BME 5742 Bio-Systems Modeling and Control

Lecture 43
Heart & Blood Circulation
The Baroreceptor Loop

Systemic Resistance Changes

- The arterioles in an exercising muscle dilate.
- Consequently, the overall systemic resistance R_s falls.
- What happens to the cardiac output and its factors (Pulse rate, Stroke Volume)?
- Starting point for analysis: Sensitivity Analysis (to R_s changes) , using the uncontrolled steady-state relationships developed earlier.

A wrong approach: Analyzing the only equation at which R_s appears

$$Q = \frac{P_{sa} - P_{sv}}{R_s}$$

Since $P_{sa} >> P_{sv}$ we may be tempted to think that P_{sv} plays a negligible role, and that either "P_{sa} must change proportionately to R_s to keep Q constant", or that "Q changes in inverse proportion to R_s to keep P_{sa} constant". Both are wrong – we must study ALL steady-state relationships simultaneously.

Let us use the solution of the simultaneous equations:

$$Q = \frac{V_0}{T_{sv} + T_{pv} + T_{sa} + T_{pa}}$$

$$P_{sa} = \frac{T_{sa} V_0}{C_{sa}(T_{sv} + T_{pv} + T_{sa} + T_{pa})}$$

$$\frac{C_{sv}}{K_R} = T_{sv}$$

$$\frac{C_{pv}}{K_L} = T_{pv}$$

$$C_{sa} R_s + \frac{C_{sa}}{K_R} = T_{sa}$$

$$C_{pa} R_p + \frac{C_{pa}}{K_L} = T_{pa}$$

Also recall the typical coefficient values: R_s=17.5, R_p=1.79, C_{sa}=0.01, C_{pa}=0.0067, C_{sv}=1.75, C_{pv}=0.08, K_R=2.8, K_L=1.12, V_0=5

Example: If R_S drops by 50%, what is the change in Q and P_{sa}?

$$Q = \frac{V_0}{T_{sv} + T_{pv} + T_{sa} + T_{pa}}$$

$$P_{sa} = \frac{T_{sa} V_0}{C_{sa}(T_{sv} + T_{pv} + T_{sa} + T_{pa})}$$

$$\frac{C_{sv}}{K_R} = T_{sv}$$

$$\frac{C_{pv}}{K_L} = T_{pv}$$

$$C_{sa} R_s + \frac{C_{sa}}{K_R} = T_{sa}$$

$$C_{pa} R_p + \frac{C_{pa}}{K_L} = T_{pa}$$

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Spreadsheet implementation of above relationships can facilitate such sensitivity analysis. Example Result:

	Normal	$R_s \rightarrow R_s/2$	Change	% Change
Q [liter/minute]	5.6	6.2	+0.6 [liters/minute]	+11%
P_{sa} [mmHg]	100	57	-43 [mmHg]	-43%

- These are the results, if no other control mechanisms exist.
- We see that the self-regulation ability of the model is insufficient, in the presence of drastic parameter changes.

Sensitivity Function Properties

$$\sigma_{YX} = \frac{\Delta \log Y}{\Delta \log X} \approx \frac{(\frac{dY}{Y})}{(\frac{dX}{X})}$$

- Sensitivity does not depend on the units of the variables. It also does not depend on the log base.
- Examples: If $Y=aX^n$ then $\sigma_{YX}=n$. If $Y=aX$ then $\sigma_{YX}=1$. If $Y=aX^{-1}$ then $\sigma_{YX}= -1$.

Sensitivities of Q and P_{sa} to R_s:

	Normal	$R_s \rightarrow R_s/2$	Change	% Change
Q [liter/minute]	5.6	6.2	+0.6 [liters/minute]	+11%
P_{sa} [mmHg]	100	57	-43 [mmHg]	-43%

Here:

$$\sigma_{QR_s} = -0.15$$

$$\sigma_{P_{sa}R_s} = 0.81$$

Balance of Sensitivities

$$P_{sa} \approx QR_s \Rightarrow -\sigma_{QR_s} + \sigma_{P_{sa}R_s} \approx 1$$

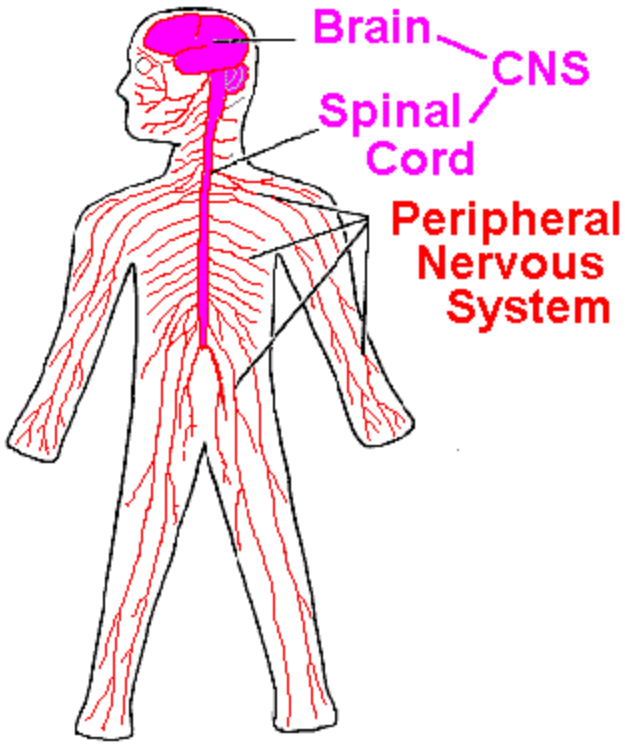
"Waterbed Effect": If we try to increase the sensitivity of cardiac output to R_s, we pay by decreased sensitivity of systemic arterial pressure to R_s

Ideally, we want:

$$\sigma_{QR_s} = -1 \qquad \sigma_{P_{sa}R_s} = 0$$

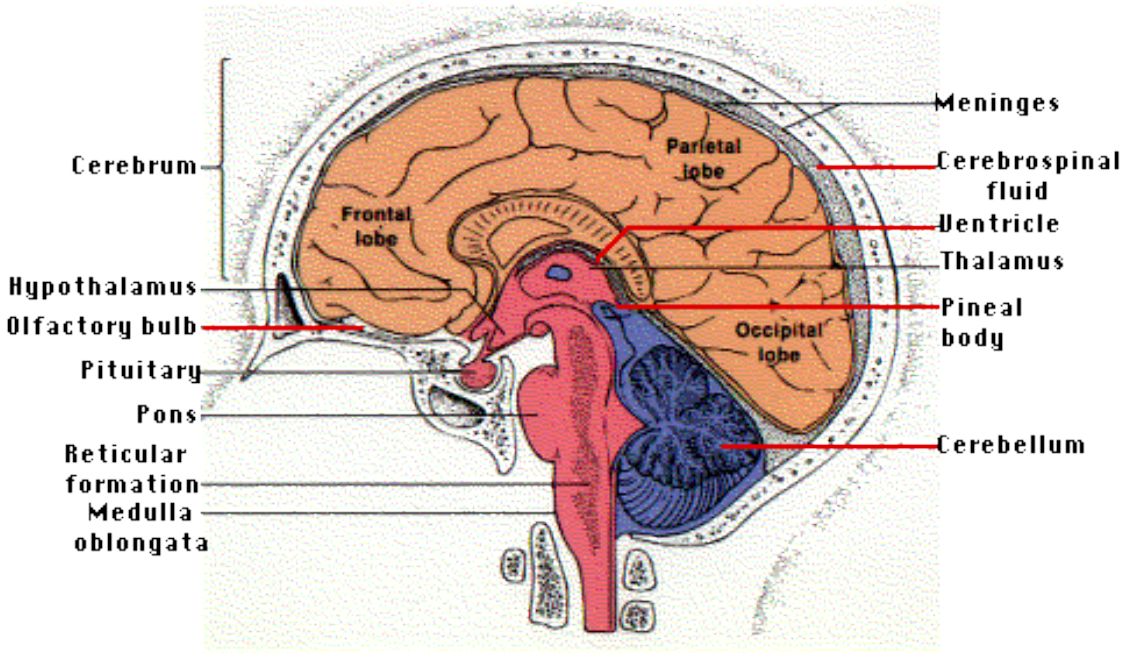
- Cardiac output becoming inversely proportional to systemic resistance (If R_s is halved, Q is doubled). According to Guyton's book – during exercise, cardiac output can become 4-7 times larger than the normal cardiac output.
- Systemic blood pressure (and consequently blood flow to the non-exercising tissues) be maintained constant.

Blood Pressure Control



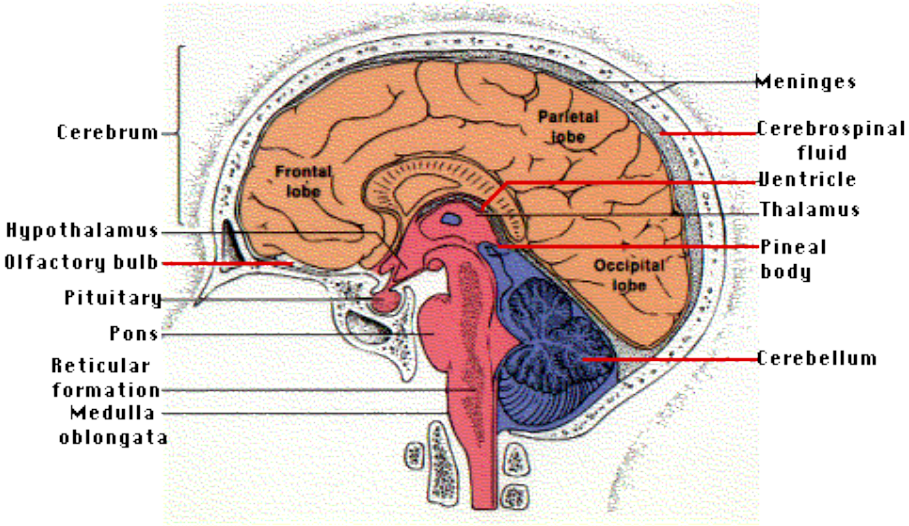
- There are several control mechanisms for the blood pressure.
- We'll describe first the Baroreceptor Loop
- The baroreceptors are receptor nerves, sensitive to pressure, that are located along the carotid arteries and on the arch of the aorta.
- These receptors (like all receptors) send the information to the Central Nervous System, in the form of impulses, by way of specific afferent neurons.

The location of the Medulla



The Medulla is one of the major parts of the brain, located just above the back neck, extending from the spinal cord, and protected by the occipital bone.

The functions of the Medulla

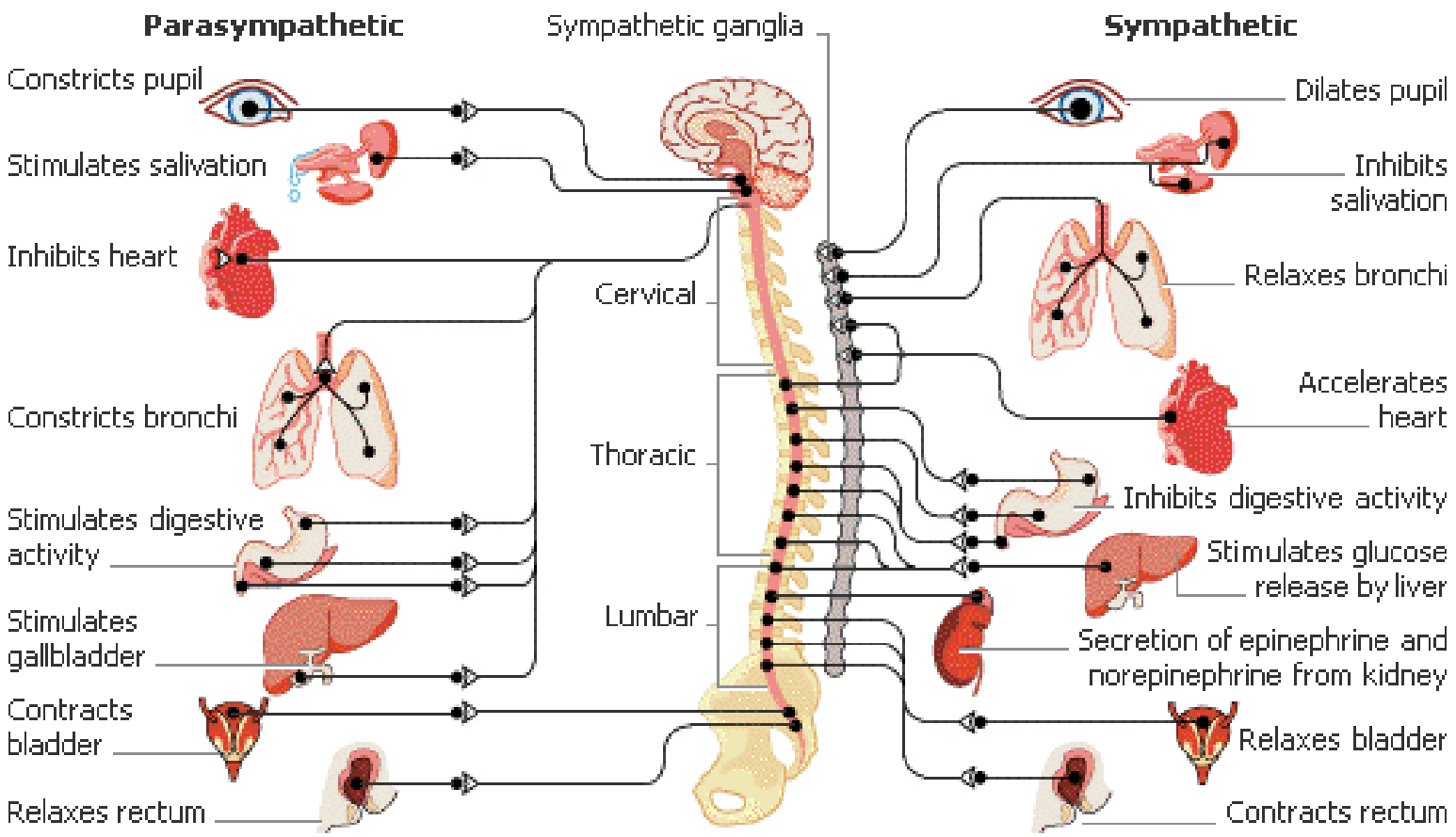


Medulla's functions involve all "vital signs": It contains the cardiac centers that regulate heart rate, vasomotor centers that regulate the diameter of blood vessels (and thereby blood pressure), and respiratory centers that regulate breathing. (There are more functions of the medulla)

Autonomic Nervous System (ANS)

- The ANS consists of the visceral motor neurons that go to all smooth muscles, cardiac muscles and glands.
- Based on the signals coming via these nerves, muscles may either contract or relax, and glands either increase or decrease their hormone secretion.

Autonomous Nervous System



ANS Two Divisions: Sympathetic and Parasympathetic Nerves -1

- In the Heart: Sympathetic nerves carry signals that command the heart to increase its pulse rate.
- For blood vessels in skin and smooth muscles: Sympathetic nerves carry the command to constrict.
- For blood vessels in skeletal muscles: Sympathetic nerves carry the command to dilate.

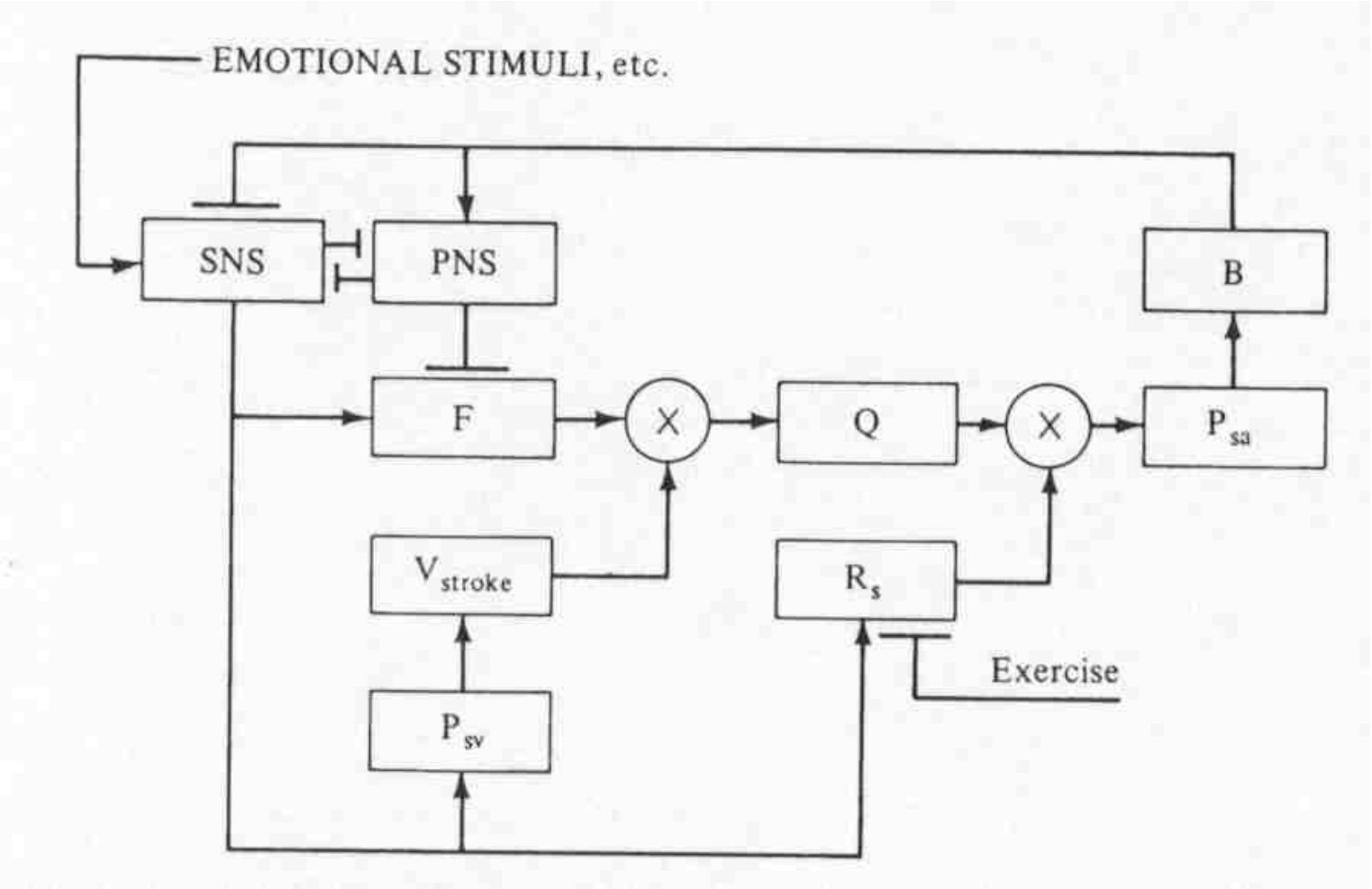
ANS Two Divisions: Sympathetic and Parasympathetic Nerves - 2

- In the Heart: Parasympathetic nerves carry signals that command the heart to decrease its pulse rate (to normal).
- No signal is carried by parasympathetic nerves to blood vessels.

The Brain's Cardiac Centers

- There are two cardiac centers in the medulla – the accelerator center and the inhibitory center. Both centers receive signals from the baroreceptors.
- The sympathetic nerves go from the accelerator center to the heart. These nerves are inhibited by the baroreceptors signals.
- The parasympathetic nerves go from the inhibitory center to the heart. These nerves are excited by the baroreceptors signals.

The Baroreceptor Loop (not annotated)



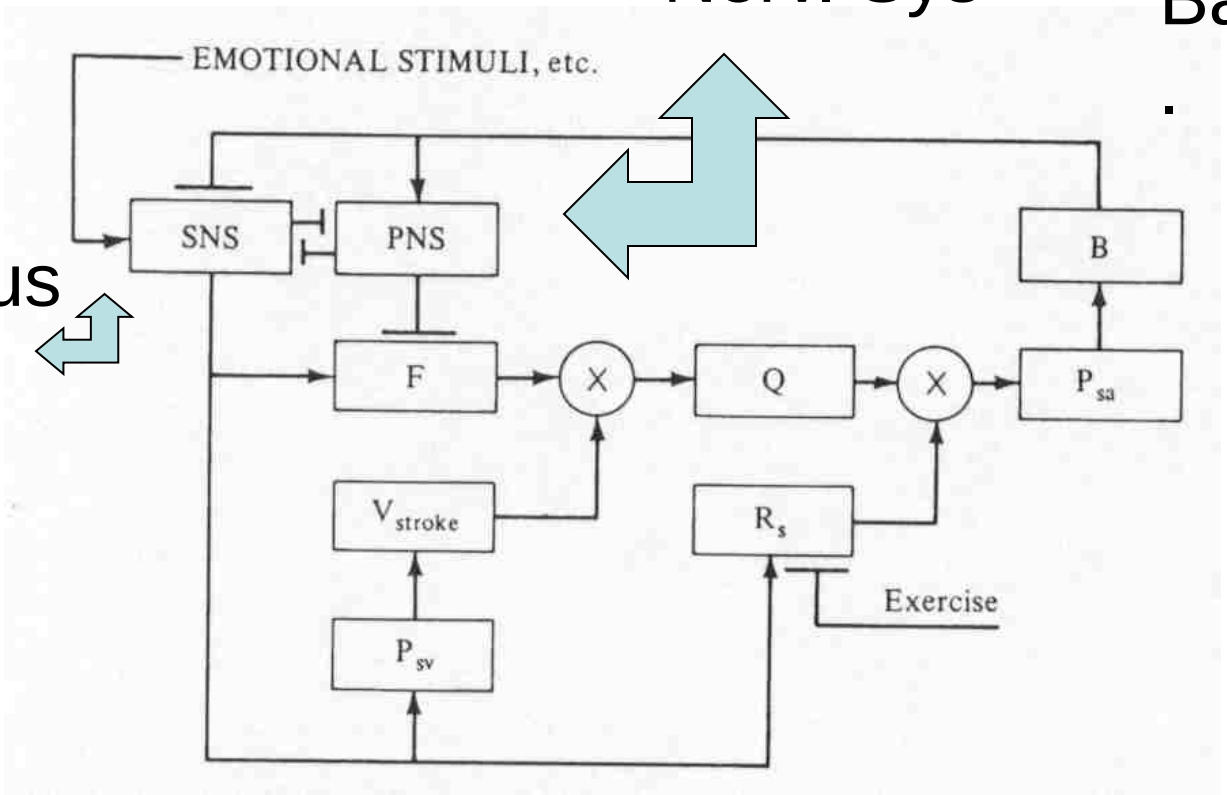
Baroreceptor Loop: Blocks Identified

(Arrows=excite/increase, Bars=inhibit/decrease)

Parasymp.
Nerv. Sys

Barorecept
.

Symp.
Nervous
Sys.

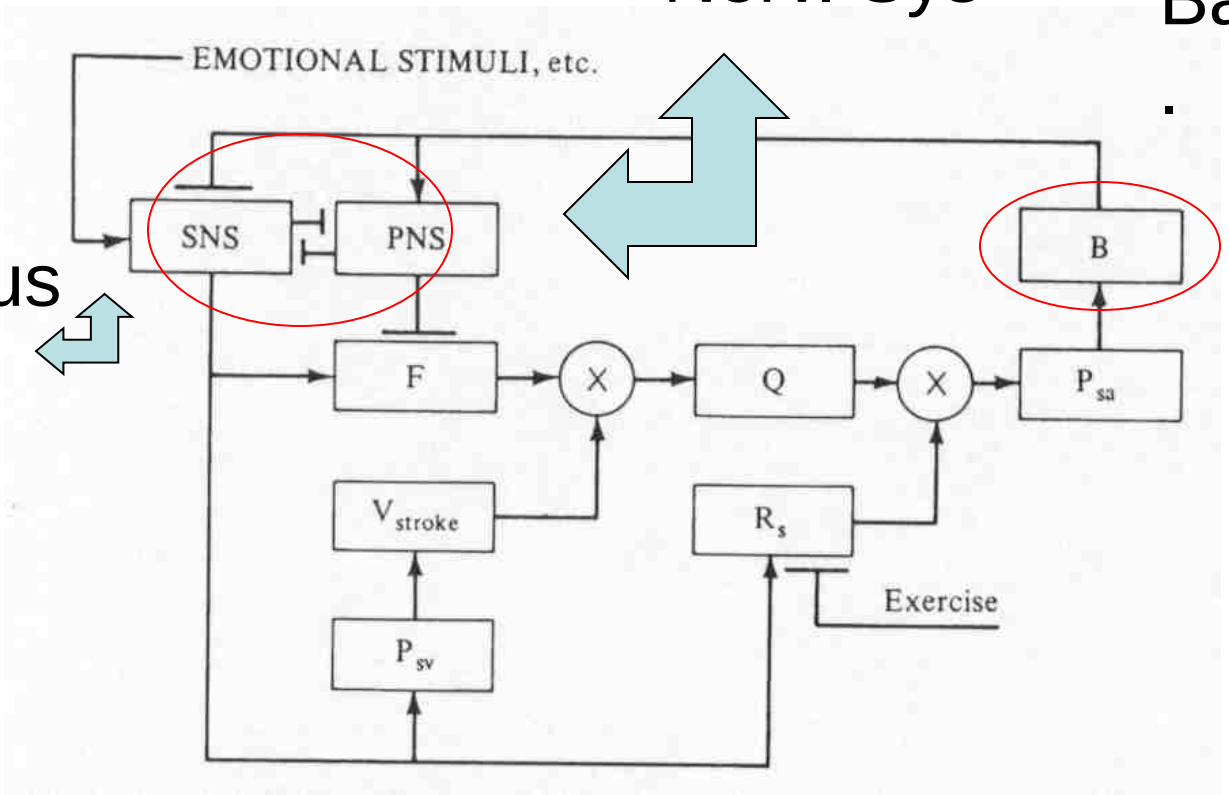


Baroreceptor Loop: Note how baroreceptor activity simultaneously excites the parasympathetic nerves and inhibits the sympathetic nerves

Parasymp.
Nerv. Sys

Barorecept
.

Symp.
Nervous
Sys.

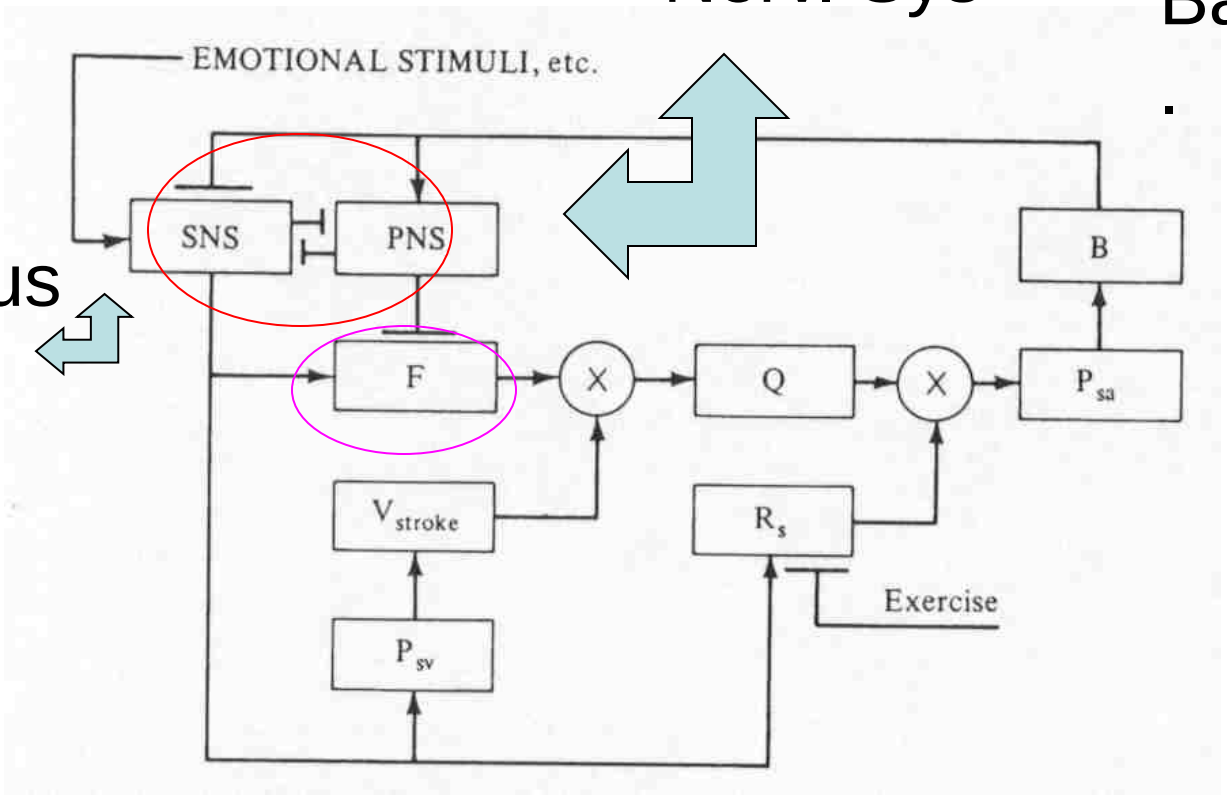


Baroreceptor Loop: The parasympathetic nerves act to decrease pulse rate F and sympathetic nerves act to increase F

Parasymp.
Nerv. Sys

Barorecept
.

Symp.
Nervous
Sys.

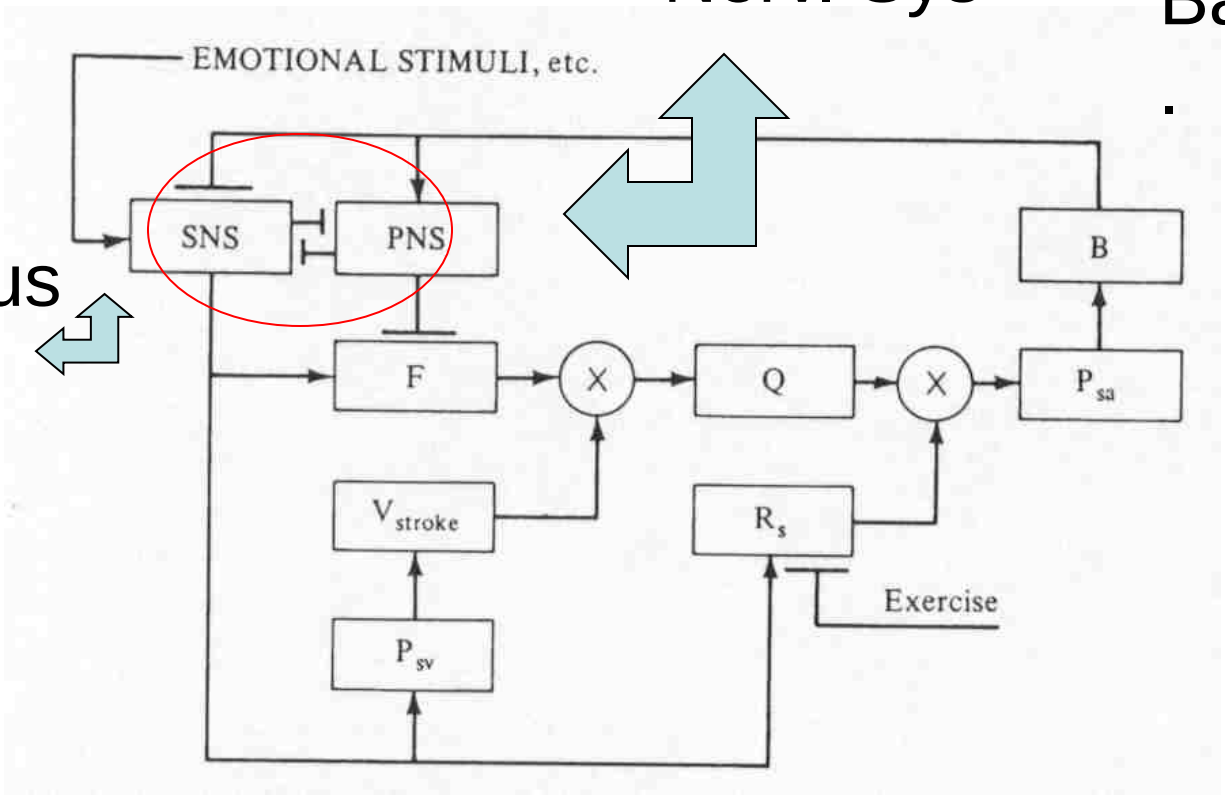


Baroreceptor Loop: The two autonomic nervous system inhibit each other

Parasymp.
Nerv. Sys

Barorecept
.

Symp.
Nervous
Sys.



Baroreceptor Loop: Sympathetic nerve signals increase venous pressure and increase systemic resistance

Parasymp.
Nerv. Sys

Barorecept
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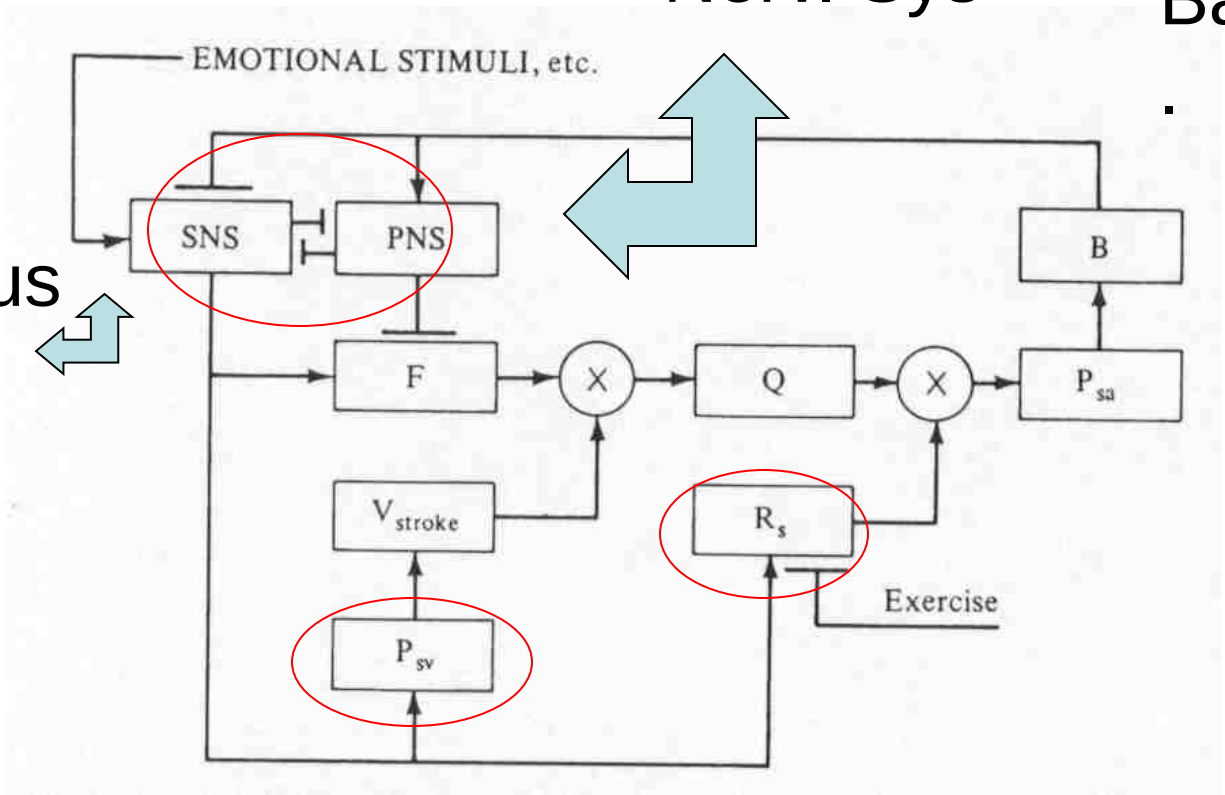
Symp.
Nervous
Sys.

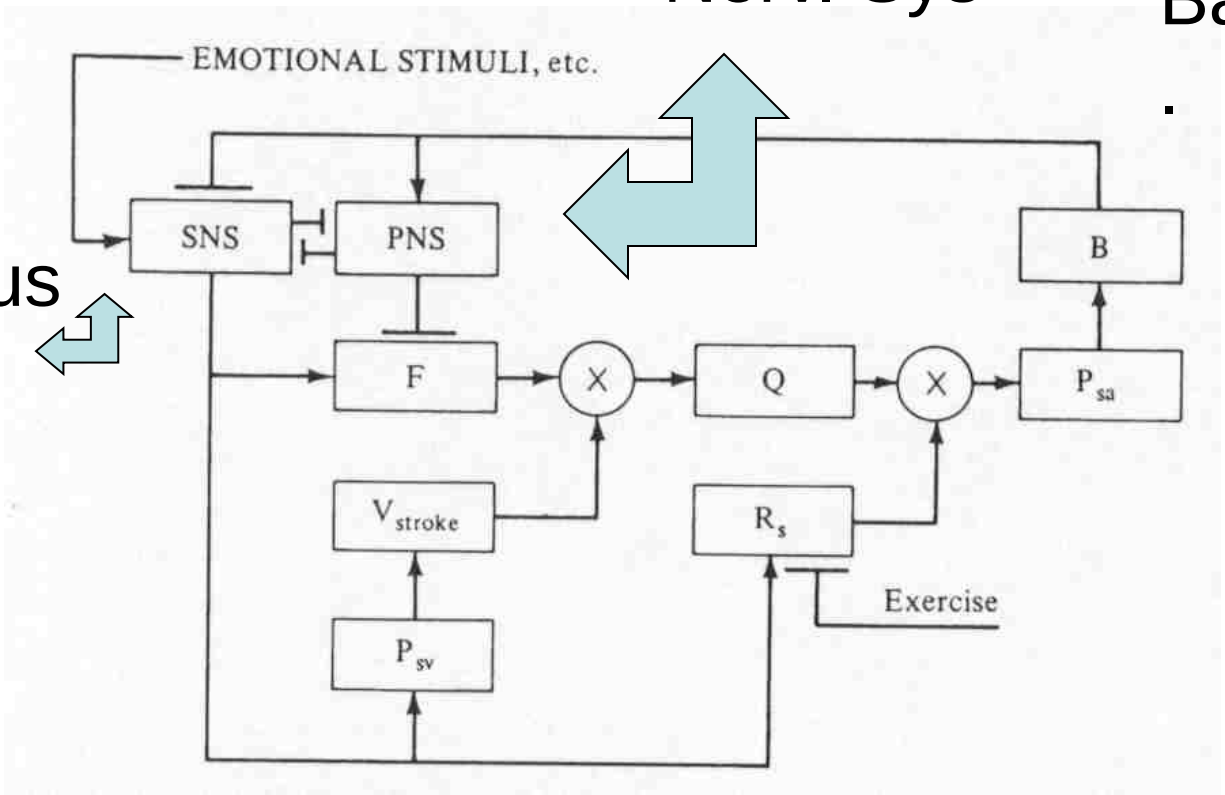


Case 1: P_{sa} increases → Baroreceptor activity increases → F decreases → Q decreases → P_{sa} is decreased

Parasymp. Nerv. Sys

Barorecept.

Symp. Nervous Sys.

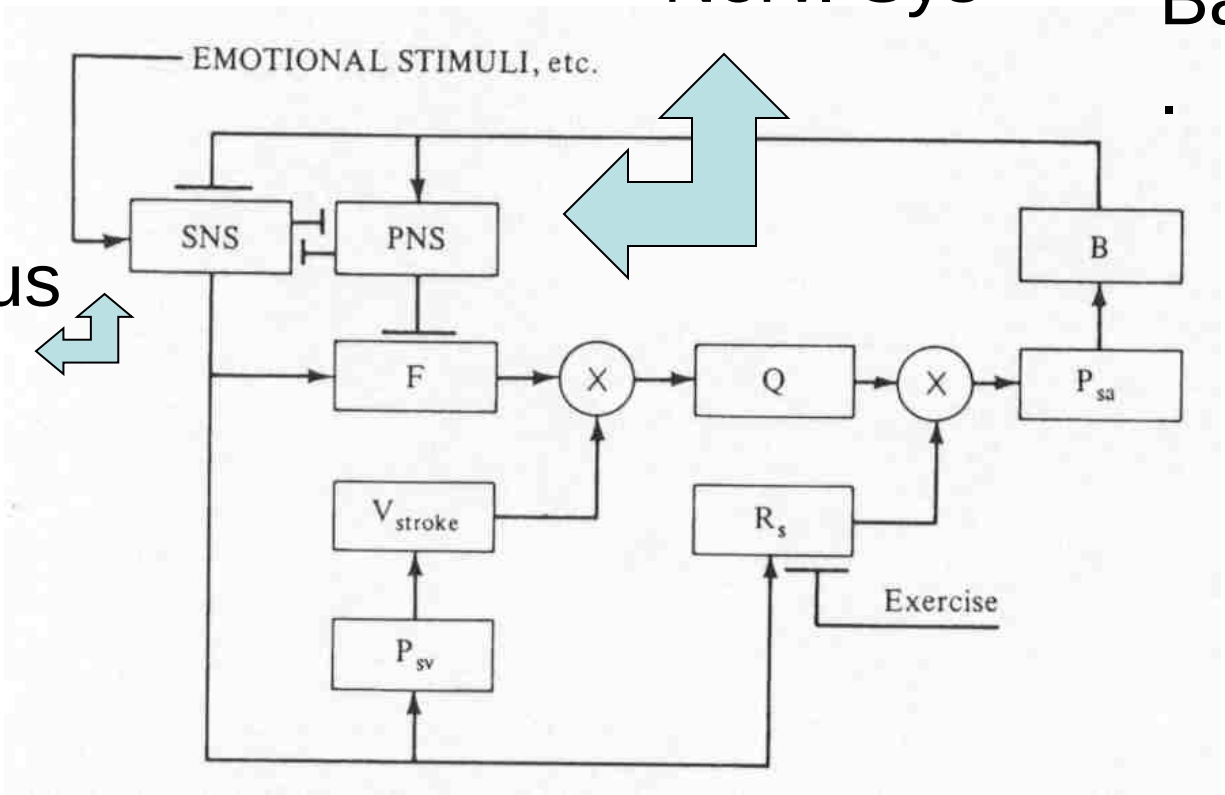


Case 2: P_{sa} decreases → Baroreceptor activity decreases → mainly F increases [and to a secondary level P_{sv} (and consequently Q) and R_s all increase] → P_{sa} is increased

Parasymp. Nerv. Sys

Barorecept.

Symp. Nervous Sys.



Case 3: If P_{sa} is high, exercise causes (in the long run) R_s to decrease, which helps to lower P_{sa}

Parasymp.
Nerv. Sys

Barorecept
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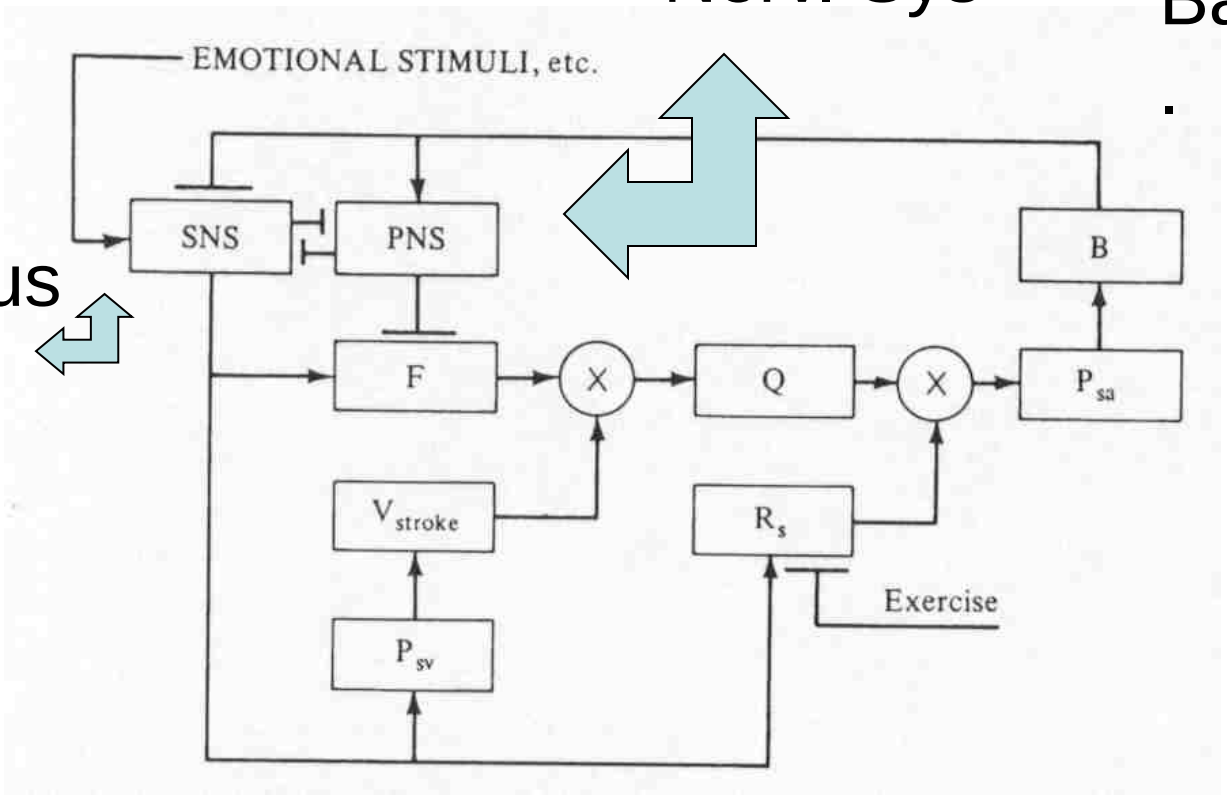
Symp.
Nervous
Sys.

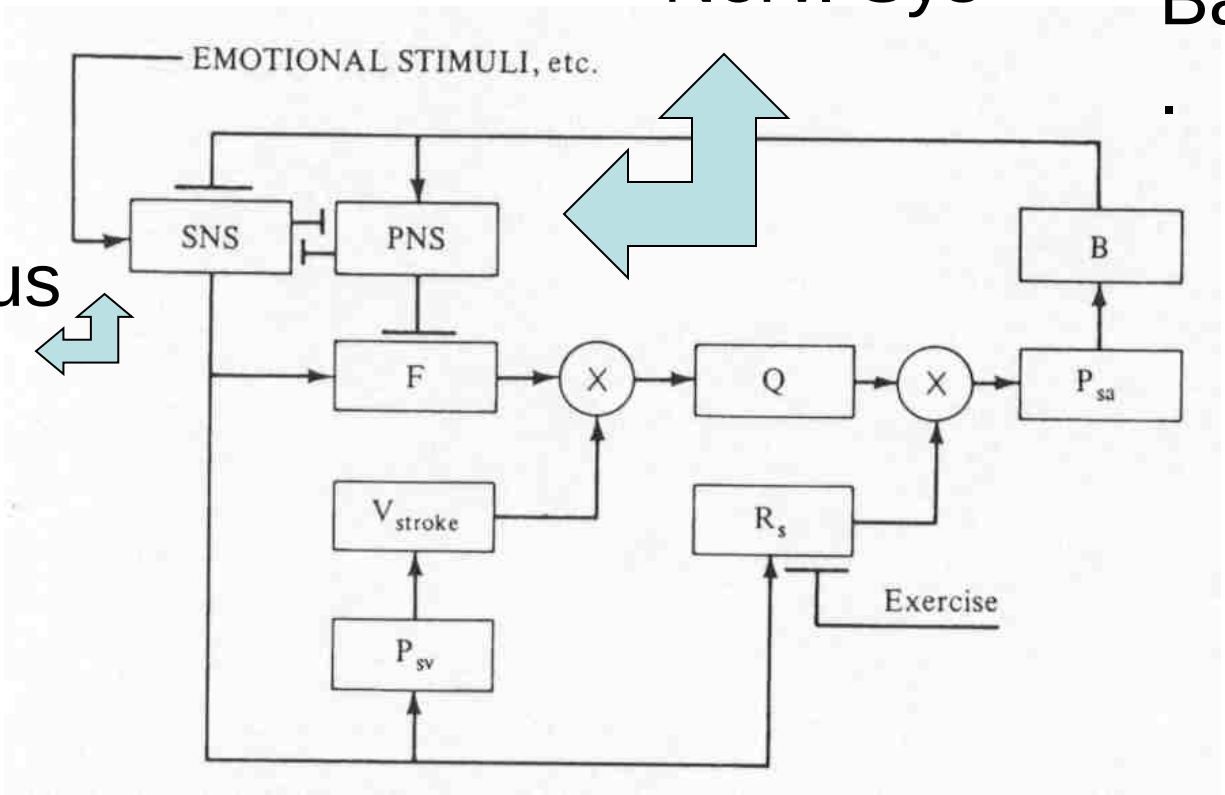


Several Feedback Loops: Negative Feedback is whenever the number of inhibitions is odd. Watch that all feedback loops here are negative!

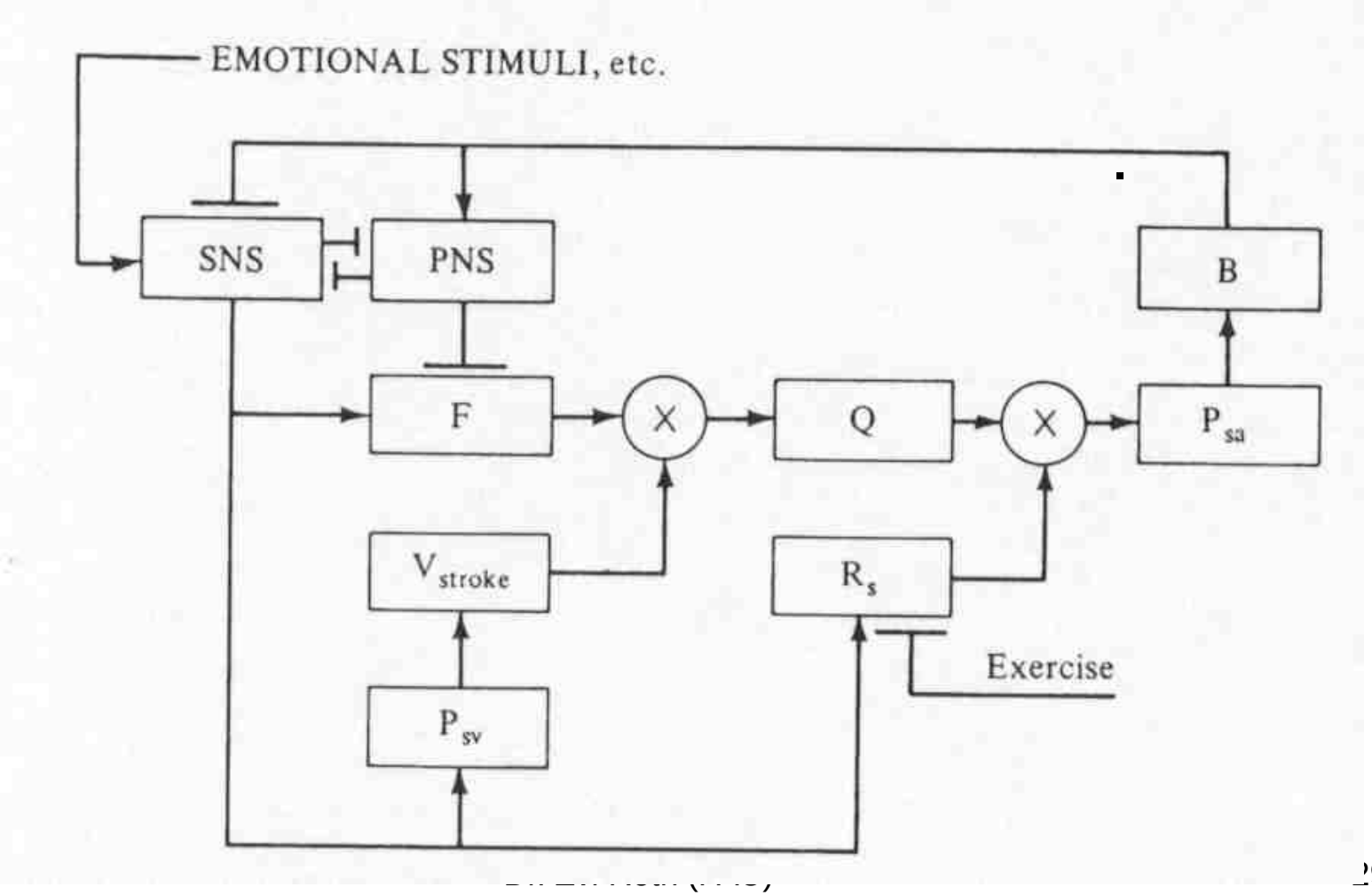
Parasymp.
Nerv. Sys

Barorecept
.

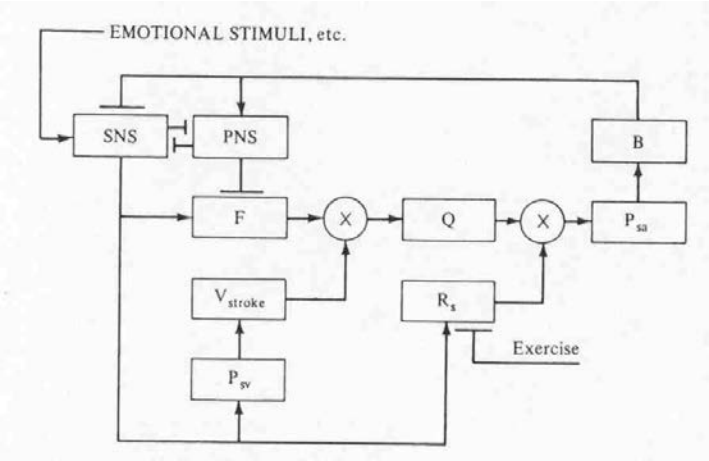
Symp.
Nervous
Sys.



Several Feedback Loops: “Negative Feedback” is whenever the number of inhibitions in a loop is odd. Watch that all feedback loops here are negative!

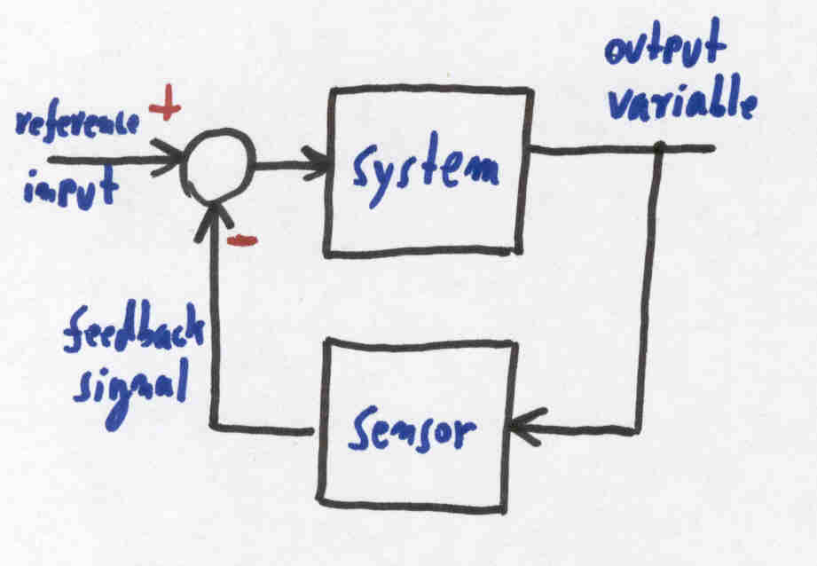


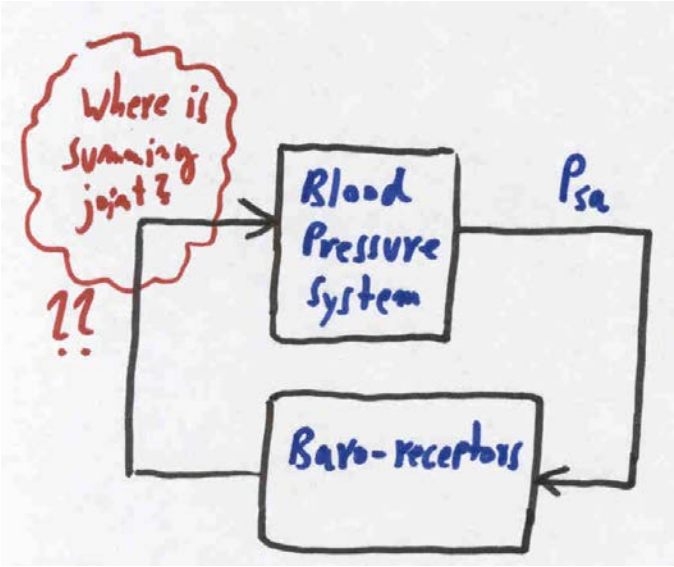
Simplified Mathematical Analysis (focusing on F, and neglecting the nervous activity influences on P_{sv} and R_s)



- The feedback system brings P_{sa} to some "desired" level P^* and it regulates it around such pressure.
- F (previously a parameter) is now one of the unknowns.

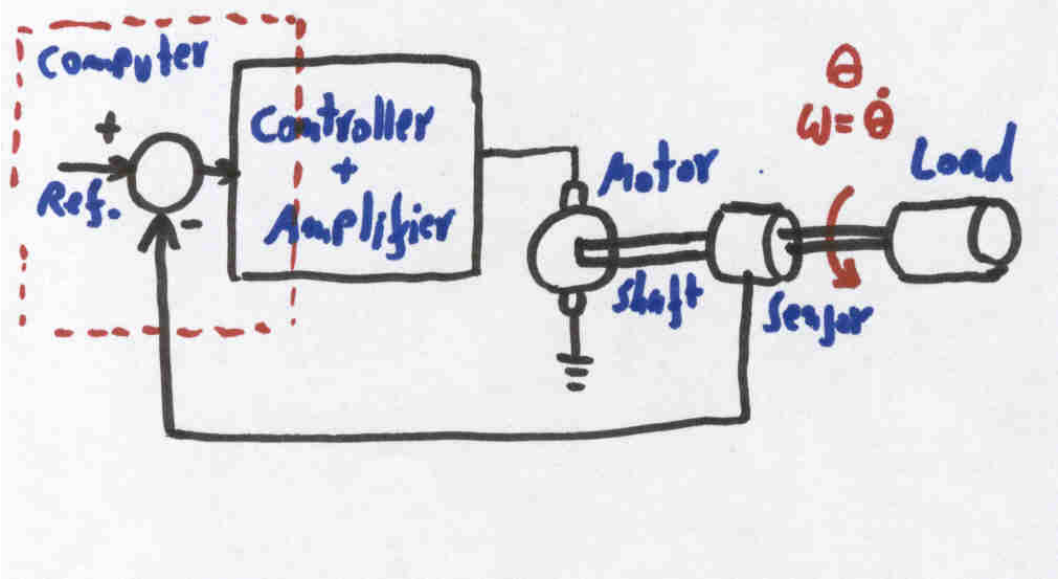
Why is it that P_{sa} ,and no other variable, is the one regulated?





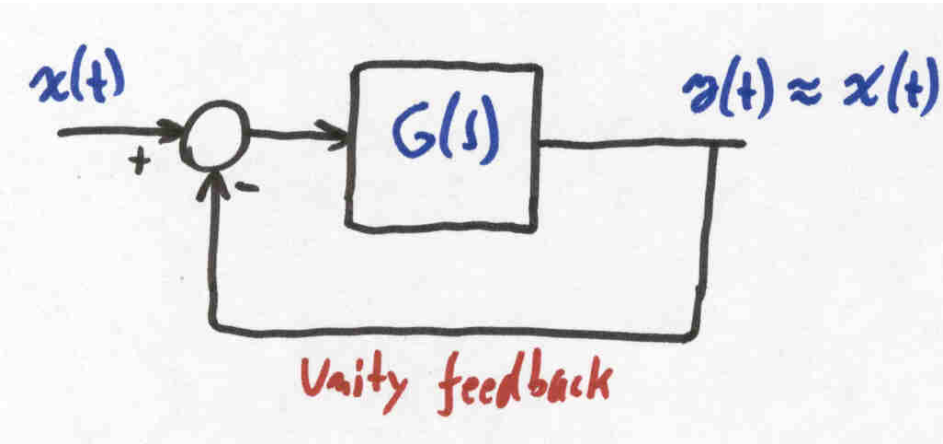
- In any negative feedback control system, the variable that is being <u>measured</u> (for signal to serve as a feedback) is the one that is <u>regulated</u>.
- Here, the baroreceptors measure P_{sa} and therefore the value of P_{sa} is regulated to be equal to a suitable reference level.

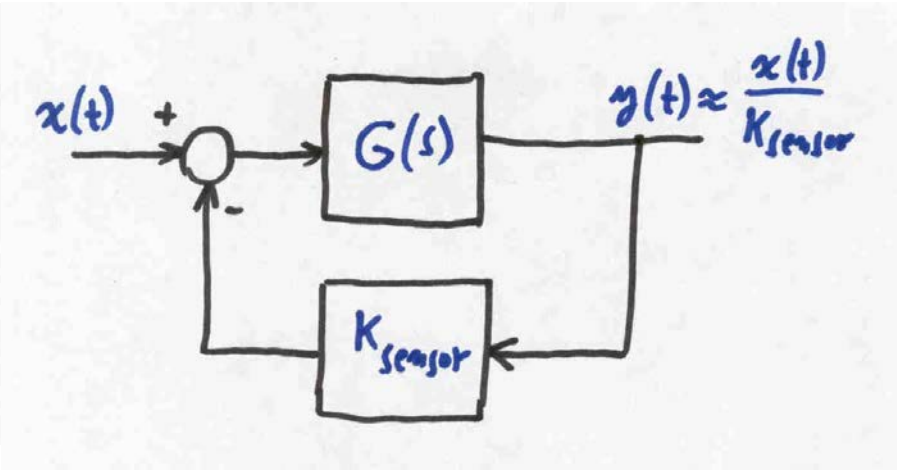
Engineering Example: Position or Velocity Control of an Electric Motor



- If motor's angular position is sensed (using a potentiometer or optical encoder) then voltage reference determines a desired final angle.
- If motor's angular velocity is sensed (using a tacho-generator) then reference determines a desired final velocity.

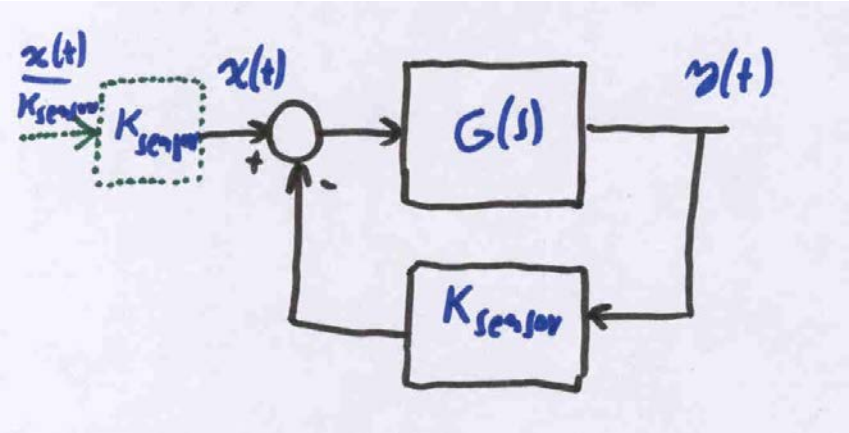
How is the reference input determined? An engineering view:

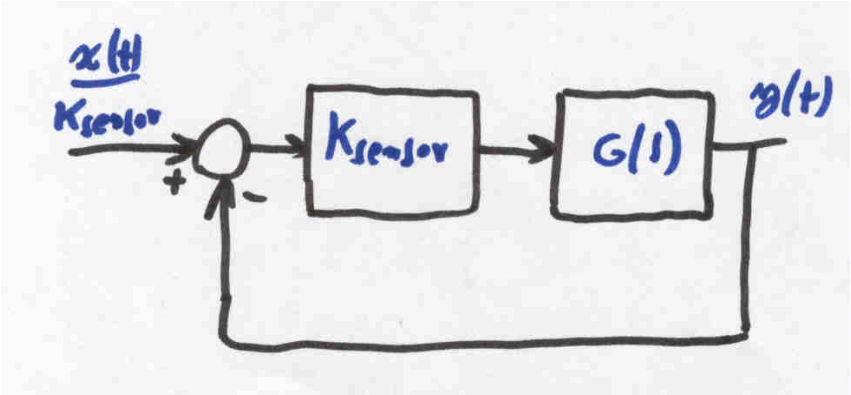




- Engineered control system usually contain a well defined summing joint, where feedback signal is subtracted from the reference input.
- Due to sensor's gain, the true reference level is a scaled version of the actual input signal.

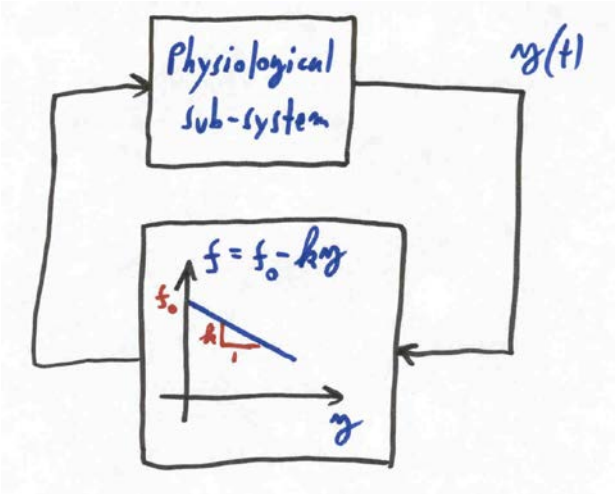
Why does output follow an input scaled by the sensor's gain?

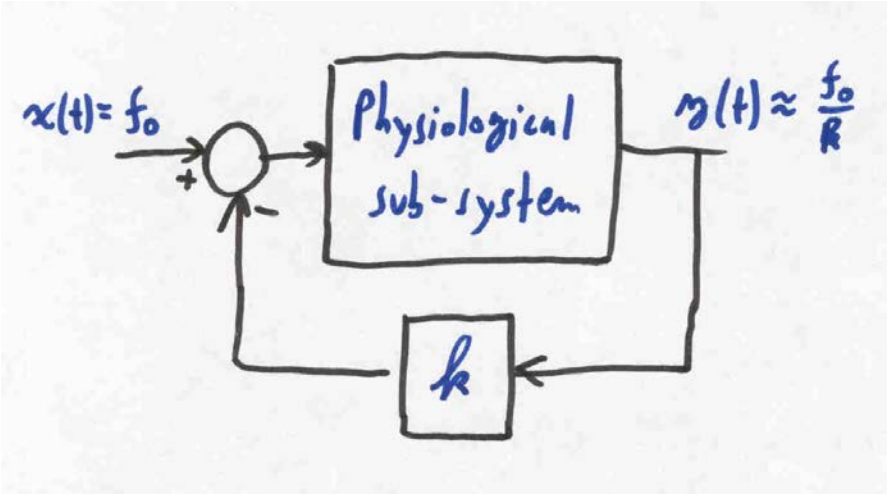




- Create a "dummy" sensor gain block processing the incoming input.
- Merge the two K_{sensor} into a single block operating on the error signal.

How is the reference input determined? A physiological view:





- Most physiological control system lack a well defined summing joint.
- Both – reference level and the negative feedback summation, are obtained due to the monotone decreasing function of the signal that relates to the feedback-sent variable.

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -1

$$Q_R = FC_R P_{sv}$$

$$Q_L = FC_L P_{pv}$$

- Now that F is variable, it no longer makes sense to use the pump constants K_R and K_L.
- Still at steady-state $Q_R = Q_L = Q$.
- C_R,C_L are the diastolic compliance of the right and left hearts

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -2

$$Q_R = FC_R P_{sv}$$

$$Q_L = FC_L P_{pv}$$

$$V_{sv} = C_{sv} P_{sv}$$

$$V_{pv} = C_{pv} P_{pv}$$

$$V_{sa} = C_{sa} P_{sa}$$

$$V_{pa} = C_{pa} P_{pa}$$

$$Q_s = \frac{P_{sa} - P_{sv}}{R_s}$$

$$V_0 = V_{sv} + V_{pv} + V_{sa} + V_{pa}$$

$$Q_p = \frac{P_{pa} - P_{pv}}{R_p}$$

Collection of all relevant equations

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -3

$$Q = Q_R = FC_R P_{sv}$$

$$Q = Q_L = FC_L P_{pv}$$

$$V_{sv} = C_{sv} P_{sv}$$

$$V_{pv} = C_{pv} P_{pv}$$

$$V_{sa} = C_{sa} P_{sa} = C_{sa} P^*$$

$$V_{pa} = C_{pa} P_{pa}$$

$$V_0 = V_{sv} + V_{pv} + V_{sa} + V_{pa}$$

$$Q = Q_s = \frac{P^* - P_{sv}}{R_s}$$

$$Q = Q_p = \frac{P_{pa} - P_{pv}}{R_p}$$

At steady-state

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -4

$$Q = FC_R P_{sv}$$

$$Q = FC_L P_{pv}$$

$$V_{sv} = C_{sv} P_{sv}$$

$$V_{pv} = C_{pv} P_{pv}$$

$$V_{sa} = C_{sa} P^*$$

$$V_{pa} = C_{pa} P_{pa}$$

$$V_0 = V_{sv} + V_{pv} + V_{sa} + V_{pa}$$

$$Q = \frac{P^* - P_{sv}}{R_s}$$

$$Q = \frac{P_{pa} - P_{pv}}{R_p}$$

With $P_{sa}=P^*$ and V_0 given, there are 8 equations with 8 unknowns

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -5

$$Q = FC_R P_{sv}$$

$$Q = FC_L P_{pv}$$

$$V_{sv} = C_{sv} P_{sv}$$

$$V_{pv} = C_{pv} P_{pv}$$

$$V_{sa} = C_{sa} P^*$$

$$V_{pa} = C_{pa} P_{pa}$$

$$V_0 = V_{sv} + V_{pv} + V_{sa} + V_{pa}$$

$$Q = \frac{P^* - P_{sv}}{R_s} \approx \frac{P^*}{R_s}$$

$$Q = \frac{P_{pa} - P_{pv}}{R_p}$$

Approximation 1: $P_{sa}=P^* >> P_{sv}$

(2% error due to approximation)

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -6

$$Q = FC_R P_{sv}$$

$$Q = FC_L P_{pv}$$

$$V_0 \approx V_{sv} + V_{sa} \Rightarrow$$

$$\Rightarrow C_{sa} P^* + C_{sv} P_{sv} \approx V_0$$

$$V_{sv} = C_{sv} P_{sv}$$

$$V_{pv} = C_{pv} P_{pv}$$

$$V_{sa} = C_{sa} P^*$$

$$V_{pa} = C_{pa} P_{pa}$$

$$Q = \frac{P^* - P_{sv}}{R_s} \approx \frac{P^*}{R_s}$$

$$Q = \frac{P_{pa} - P_{pv}}{R_p}$$

Approximation 2: Neglect pulmonary volumes compared to systemic volumes (10% error due to approximation)

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -7

$$Q = FC_R P_{sv}$$

$$Q = FC_L P_{pv}$$

$$V_0 \approx V_{sv} + V_{sa} \Rightarrow$$

$$\Rightarrow C_{sa} P^* + C_{sv} P_{sv} \approx V_0$$

$$V_{sv} = C_{sv} P_{sv}$$

$$V_{pv} = C_{pv} P_{pv}$$

$$V_{sa} = C_{sa} P^*$$

$$V_{pa} = C_{pa} P_{pa}$$

$$Q = \frac{P^* - P_{sv}}{R_s} \approx \frac{P^*}{R_s}$$

$$Q = \frac{P_{pa} - P_{pv}}{R_p}$$

Find P_{sv}

Find Q

Find F

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -8

$$Q = FC_R P_{sv} \Rightarrow$$

$$\Rightarrow \boxed{F = \frac{P^* C_{sv}}{R_s C_R (V_0 - C_{sa} P^*)}}$$

$$\boxed{Q = \frac{P^*}{R_s}}$$

$$C_{sa} P^* + C_{sv} P_{sv} \approx V_0 \Rightarrow$$

$$\Rightarrow \boxed{P_{sv} = \frac{V_0 - C_{sa} P^*}{C_{sv}}}$$

Approximated Results

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -9

$$Q = FC_R P_{sv} \Rightarrow$$

$$\Rightarrow \boxed{F = \frac{P^* C_{sv}}{R_s C_R (V_0 - C_{sa} P^*)}}$$

$$\boxed{Q = \frac{P^*}{R_s}}$$

$$C_{sa} P^* + C_{sv} P_{sv} \approx V_0 \Rightarrow$$

$$\Rightarrow \boxed{P_{sv} = \frac{V_0 - C_{sa} P^*}{C_{sv}}}$$

Controlled Circulation Performance:

$$P_{sa} = P^* = const \Rightarrow \sigma_{P_{sa} R_s} = 0 \qquad \sigma_{QR_s} = -1$$

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -9

$$Q = FC_R P_{sv} \Rightarrow$$

$$\Rightarrow \boxed{F = \frac{P^* C_{sv}}{R_s C_R (V_0 - C_{sa} P^*)}}$$

$$\boxed{Q = \frac{P^*}{R_s}}$$

$$C_{sa} P^* + C_{sv} P_{sv} \approx V_0 \Rightarrow$$

$$\Rightarrow \boxed{P_{sv} = \frac{V_0 - C_{sa} P^*}{C_{sv}}}$$

Controlled Circulation Performance: As P_{sv} and stroke volume $V_{stroke} = C_R P_{sv}$ are both independent of R_s →increased cardiac output is due to increase in F

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -10

$$Q = FC_R P_{sv} \Rightarrow$$

$$\Rightarrow \boxed{F = \frac{P^* C_{sv}}{R_s C_R (V_0 - C_{sa} P^*)}}$$

$$\boxed{Q = \frac{P^*}{R_s}}$$

$$C_{sa} P^* + C_{sv} P_{sv} \approx V_0 \Rightarrow$$

$$\Rightarrow \boxed{P_{sv} = \frac{V_0 - C_{sa} P^*}{C_{sv}}}$$

In uncontrolled circulation sensitivity of Q to V_0 is 1; In controlled – sensitivity is 0!→ Blood loss does not affect Q: F increases to compensate for loss of stroke volume.

Simplified Mathematical Model of Blood Pressure Control by Baroreceptor Loop -11

$$Q = FC_R P_{sv} \Rightarrow$$

$$\Rightarrow \boxed{F = \frac{P^* C_{sv}}{R_s C_R (V_0 - C_{sa} P^*)}}$$

$$\boxed{Q = \frac{P^*}{R_s}}$$

Blood Loss: Model breaks down when $V_0 = C_{sa} P^*$ which means an empty systemic venous system.

$$C_{sa} P^* + C_{sv} P_{sv} \approx V_0 \Rightarrow$$

$$\Rightarrow \boxed{P_{sv} = \frac{V_0 - C_{sa} P^*}{C_{sv}}}$$