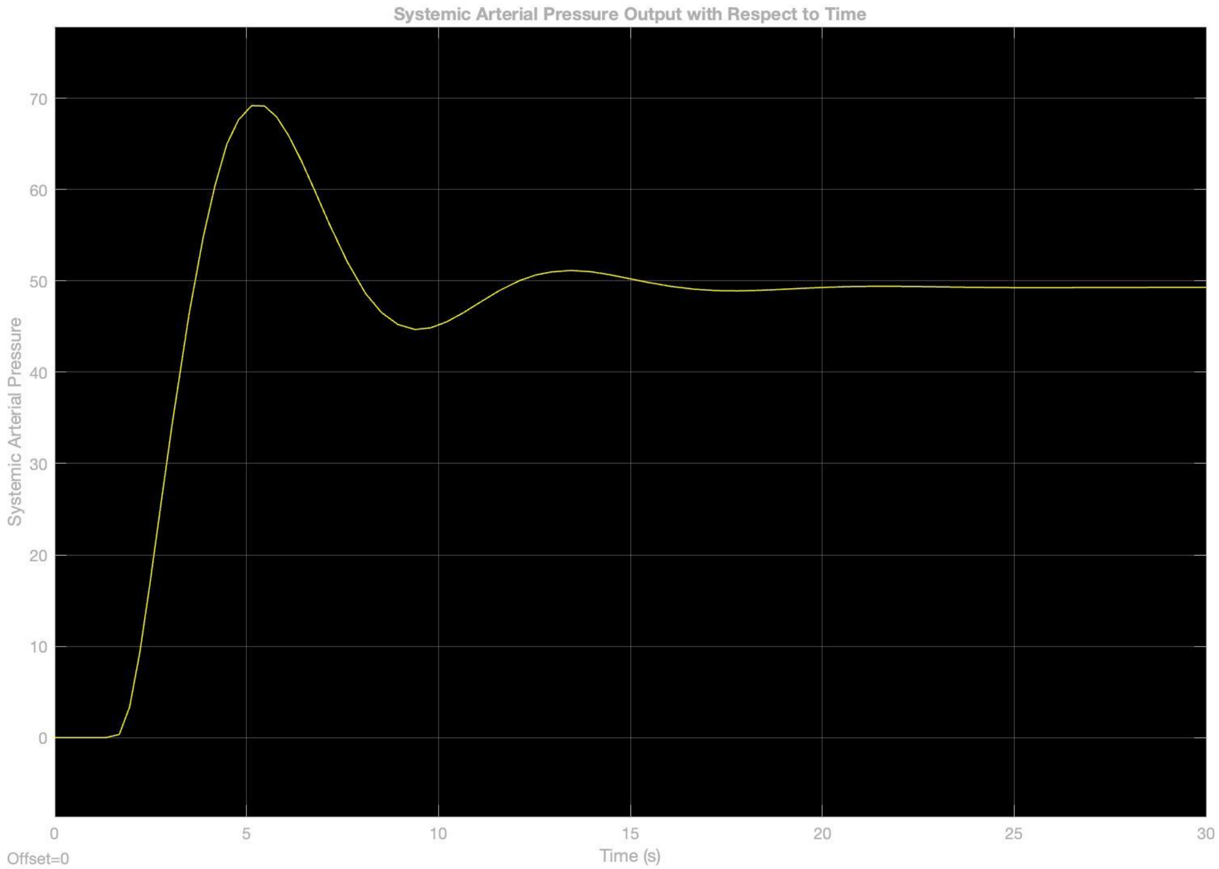


- Transfer functions based on anesthetized rabbits were found from literature. Models were adjusted to humans through modelling carotid sinus pressure as a function of resting hea

fc1	0.035
fc2	0.6
fn	0.49
zeta	0.92

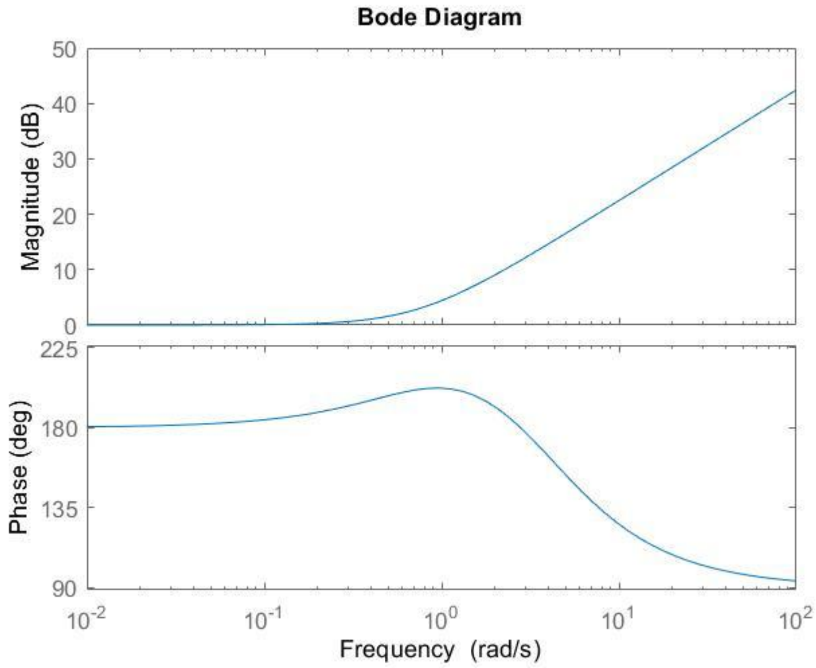
System Block Diagram in Simulink

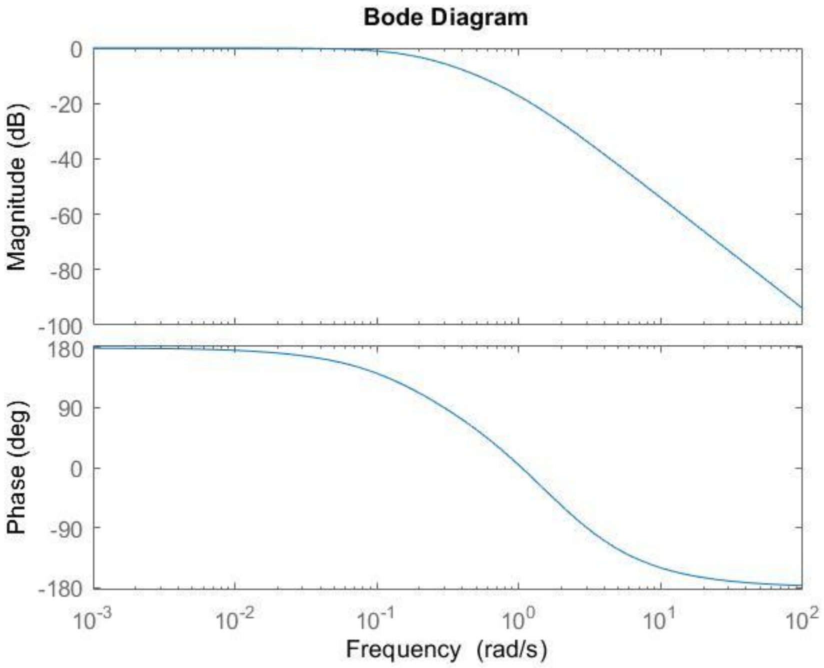




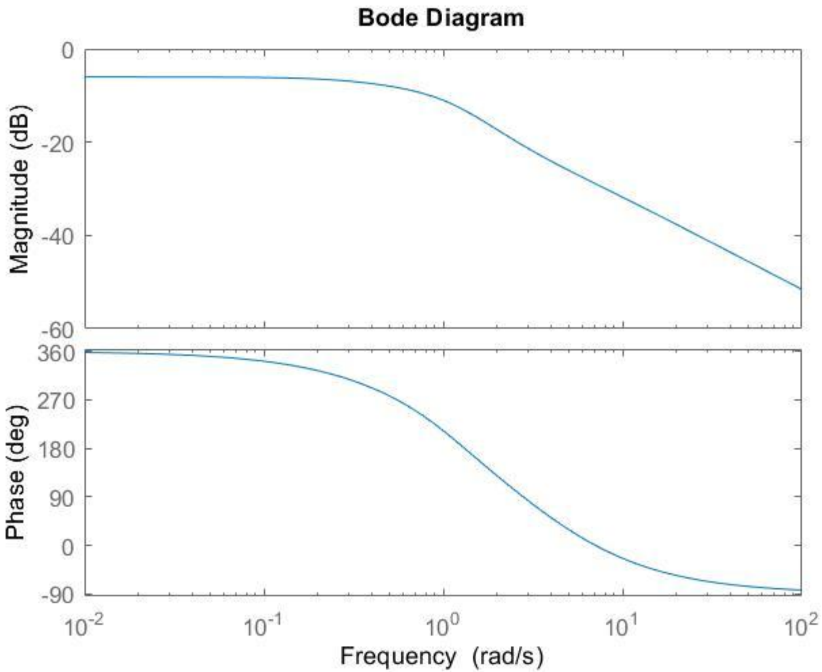
- For an input resting heart rate of 75 bpm, or ~1.25 beats per second.
- Negative feedback is apparent, with steady-state settling at around 50 mmHg

Neural Arc & Peripheral Arc Bode Plots





Closed Loop System Bode Plot



Sensitivity Analysis

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

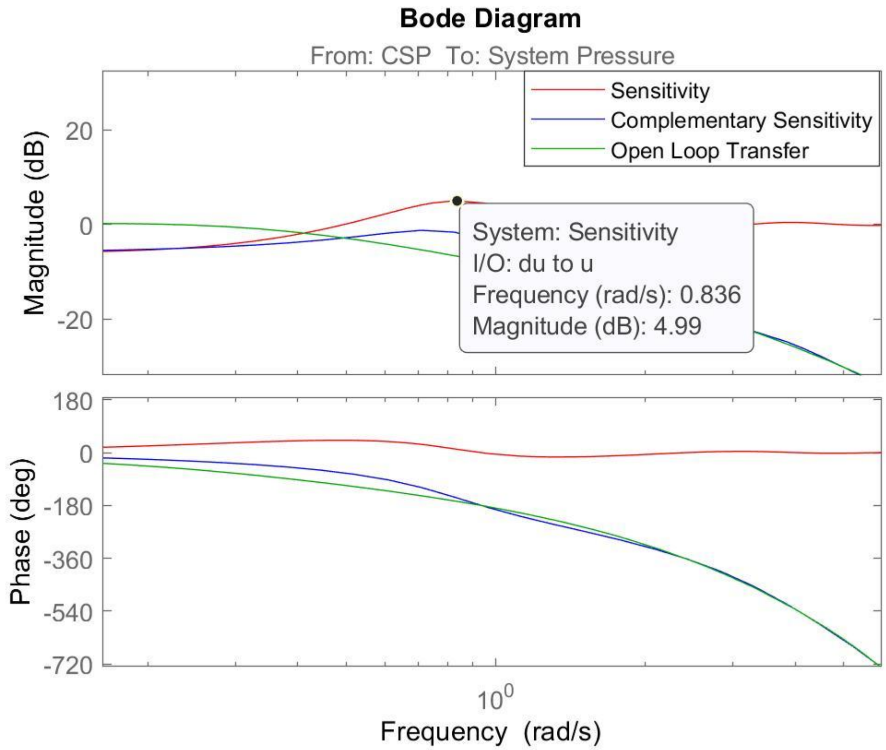
Women: 77, men 72

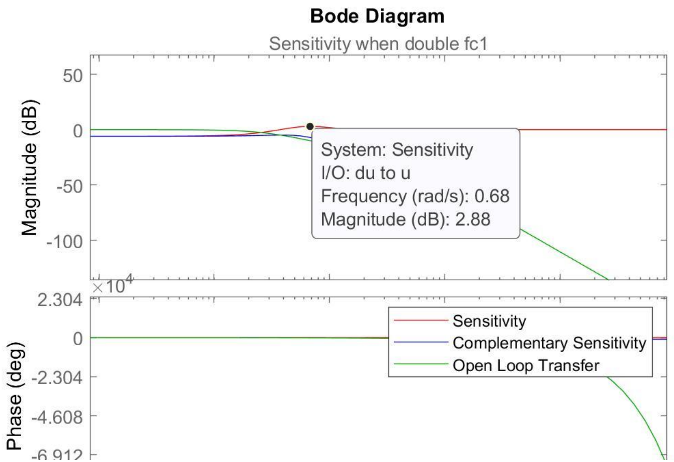
Assuming 95mL stroke volume and .83 mmHg/s/mL TPR [9]

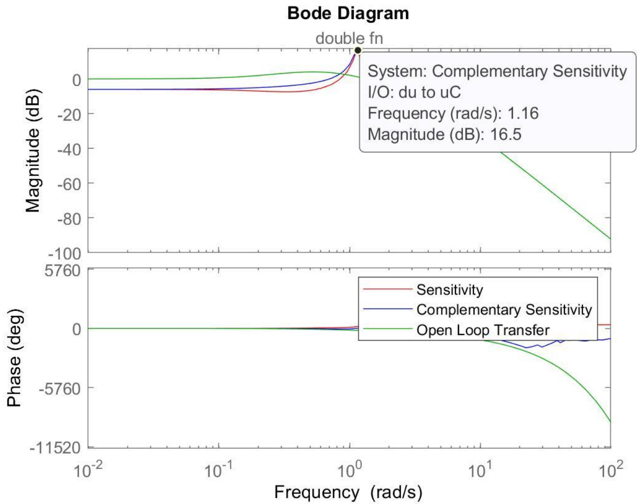
Sensitivity=1/[1+P(s)*H(s)]

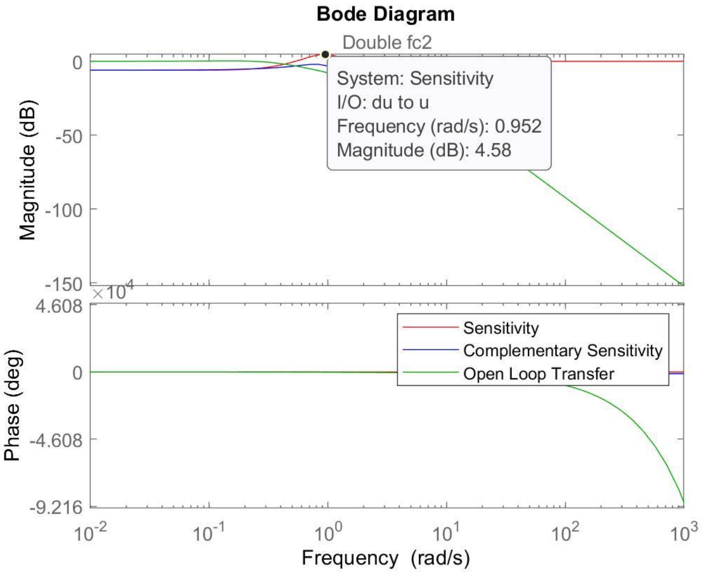
```
s^4 + 6.859 s^3 + 14.36 s^2 + 10.01 s + 1.447
---------------------------------------------
s^4 + 7.123 s^3 + 13.07 s^2 + 10.81 s + 2.895
```

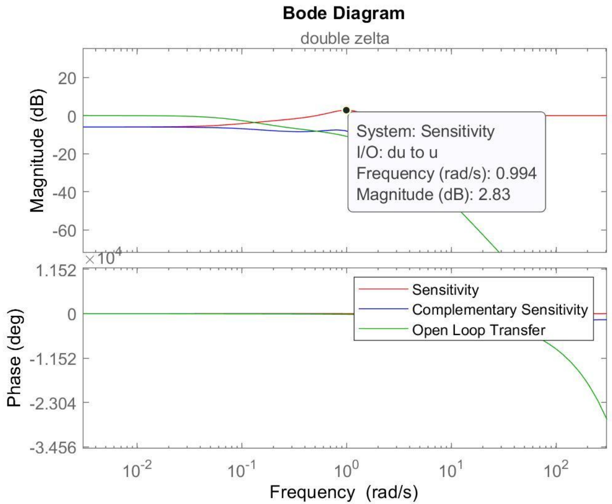
Maximum sensitivity at w=0.836 (rad/s) at original parameter values (10^(5/20)=1.77)




Bode Diagram
Sensitivity when double fc1
Magnitude (dB)
Phase (deg)
System: Sensitivity
I/O: du to u
Frequency (rad/s): 0.68
Magnitude (dB): 2.88
Sensitivity
Complementary Sensitivity
Open Loop Transfer


Bode Diagram
double fn
Magnitude (dB)
Phase (deg)
Frequency (rad/s)
System: Complementary Sensitivity
I/O: du to uC
Frequency (rad/s): 1.16
Magnitude (dB): 16.5
Sensitivity
Complementary Sensitivity
Open Loop Transfer

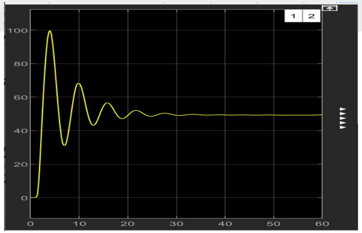

Bode Diagram
Double fc2
Magnitude (dB)
Phase (deg)
Frequency (rad/s)
System: Sensitivity
I/O: du to u
Frequency (rad/s): 0.952
Magnitude (dB): 4.58
Sensitivity
Complementary Sensitivity
Open Loop Transfer


Bode Diagram
double zelta
Magnitude (dB)
Phase (deg)
Frequency (rad/s)
System: Sensitivity
I/O: du to u
Frequency (rad/s): 0.994
Magnitude (dB): 2.83
Sensitivity
Complementary Sensitivity
Open Loop Transfer

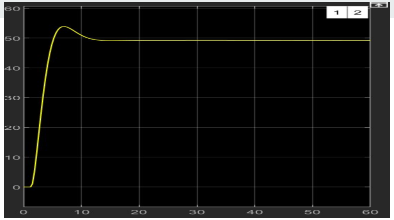
Sensitivity stability

Variable	S	Stability
CSP	1	60-160 mmHg
fc1	<<1	>=0.026 (75%)
fc2	<<1	>=0.3 (50%)
fn	<<1	<=0.6125 (125%)
zeta	<<1	1>Z>=0.46 (50%)

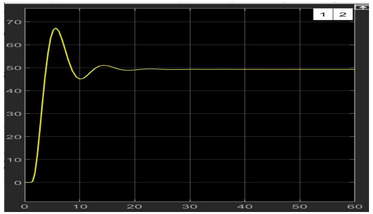
fc1=0.035 50%fc1



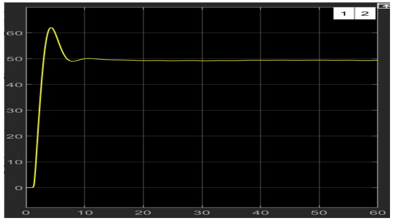
200%fc1



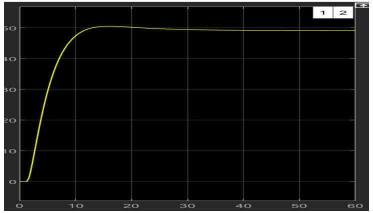
fc2=0.6 50%fc2



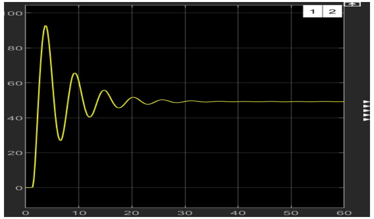
200%fc2



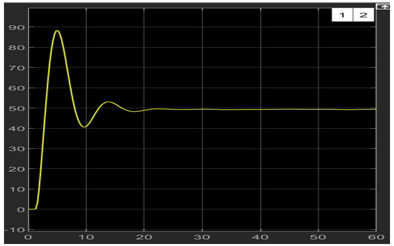
fn=0.49 50%fn



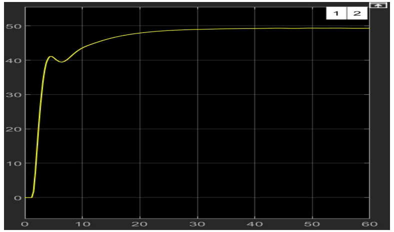
150%fn



Zeta=0.92 50%Zeta



200%Zeta



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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Thank you for listening!