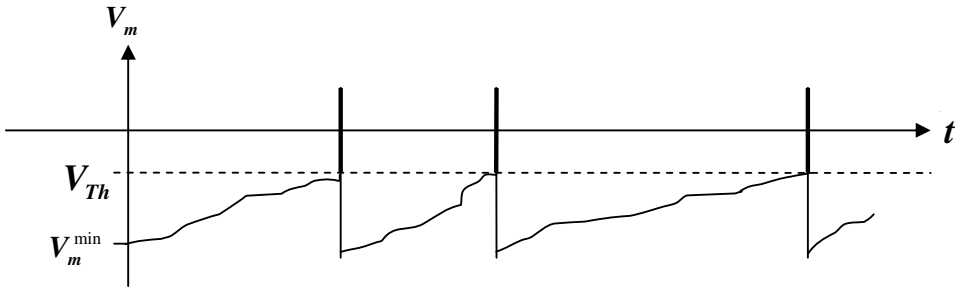
NEURAL CONTROL OF THE CARDIOVASCULAR SYSTEM

Long term blood pressure control is achieved by adjusting total blood volume to the level required. Within 30 minutes or less fluid can be expelled or taken up at the capillary level. If one considers control over longer periods (several hours to days), the kidneys are effective. By adjusting their water excretion rate they can adjust blood volume and hence blood pressure.

Rapidly occuring (tens of seconds to few minutes) pressure transients in the central large arteries are sensed by tension-sensitive nerve endings which are called baroreceptors. These are located on the wall of the aorta at the aortic arch and on the wall of the carotid sinuses in areas just distal to the bifurcation of the common carotid areteries. Wall tension depends on local blood pressure and therefore baroreceptor firing rate depends on blood pressure, such that increase blood pressure results in increased firing rate, f_b. This information is relayed to the Cardiovascular Control Center (CCC) in the brain stem. This center receives other information as well among which we can mention O_2 and CO_2 concentrations in the arteries, and information coming from higher brain centers. Neurons of the CCC process all information they receive and their axons innervate the heart and blood vessels through two pathways, namely the sympathetic and the parasympathetic nerves.

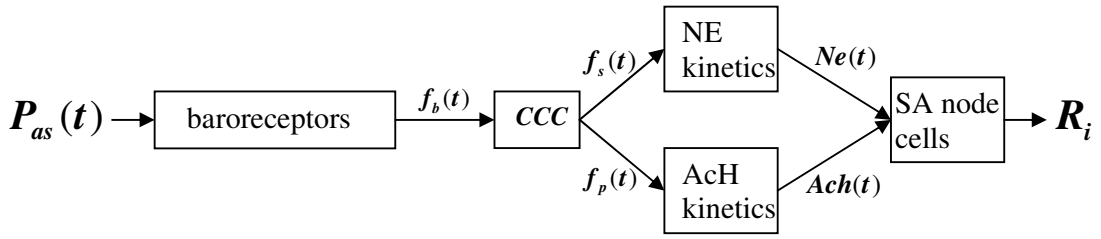
Let us first concentrate on the effects of the firing artes of the sympathetic nerves, f_s, and the parasympathetic nerves, f_p, innervating the SA node cells. The beating rate of the SA node cells depend on the norepinephrine and acetylcholine concentrations, $Ne(t)$ and $Ach(t)$, in the instertitial fluid around these cells. $Ne(t)$ depends on $f_s(t)$ and $Ach(t)$ depends on $f_p(t)$.

A typical SA node cell memnbrane potential is as below



This is a simplistic illustration and it does not show the details of the action potentials but only their occurences. V_m increases slowly until a threshold voltage V_{Th} is reached at which time an AP occurs, and V_m is reset back to its lowest value $V_m^{\min}$. The instantenaous slope of the slowly rising V_m is dependent on $Ne(t)$ and $Ach(t)$. If the slope is larger on the average , then the next beat occurs earlier and vice versa.

Overall block diagram for the control of SA node cells' beating times and hence for the control of the heart period, T , (and the heart rate HR) is as follows:



where R_i, $i = ...,1,2,3,...$ denote the times at which the heart beats. Many different models for this overall system are proposed ranging from simple to complex ones. In the simple model explained below the $f_b(t)$, $f_s(t)$, and $f_p(t)$ variables are not explicitly shown. Thus $Ne(t)$ and $Ach(t)$) are related to $P_{as}(t)$ directly:

$$\frac{dNe(t)}{dt} = K_{Ne}[P_{const} - P_{as}(t-\tau_{sym})] - k_{Ne}Ne(t)$$

$$\frac{dAch(t)}{dt} = K_{Ach}P_{as}(t-\tau_{Ach})] - k_{Ach}Ach(t)$$

where

$K_{Ne} = K_{Ach} = 0.3, P_{const} = 120$ ***mmHg***

$\tau_{Ne} = 2.5$ ***seconds***, $\tau_{Ach} = 0.5$ ***seconds***

$k_{Ne} = 0.239, k_{Ach} = 2$

Solving these two differential equations one can find $Ne(t)$ and $Ach(t)$ for a given $P_{as}(t)$.
To find the times of the heart beats we must relate the slope of the rising portion of $V_m(t)$ to $Ne(t)$ and $Ach(t)$.
Define $U(t) = V_m(t) - V_m^{\min}$, and assume that the last beat has occured at $t = 0$. For $t \geq 0$

$$\frac{dU}{dt} = C + c(t), \text{ and } U(0) = 0$$

where

$C = 180$ ***and***

$c(t) = BRS \times [0.25(15 - Ach(t)) + 0.25(Ne(t) - 20)]$

where BRS is called the "baroreflex gain" and is between 0 and 50.
Once U reaches $V_{Th} - V_m^{\min}$, a new heart beat occures and U is reset to zero. We take $V_{Th} - V_m^{\min} = 144$.

Another effect of increased $Ne(t)$ is to increase ***SLS and SRS*** (see the section on the model of the ventricle).
Also increased $f_s(t)$ increases R_S by constricting small blood vessels. Yet another effect of increased $f_s(t)$ is decreased C_{VS}.

In summary

$f_s \uparrow \Rightarrow HR \uparrow, SLS \uparrow, SRS \uparrow, R_S \uparrow, C_{VS} \downarrow \Rightarrow P_{as} \uparrow$
$f_p \uparrow \Rightarrow HR \downarrow \Rightarrow P_{as} \downarrow$

That is, the overall effect of increased symphatetic firing rate is increase arterial blood pressure, and the the effect of increased parasympathetic firng rate is decreased arterial blood pressure.

Thus if P_{as} increases, Ach increases but Ne decreases as seen in the above differential equations. Increased Ach decreases $c(t)$. Decreasing Ne also decreases $c(t)$. Therefore overall effect is less frequent beating and decreased HR. This then decreases P_{as}, completing the negative feedback cycle.

Results of some simulations are given below to explain the steady state effect of neural feedback:

In the following we assume that baroflex feedback changes HR only and not the other parameters such as SLS, SRS, R_S, C_{VS}.

i) Let us take BRS = 25. Also assume Pas is constant, i.e. it does not vary with time. Since we are dealing with the steady state relation we can simplify the baroreceptor model by making the derivatives equal to zero.

$0=K_{sym}*(P_{const} –Pas) – NE*k_{sym}$
$0= K_{Ach}*Pas – Ach*k_{Ach}$
where NE, Ach and Pas are the steady state values.

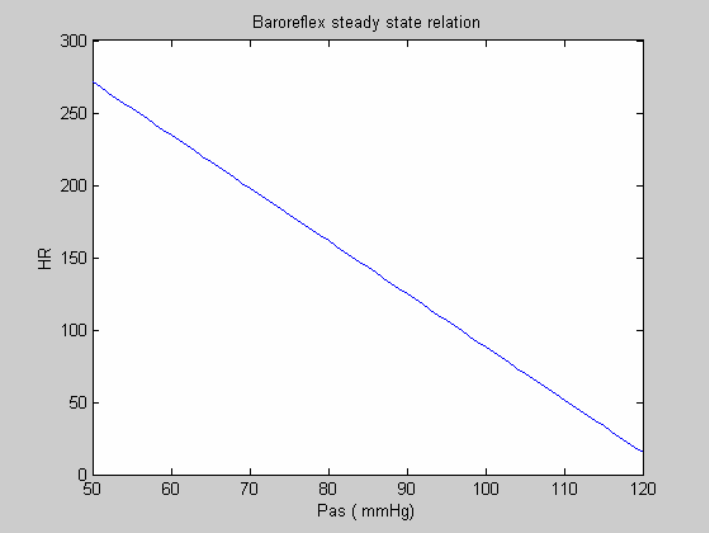
Solving for NE and Ach from these equations, we get

$NE = K_{sym}*(P_{const} –Pas) / k_{sym}$
$Ach = K_{Ach}*Pas/k_{Ach}$

The steady state value of c
$c_{ss} = BRS*0.25*(15-Ach + NE – 20) = A – B*Pas$
where $A = 0.25*BRS*(-5+(K_{sym}/k_{sym})*Pconst)$
$B = 0.25*BRS* (K_{sym}/k_{sym} + K_{Ach}/k_{Ach})$

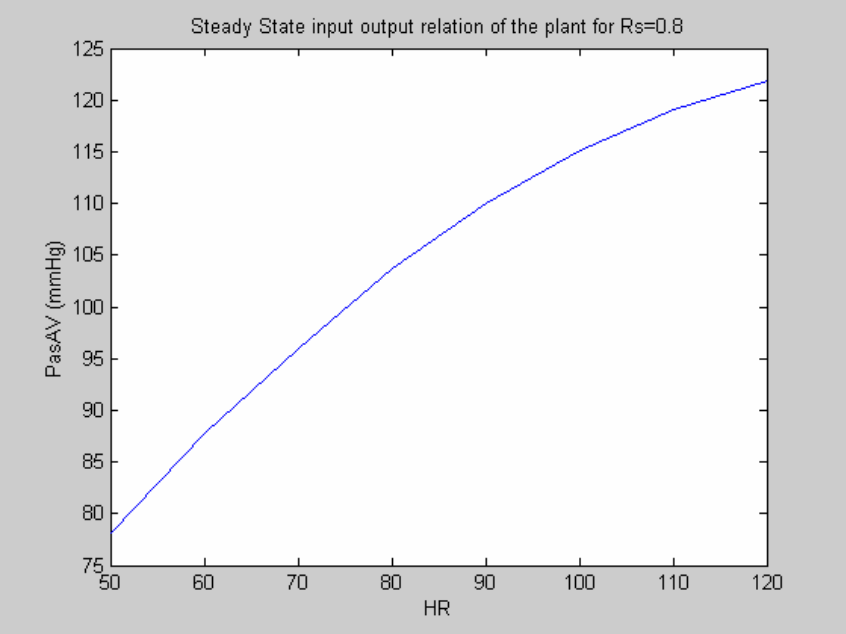
$dU/dt = C + c_{ss}$
The time it takes for U to reach 144, i.e. Heart Period, $T = 144/(C+c_{ss})$

Therefore Heart Rate HR is
$HR = 60/T = (60/144)*(C+c_{ss}) = C – D*Pas$
where $C = (60/144)*(C+A)$, $D = (60/144)*B$
If we substitute the numerical values for the constants
C = 454.2386 D = 3.6595 we get

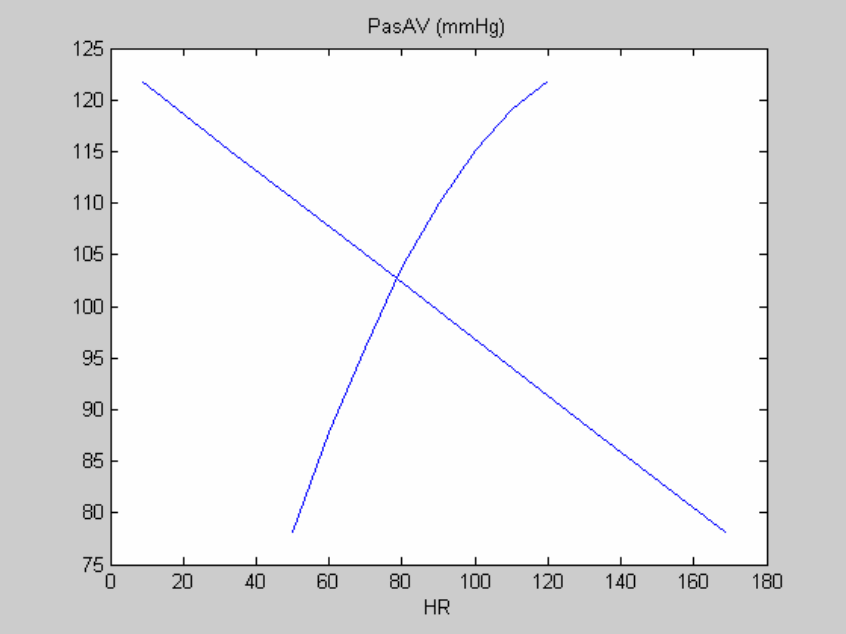


This graph shows that as Pas is increased HR decreases.

ii) Using the previously given complete CVS model we can calculate the steady state average values for Pas for different values of HR, as shown in the below model for Rs = 0.8.

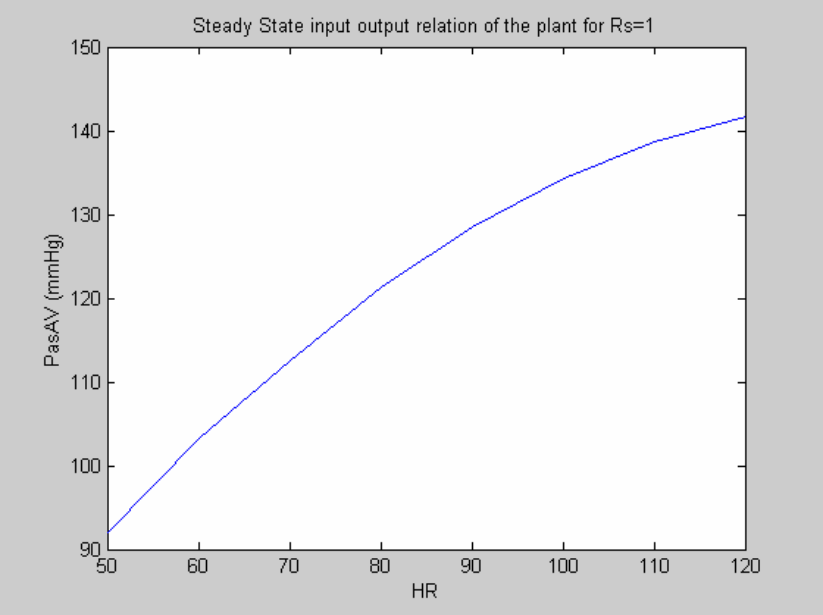


iii) Since the function from Pas to HR, and the function from HR to Pas work together in a real intact CVS, the solution for Pas and HR is forund by finding the intersection of the two curves given in i) and ii).

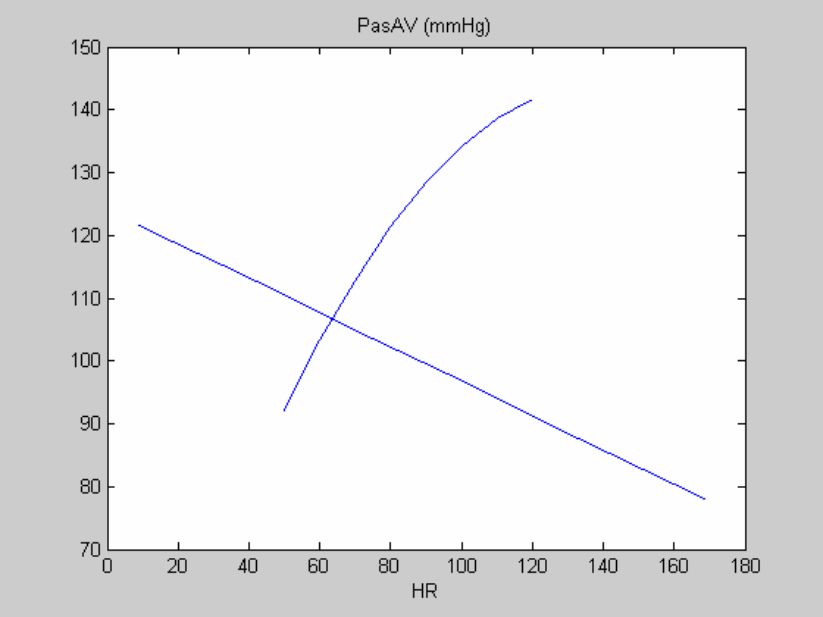


The intersection point is Pas_{Av} = 102.64 mmHg, HR = 78.64 beats/min. This is the solution for when there is baroreceptor feedback and when Rs = 0.8.

iv) Same plot as in ii) is obtained for Rs = 1.

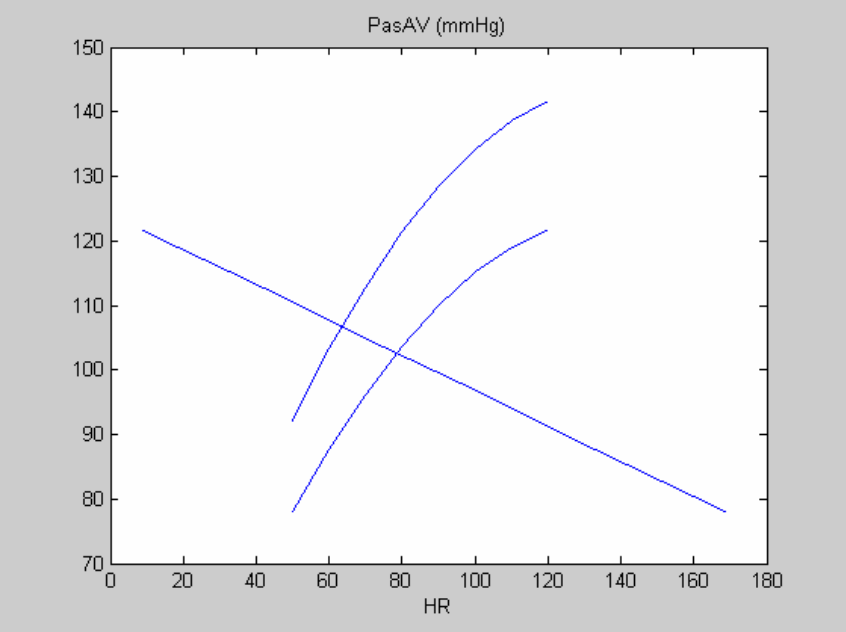


v) Again just as we have found the intersection point in iii) we again find the intersection point for Rs = 1 this time.



The intersection point is Pas_{Av} = 106.72, HR = 63.71 for when there is feedback and for Rs = 1.

vi)



The two graphs in iii and iv are superimposed on each other to see the results better. When there is feedback Pas increases from 102 to 106 for when Rs increases from 0.8 to 1 respectively. However if there were no feedback and HR were fixed at the value 78.64, then Pas would increase to 120. This result shows that with the presence of Baroreflex control, when Rs increases the system does not allow for a large increase in Pas by lowering HR.

Here is the code for the above simulations:

```
clear all;close all;

%css = A-B*Pass
Ksym=0.3;
ksym=0.239;
Kach=0.3;
kach=2;
Pconst=120;
BRS=25;
A=0.25*BRS*(-5+Ksym*Pconst/ksym)
B=0.25*BRS*(Ksym/ksym+Kach/kach)
%HR = C - D*Pass
C=60*(180+A)/144
D=60*B/144


HR(1)=50;
HR(2)=60;
HR(3)=70;
HR(4)=80;
HR(5)=90;
HR(6)=100;
HR(7)=110;
HR(8)=120;


Rs=0.8;
PasAV(1)=78.074;
PasAV(2)=87.755;
PasAV(3)=96;
PasAV(4)=103.681;
PasAV(5)=110.056;
PasAV(6)=115.18;
PasAV(7)=119.117;
PasAV(8)=121.836;

Rs=1;
PasAV2(1)=92.084;
PasAV2(2)=103.23;
PasAV2(3)=112.62;
PasAV2(4)=121.33;
PasAV2(5)=128.49;
PasAV2(6)=134.225;
PasAV2(7)=138.61;
PasAV2(8)=141.63;
```

```
for i=1:8
   HRbaro(i)=C-D*PasAV(i);
end


figure(1);plot(HR,PasAV2);title('PasAV (mmHg)');xlabel('HR');
hold on;
plot(HR,PasAV);
plot(HRbaro,PasAV);

figure(2);
Pin=(50:1:120);
HRout=C-D*Pin;
plot(Pin,HRout);title('Baroreflex steady state relation');
xlabel('Pas ( mmHg)');ylabel('HR');

figure(3);
plot(HR,PasAV);title('Steady State input output relation of the plant for Rs=0.8');
xlabel('HR');ylabel('PasAV (mmHg)');

figure(4);plot(HR,PasAV);title('PasAV (mmHg)');xlabel('HR');
hold on;
plot(HRbaro,PasAV);

figure(5);
plot(HR,PasAV2);title('Steady State input output relation of the plant for Rs=1');
xlabel('HR');ylabel('PasAV (mmHg)');

figure(6);plot(HR,PasAV2);title('PasAV (mmHg)');xlabel('HR');
hold on;
plot(HRbaro,PasAV);
```