Unit 9
CARDIOVASCULAR CONTROL

In this chapter we will learn about the wiring that allows for neural control of cardiovascular function. We will discover the anatomy, physiology and major reflexes and the current and future mathematical theory to describe the control objective.

Unit 9 Learning Objectives

Physiology and Anatomy
- **Autonomic Nervous System**
  - **Sympathetic**
  - **Parasympathetic**
- **Major CV reflexes**
  - **Baroreceptor**
  - **Chemoreceptor**
  - **CNS Ischemic Response**
  - **Cushing reaction**

Cardiovascular Coupling
- **Maximal External Work Transfer**
- **Maximum Power Transfer**
- **Maximum Efficiency**
- **Survival Reserves**
- **Towards a New Construct**

Physiology and Anatomy

The autonomic nervous system (ANS) is comprised of the sympathetic and parasympathetic nervous systems, (SNS and PNS respectively). In total, the ANS is said to be responsible for the 4 F's flight, fight, feeding and reproduction. In this course we will concentrate on the flight and fight aspects only! In figure 9-1 and 9-2, one can see connection between the vasomotor centers in the medulla and the heart and blood vessels for SNS and PNS. As a general rule, the SNS is considered to govern mostly excitatory cardiovascular functions — constriction of the vasculature (Figure 9-3) and increases in heart rate and contractile properties of the heart to name a few. Usually the PNS is considered to have inhibitory effects upon the cardiovascular system — relaxation of the vasculature and decreases in heart rate and contractile properties. While these examples are generalizations of far more complex processes, they serve to illustrate that the neural activity responsible for cardiovascular control is a fine balance between these two systems. The ANS interacts with the central nervous system (CNS) through diffuse and multiple neural pathways (Figure 9-4). We've all experienced a powerful emotional experience and felt the pounding of our heart as the ANS has done its work as an example of this CNS/ANS communication.

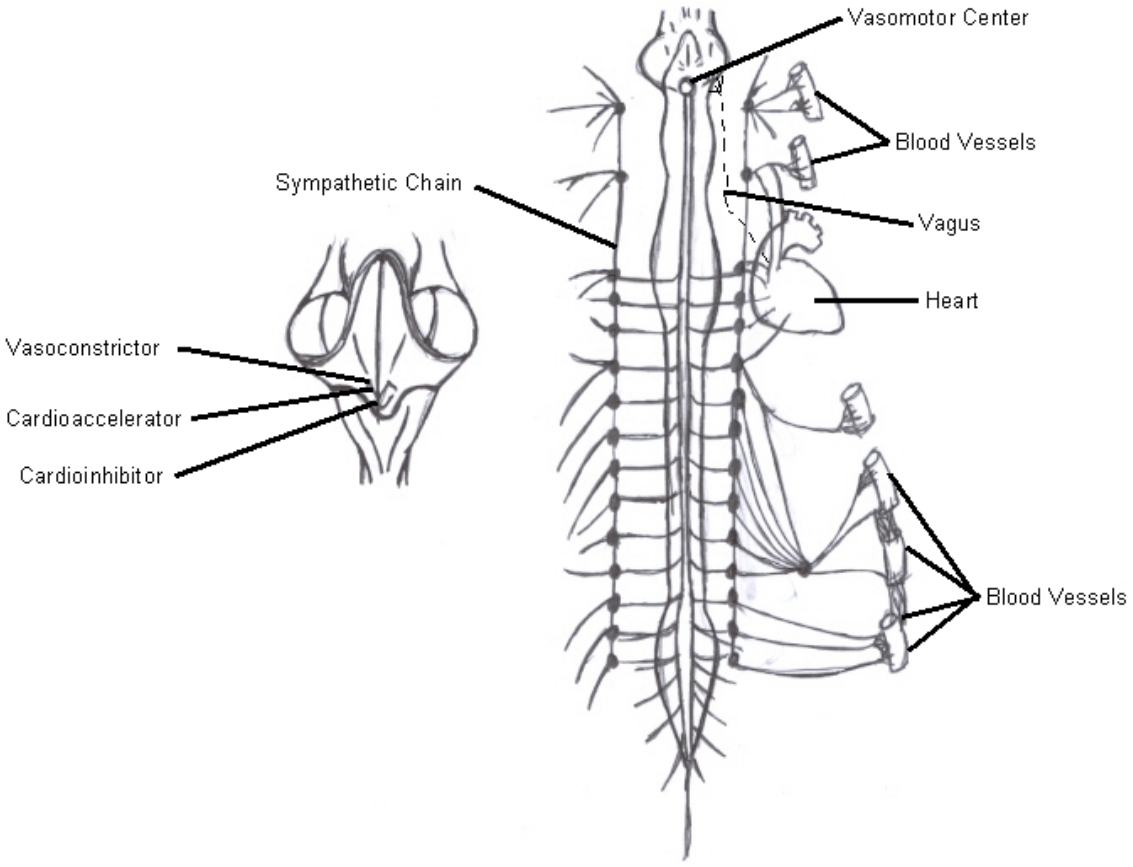


Figure 9-1 Sympathetic Nervous System

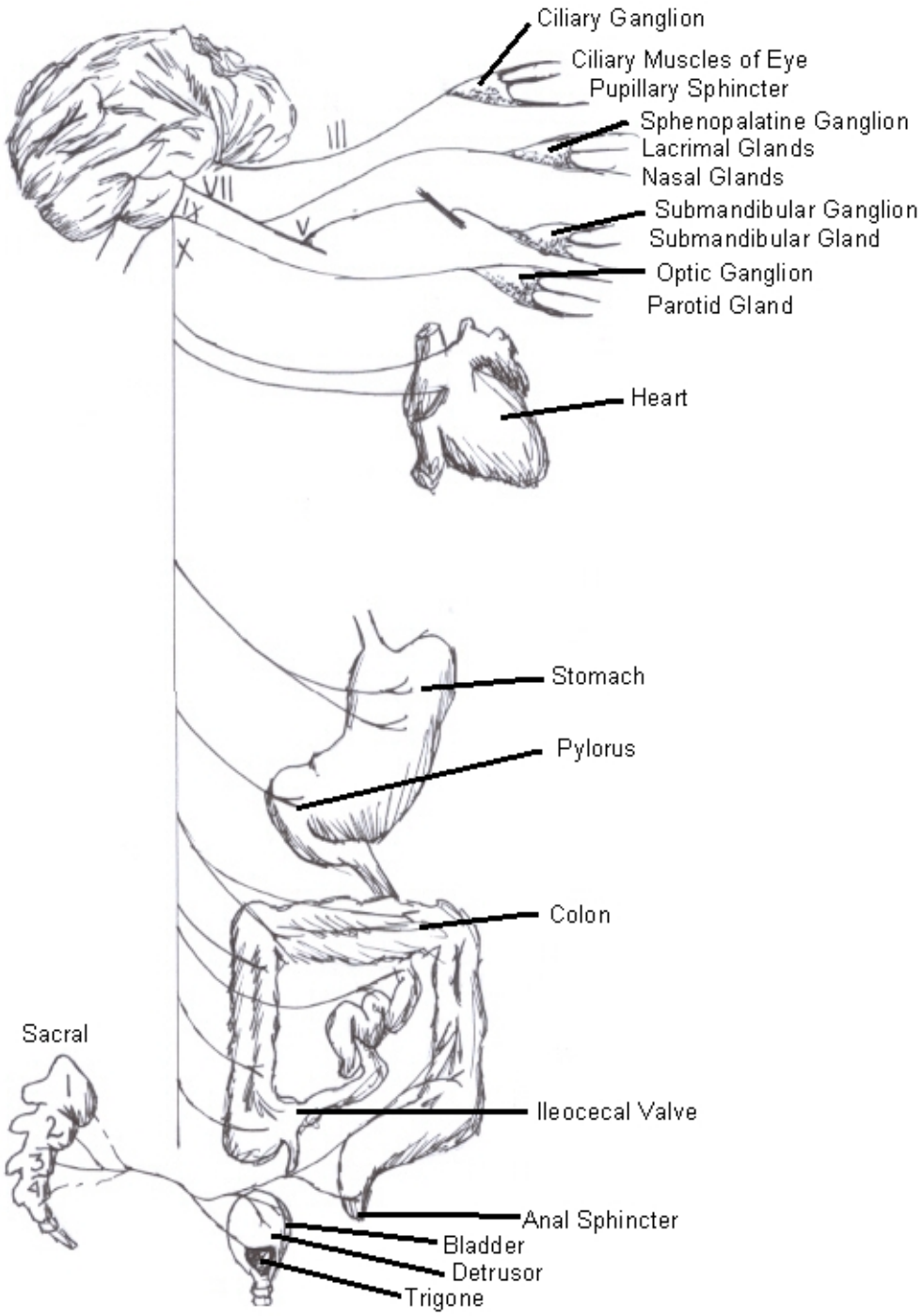


Figure 9-2

Figure 9-2 Parasympathetic Nervous System

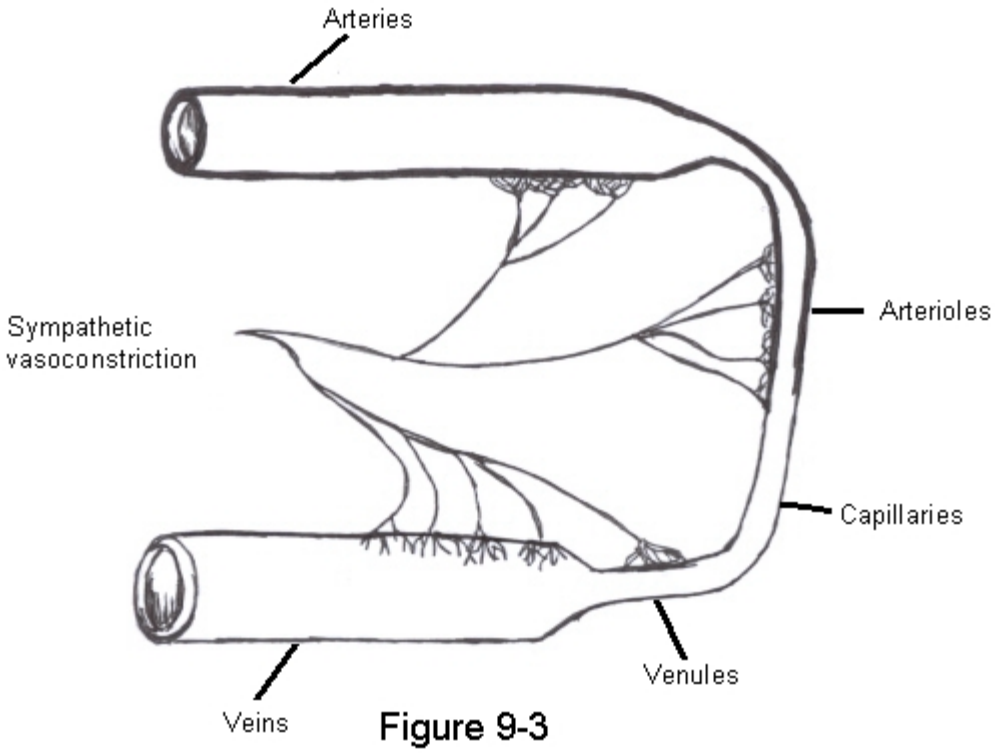


Figure 9-3 Sympathetic Innervation of Peripheral Circulation

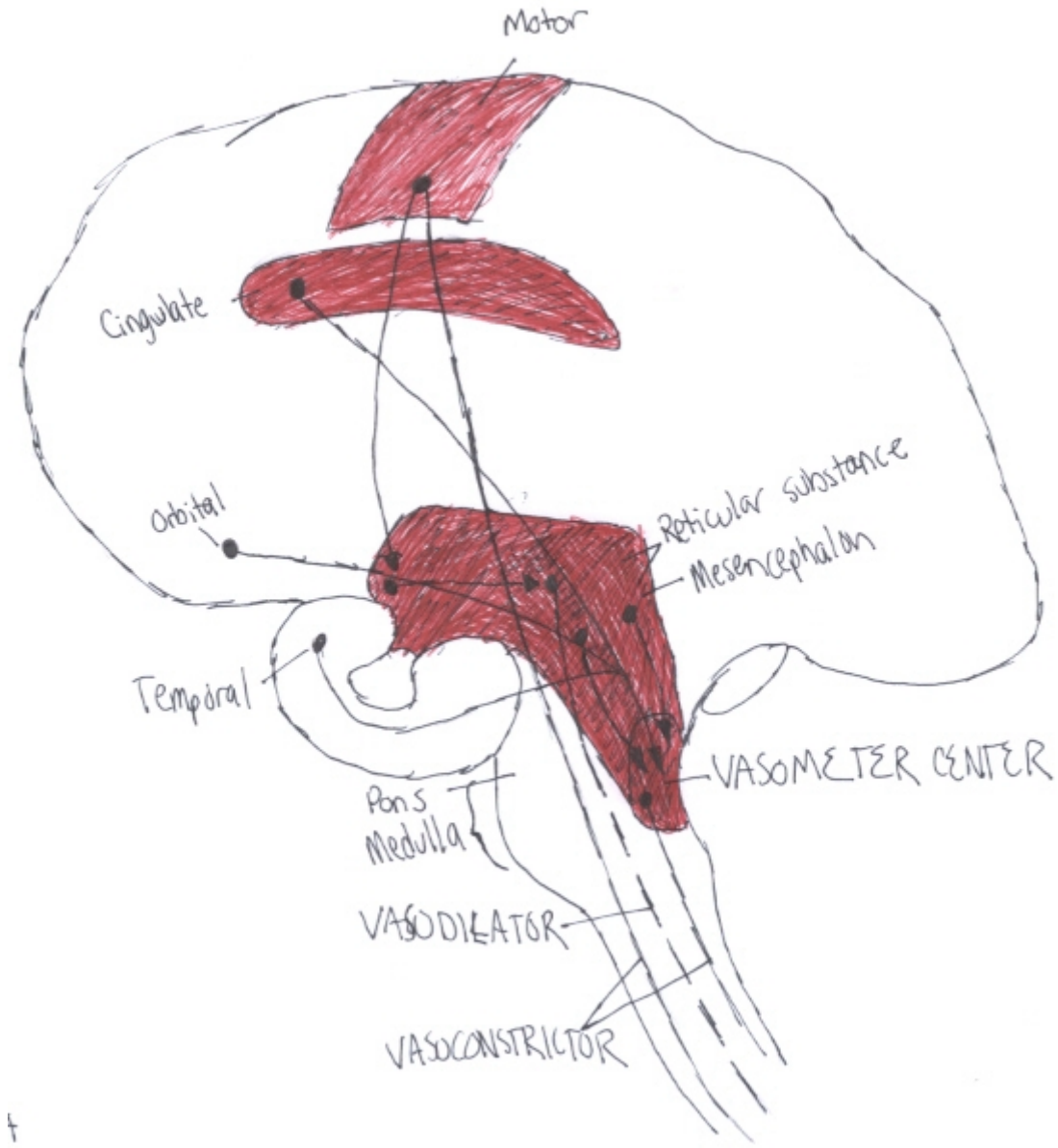


Figure 9-4 Areas of the brain important to the circulation, dashed lines represent inhibitory pathways

Major neural reflexes of the cardiovascular system include 1) baroreceptor, 2) chemoreceptor, 3) CNS ischemic response, and 4) atrial and pulmonary artery stretch. In this chapter we will concentrate on the baroreceptor reflex.

The basic anatomy of the baroreceptor reflex is shown in Figure 9-5

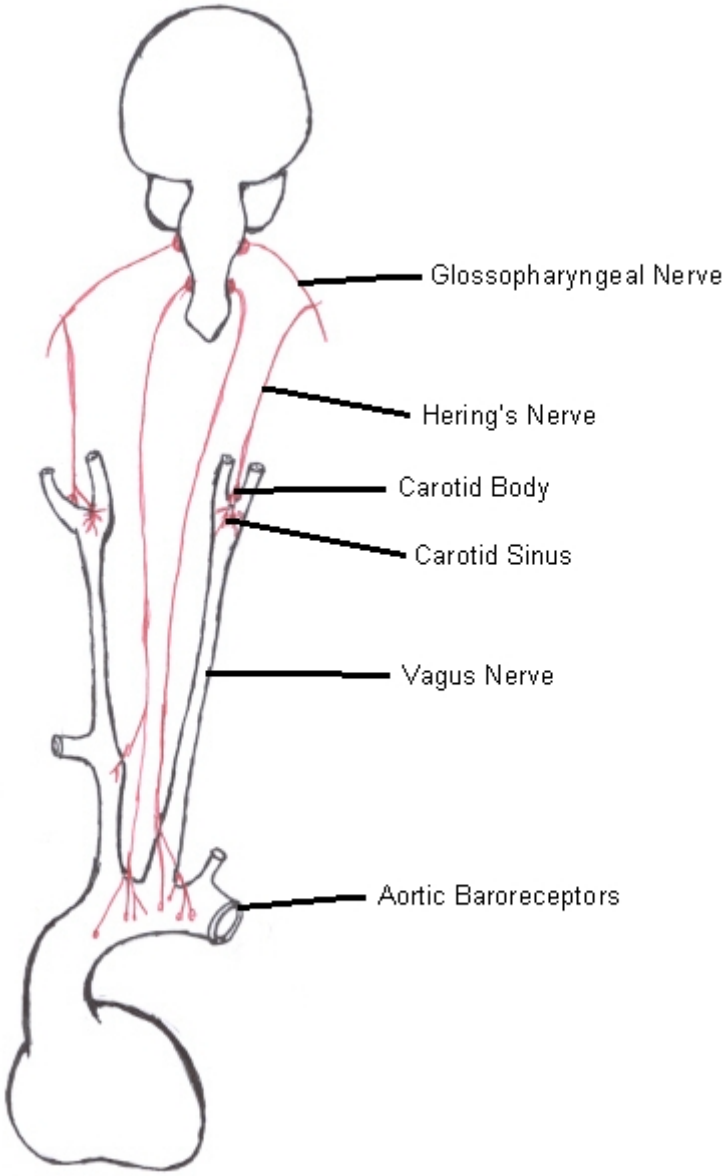


Figure 9-5 Baroreceptor System

The baroreceptors (pressure sensors) are located in the arch of the aorta and in the carotid sinus. These receptors sense changes in pressure in send the neural information up the Vagus and Hering's nerves. The cardiovascular control centers located in the medulla use this information to adjust cardiovascular

parameters, via the ANS. A typical function curve for a set of baroreceptors is shown in Figure 9-6.

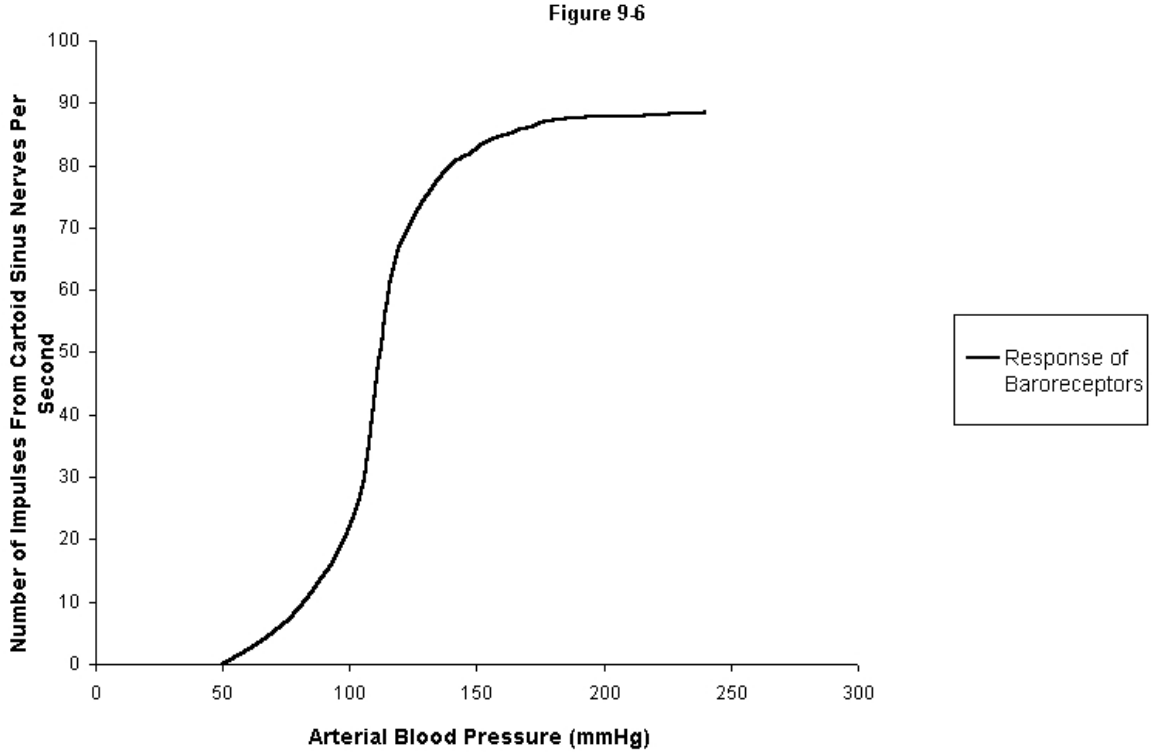


Figure 9-6 Baroreceptor Function Curve

As the blood pressure increases, so does the neural frequency. After a long-term exposure to a higher (or lower) pressure, the baroreceptor tends to "reset" and adjust its neural output to operate at the maximum sensitivity region of the curve. Thus, the baroreceptor reflex is not the method by which long-term pressure regulation is accomplished. However, for the short term, quick acting, pressure regulation, the baroreceptor reflex is the dominant control method. Figure 9-7 shows what happens when baroreceptor reflex is surgically taken out of the loop.

Without the baroreceptor reflex, a much wider variation in the arterial pressure occurs. If one observes astronauts in Earth's gravity after prolonged exposure to zero-gravity, they often have difficulty maintaining blood pressure, among other physiological complications. This is due, in part, to the de-conditioning of the baroreceptor reflex during long exposure to zero-gravity. In fact, two astronauts from the recent Shuttle flight (STS 102) had to be carried off the Shuttle, due in part, to their de-conditioned baroreceptor reflex.

The chemoreceptor reflex is similar to the baroreceptor reflex, except that oxygen levels are sensed in the aortic arch and carotid sinus. When the levels are low, the sensors send their information to excite the cardiovascular centers. Typically

this system is not activated unless the arterial pressure drops below about 80 mmHg.

CNS ischemic response is a highly potent reflex. When the CNS oxygen levels drop, the CNS sends excitatory signals to the ANS to constrict all peripheral vessels, increase heart rate, and cardiac contractile properties to dramatically increase the arterial pressure, which better perfuses the brain. Cushing's response is a special case of the CNS ischemic response. If the cerebral spinal fluid pressure is increased, this tends to collapse some of the cerebral arteries, which causes oxygen levels to drop. The CNS ischemic response is activated to increase the arterial pressure, thereby returning the cerebral oxygen levels back to normal.

Finally, one of the atrial stretch reflexes is the Bainbridge reflex. Here, a stretch in the atria causes the heart rate to increase — a good thing. Because of the increased heart rate more blood will be pumped by the heart, thereby reducing the atrial stretch.

There are many more reflexes, both short-term and long-term, not discussed here. The reader is referred to Handbook of Physiology Series for more complete details.

Cardiovascular Coupling

Cardiovascular coupling is the study (sometimes mystical) of how the heart delivers hemodynamic energy to the vasculature. Many approaches have been taken, and yet, the true nature of the process that governs the transfer of hemodynamic energy from heart to vessel remains unclear. In the following discussion, it is hoped that some basic foundational elements involved in the hemodynamic energy transfer process may be revealed. Ultimately, cardiovascular coupling is the ***governing control principle(s)*** of cardiovascular control mediated by the neural and humoral mechanisms.

Many have attempted to discover the governing control principle underlying cardiovascular control. Avenues taken include usually reduce to some form of maximum power transfer and/or maximum efficiency. We will start with the dominant current view, develop some of our own views from a common sense approach and conclude with a paper on a new concept.

Popular Current View (Maximal External Work, a form of maximum hemodynamic power transfer)

We know from Ohm's law that the average aortic pressure $\overline{AoP}$ is related to the average aortic flow, $\overline{AoF}$, by the average arterial resistance, R.

$$\overline{AoP} = R\,\overline{AoF}$$

One can assume, with minimal effect, that the end-systolic pressure, P_{ES}, is roughly equal to $\overline{AoP}$. Further, we know that $\overline{AoF}$ can be written as the stroke volume, SV divided by the length of one heartbeat, T.

$$\overline{AoF} = \frac{SV}{T}$$

If we make the substitutions for $\overline{AoP}$ and $\overline{AoF}$, into Ohm's law we have:

$$P_{ES} = R\,\frac{SV}{T}$$

Now define the ratio $\frac{R}{T}$ as effective arterial elastance, (as this ratio has the units of elastance).

$$E_A = \frac{R}{T}$$

This results in an equation for the arterial system:

$$P_{ES} = E_A\,\mathrm{SV}$$

Now we have an equation that represents the ***average*** arterial behavior over time. For example, if SV = 0 (no volume is injected into the arterial system over a length of time), the result will be P_{ES} = 0. When a larger SV is injected into the arterial system a larger P_{ES} will result. The relationship of ***average*** injected stroke volume to P_{ES} is described by the ***effective arterial elastance,*** E_A**.** This is not truly an elastance because to maintain P_{ES}, one must continue to inject an

average SV. A real (and constant) elastance would require no injection of volume to maintain the pressure level at P_{ES}. It is unfortunate that it was termed effective arterial elastance as much misinterpretation has resulted where it is thought of as an elastance. Perhaps it can be better understood by a simple example in Figure 9-8. If one has a bucket with a drain in the bottom (i.e. arterial system with capacity and resistance), it would take a continuous injection of water (i.e. SV) to maintain a certain level of water in the bucket (i.e. P_{ES}). If no water is put into the bucket for a period of time, the water level will go to zero. To increase the average water level in the bucket, one must increase the average water injected (SV) into the bucket. Thus, one can calculate E_A for a bucket. A small E_A would mean it takes large volumes of water (SV) to raise the water level slightly (P_{ES}) – a small outflow resistance and a large capacity. A large E_A means it takes very little volume (SV) to raise the water level (P_{ES}) – large outflow resistance and small capacity bucket.

In summary, E_A, is a term that represents both the capacity (inverse elastance) of the bucket and the rate at which water drains out of the bucket, R. More exactly, E_A represents the interaction between the injection rate, capacity and

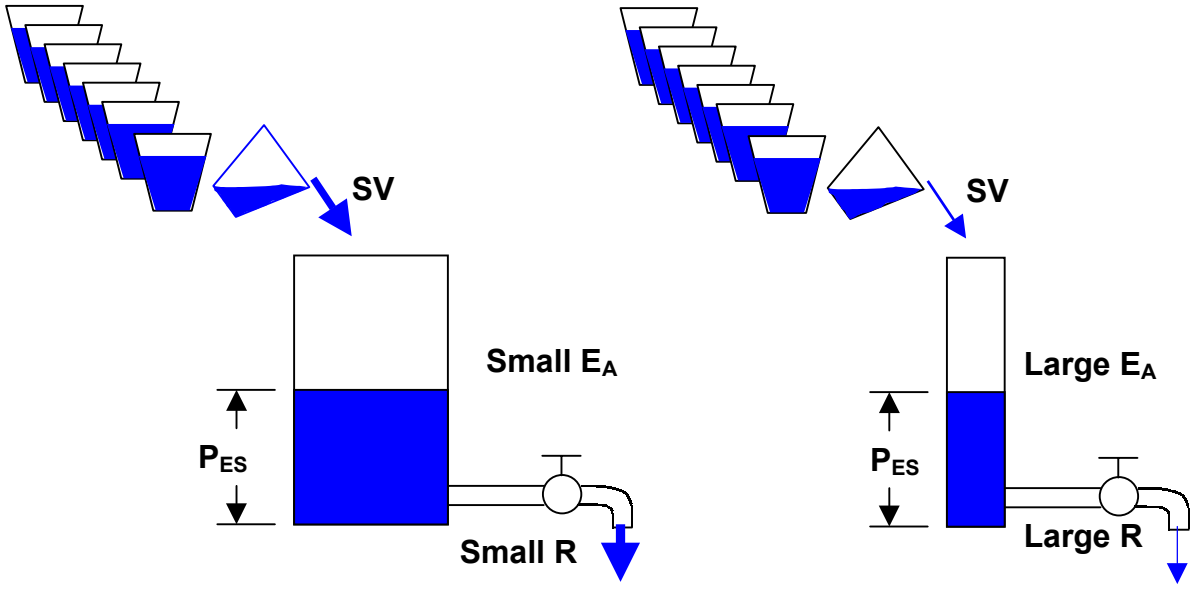


Figure 9-8 Simple representation of Physical meaning of E_A

the drain rate. In hemodynamic terms, it is an ***index*** of the windkessel effect! Having E_A allows us to plot it on a pressure volume loop (Figure 9-9). When SV=0, P = 0 (and volume is at end-diastolic volume, point 1), when SV = SV, P = P_{ES} (volume is at end systolic volume, point 2).

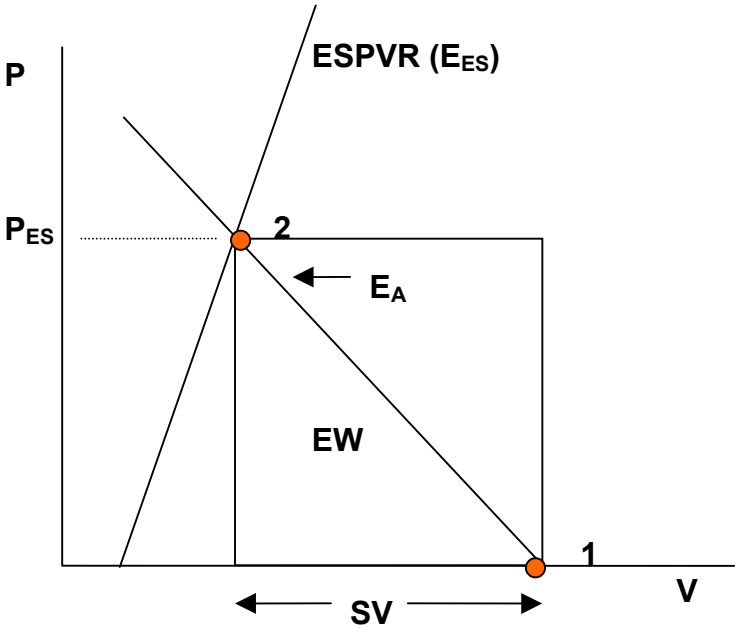


Figure 9-9 Both Arterial and Cardiac Parameters on PV Loop

We now have a representation of the heart (PV loop and ESPVR or E_{ES}) and the arterial system, E_A on the same graph. The next question is, "What value of E_A maximizes external work, EW)?"

$$P_{ES} = E_A \text{ SV}$$

$$P_{ES} = E_{ES}\left[\text{EDV - SV - } V_o\right], \text{ (note, no viscous loss term)}$$

Making appropriate substitutions and rearranging terms results in:

$$SV = \frac{E_{ES}(EDV - V_O)}{E_{ES} + E_A}$$

$$P_{ES} = \frac{E_{ES}E_A(EDV - V_O)}{E_{ES} + E_A}$$

$$EW = P_{ES}SV$$

Substituting yields,

$$EW = \frac{E_{ES}^2 E_A (EDV - V_O)^2}{(E_{ES} + E_A)^2}$$

We want to maximize EW with respect to E_A. We do this by taking the partial derivative of EW with respect to E_A and setting it equal to zero.

$$\frac{\partial EW}{\partial E_A} = 0 = E_{ES}^2 (EDV - V_O)\left[\frac{-2E_A}{(E_A + E_{ES})^3} + \frac{1}{(E_A + E_{ES})^2}\right]$$

A trivial solution occurs when either, $E_{ES} = 0$, or $(EDV - V_O) = 0$, thus

$$\left[\frac{-2E_A}{(E_A + E_{ES})^3} + \frac{1}{(E_A + E_{ES})^2}\right] = 0$$

Solving this yields

$$E_A = E_{ES}.$$

In other words, when $E_A = E_{ES}$, the PV loop is a square and external work is maximized!

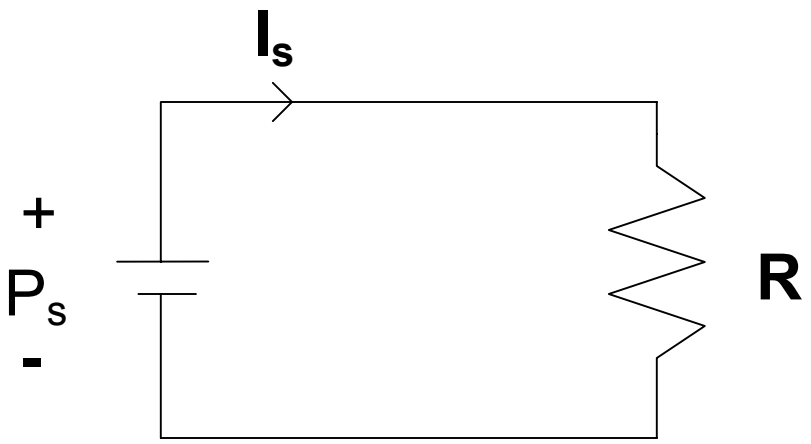
Some investigators have experimentally found that $E_A = E_{ES}$ and others have not. Mountains of journal papers have been published using this method and a commercial software package is available that will calculate E_A for the user. This concept is based on a cardiac model without source losses and an arterial model that is based on the clinical definition of TPR.

Now let's investigate other approaches.

A simple model:

Perhaps the simplest approach to examining the process of hemodynamic energy transfer is to look at the process through an electrical circuit model of the heart and vasculature. In this approach, let us consider the heart to produce a mean pressure that delivers a mean flow to a mean resistance.

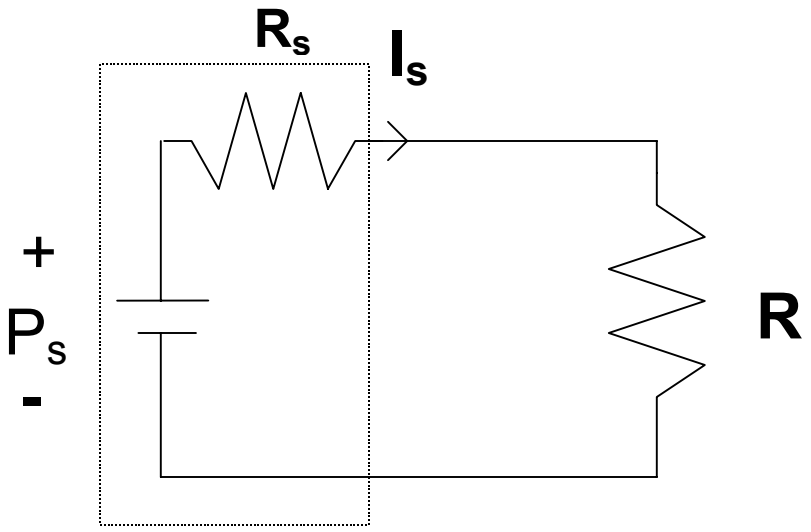
In electrical circuit terms,



Here a battery creating Ps volts (pressure) represents the heart and a resistance R represents the flow impediment of the vasculature. In this simple case all the hemodynamic energy that is created in the heart (battery) is transferred to the resistance. Putting numbers to this concept, let us assume the battery, $\mathbf{P_s}$, produces 100 mmHg and the resistance, **R**, is 1 mmHg sec/cc. Using Ohm's law, the current $\mathbf{I_s}$ is calculated to be 100 cc/sec. Thus the heart is producing 100 mmHg x 100 cc/sec of hemodynamic power (10,000 mmHg cc/sec) and all of this power $\mathbf{(I_s^2R)}$ is dissipated across the resistance, **R**. Thus it can be said that all of the power that leaves the battery is dissipated in the load resistance. The efficiency of the process is 100%, that is power dissipated in load divided by power output by the heart $\mathbf{(I_s^2R)/(P_sI_s) = 1.}$

The next model:

No battery, or pressure source, is perfect. That is, not all the energy created within the source actually leaves the source in the form of hemodynamic energy. The lost hemodynamic energy (ideal source energy – actual source energy) can be due to things like internal friction and the energy lost as heat. A simple way to represent this loss is to add a resistance element to the source, $\mathbf{R_s}$. That way anytime the source produces flow, some of the energy is lost in the form of heat. The dashed box represents the boundary of the source and that the source resistance cannot be seen external to the source as it is an integral part of the source.

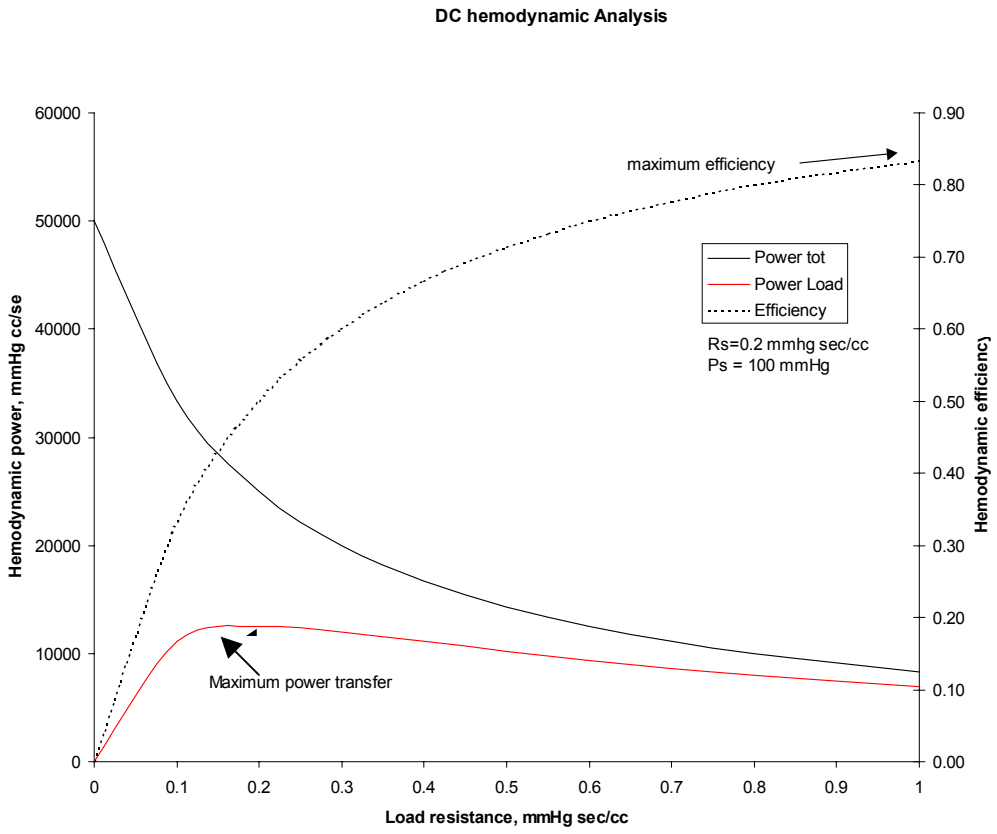


In this situation, not all the hemodynamic energy created by the ideal source $\mathbf{P_s}$ is delivered to the load **R.** Some of the energy is lost as heat due to $\mathbf{R_s}$. Putting numbers to this concept, let $\mathbf{P_s}$ = 100 mmHg**, R =** 1 mmHg sec/cc and $\mathbf{R_s}$ is 0.2 mmHg sec /cc. The current, $\mathbf{I_s}$ is $\mathbf{P_s}$ / (**R** + $\mathbf{R_s}$**)** which computes to 83 cc/sec. Now the total power delivered by the ideal source, $\mathbf{P_s}$, is $\mathbf{P_s}$ x $\mathbf{I_s}$ (8,333 mmHg cc/sec) and the hemodynamic power transferred to the vascular load, R, is $\mathbf{I_s}^2$ **R** (6,944 mmHg cc/sec). This results in an internal power loss in the source of

1389 mmHg cc/sec (8,333 – 6944 mmHg cc/sec). As a result the efficiency is 83% (power delivered to the load) / (power delivered by the ideal source).

Based on this model, one might surmise that a possible strategy of the cardiovascular system is to maximize efficiency during "rest" periods and maximize hemodynamic power during stressful periods (i.e. exercise or fight or flight situations).

Maximum efficiency is a condition where **R** >> $\mathbf{R_s}$ as most of the power will be delivered to the load **R**. In fact, if $\mathbf{R_s}$ = 0, then maximum efficiency is guaranteed**.** Physiologically, at rest, **R** will be at its greatest value and a high probability exists



that **R** >> $\mathbf{R_s}$. Assuming $\mathbf{R_s}$ remains constant, as **R** decreases and approaches $\mathbf{R_s}$ **,** a condition occurs which represents maximum power transfer. Note that the efficiency at maximum power transfer is only 50%.

Concepts in vascular-arterial coupling literature often allude to “impedance matching” (i.e. $\mathbf{R = R_s}$) based on this type of analysis. Of course the heart is not a

DC pressure source and that the peripheral vasculature in not just a resistance. In fact, the heart is periodic and the vasculature has elasticity as well as resistance and the two are connected through a one-way valve. We can use our elastance — resistance cardiac model and our n-element arterial model to analyze the maximum power/maximum efficiency debate. But before we do that, let's use some common sense in thinking about the possible governing control principle for CV control, if we were to design one from scratch.

Let's starts with the premise that the main function of the cardiovascular system is to provide adequate metabolic energy to all tissue. This means that we must have adequate oxygenated volumetric flow to all tissues. It then might follow that we may want to deliver the required volumetric flow to the tissues with the least amount of energy expenditure. This would make sense from a survival point of view. Why use more energy than necessary to deliver the required amount of oxygenated volumetric flow? In this context maximizing external work DOES NOT make sense. Even if maximum power were required, we'd like to transfer the volume from the ventricle to the arterial load as efficiently as is possible.
So what approaches to minimize energy expenditure are available to us? Let's return to the PV loop to look at some options and the resulting ramifications. If we want to reduce the amount of energy required to move the stroke volume into the arterial load, we can simply reduce the arterial pressure from 100 mmHg to 10 mmHg as shown in Figure 9-10! Thus we only need 1/10th the energy expended to move the same amount of stroke volume. Obviously a good deal right? Of course, we understand that in the earth's gravitational field we wouldn't survive long with 10 mmHg arterial pressure. In fact, material transfer across the capillary membranes would be curtailed! This example shows that minimizing energy expediture to move volume cannot be the only consideration. We must

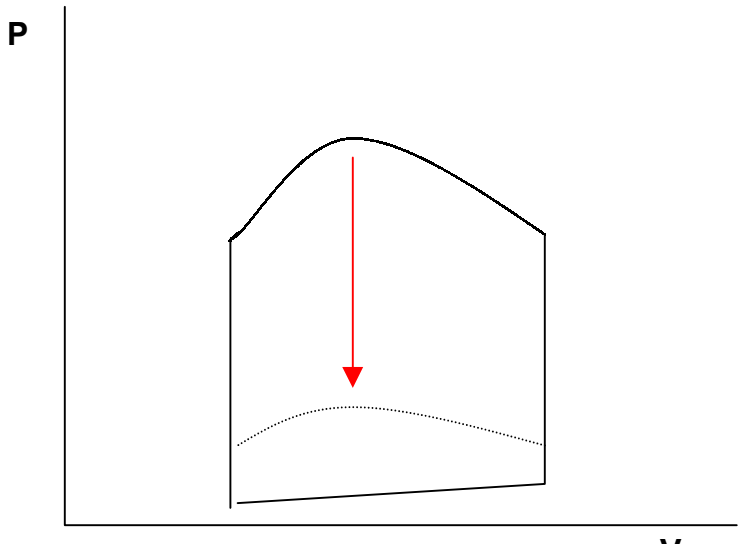


Figure 9-10 Significant Reduction in EW by Reducing Arterial Pressure

minimize energy expenditure with a careful eye towards maintaining an adequate arterial pressure necessary for survival.

Ok, we'll have to accept that we need a certain arterial pressure for survival. The other option we have is to reduce stroke volume. As it turns out, at rest, we extract only about 25 % of the oxygen from the hemoglobin of the red blood cell as it traverses our system circulation. Thus it is conceivable that we could reduce our volumetric flow to 25% percent of its normal value and still deliver adequate oxygen to tissue. Examine the equation below:

$$Q_{metabolic} = K\dot{m}\Delta O_2$$

Here, $Q_{metabolic}$, represents the rate of metabolic energy required by the body at any one time. For example, at rest, $Q_{metabolic}$, approaches our basal metabolic rate and then as we exercise $Q_{metabolic}$ increases to meet the larger metabolic demand. The constant K, represents the energy equivalent of oxygen, about 4.2 Cal/LO_2. The variable, $\dot{m}$, represents the total mass flow rate of blood to the systemic circulation, the cardiac output in units of mass/time. The variable ΔO_2, represents the difference in oxygen from the arterial to the venous system. Since we remove only about 25% of the available oxygen from the blood at rest,

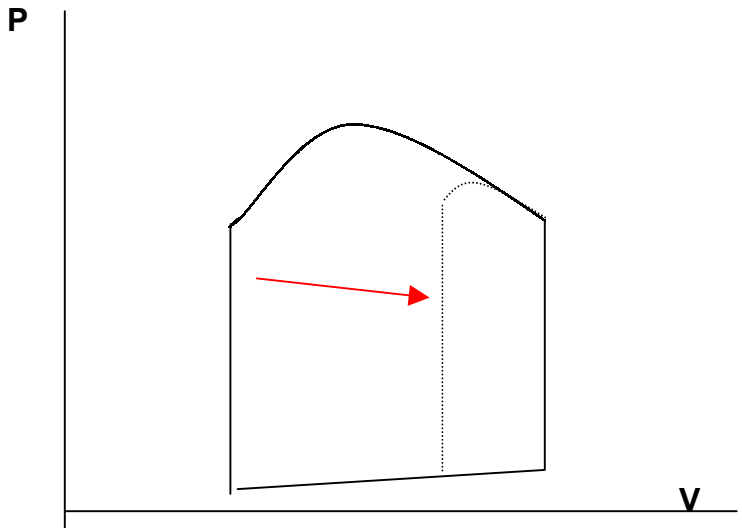


Figure 9-11 Significant Reduction in Energy Expenditure by reducing SV

we can decrease stroke volume (Figure 9-11) and then remove closer to 100% of the oxygen.

But removing closer to 100% oxygen removal means that if we need a short increase in energy in a very short period of time, we'd have to increase heart rate. This would not be as advantageous for survival as having extra oxygen available all the time. Through increases in oxygen extraction and heart rate we can raise the metabolic energy delivery 24 fold for a short time!

It seems that a viable concept for cardiovascular control is to deliver adequate oxygenated volumetric flow, with minimal energy requirements, all the while maintaining critical survival reserves such as arterial pressure, heart rate and ΔO_2. An interesting test of this concept is to observe hibernating animals. When hibernating, survival reserves appear to be sacrificed for the sake of minimizing energy requirements. Armed with this common sense approach we can test the theory using our somewhat limited cardiac and vascular models.

Summary:
While the final verdict is still out on what the governing principles for cardiovascular coupling and control, we've investigated the current thinking and

thought about from our own perspective. In the final analysis, perhaps the governing principle is to deliver an adequate oxygenated volumetric flow, with minimum effort, while maintaining survival reserves. Minimal effort would depend on the source resistance, characteristic impedance and wave reflection properties. These are critical to the momentary and intermittent transfer of volume from the heart to the arterial load. For example, the all the stroke volume must be transferred during the ejection phase. Immediately upon valve opening, the volume is transferred to the characteristic impedance of the proximal aorta and the relation between pressure and flow is dominated by the characteristic impedance. The pressure and flow waves travel forward, away from the heart. As the pressure and flow waves begin arriving back at the heart, the relationship between pressure and flow is now more complex and may be closer to the input impedance and it can be dominated by wave reflections. Thus expending minimal effort to transfer the volume from the ventricle to the arterial system during the ejection phase is a rather complex process, all the while trying to optimize the survival reserves such as arterial pressure, heart rate and ΔO_2.

There is another approach related to the above discussion. It is based upon the 2nd law of Thermodynamics and I will place this paper on the DOC SHARING PORTION of the class, read it if you're interested in it, but you are not responsible for the information contained within it.