Modeling hemorrhage control

- Overview of cardiovascular control system
- Definiton of control problem
- Model application

Introduction

- It was noted in a recent issue of the New England Journal of Medicine that "The art of fluid administration and hemodynamic support is one of the most challenging aspects of treating critically ill patients. Considering that every year in the United States over 11 million units of red cells are transfused in more than 3 million patients, there is a surprising paucity of data to guide decisions on transfusion."
- The article notes that there exists a transfusion algorithm developed by the American College of Physicians based on a consensus of experts, and not on data. It also notes that transfusion regimens in critically ill patients varies widely, with "an estimated 66 percent of transfusions are administered inappropriately."
- Thus a fuller understanding of the control interactions of the various control systems of the cardiovascular and respiratory systems as it relates to blood volume control is essential.

General CVR system physiology I

- The purpose of the cardiovascular system is to transport CO_2, and O_2, nutrients, and hormones via blood flow to various tissues of the body.
- The purpose of the respiratory system is to exchange CO_2 produced by metabolism in the tissues for O_2 which is necessary for metabolism.
- These two systems are linked in a number of ways and influence each other.
- There are control systems which sense changes in these systems and respond in ways which stabilize the systems.

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  - The systemic circuit transports blood from the left heart to the tissues and back to the right heart. CO_2 is collected as an unwanted metabolic byproduct and O_2 is delivered to the tissues for metabolism. Other nutrients and wastes are also transported.

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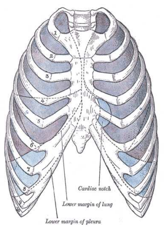
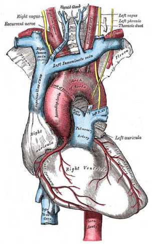
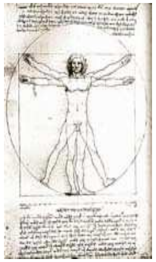
  - Each circuit is subdivided into arterial and venous volume components with the lungs or tissues acting as resistances.
- The cardiovascular system can respond to a number of perturbations in the system via control mechanisms which monitor key elements.

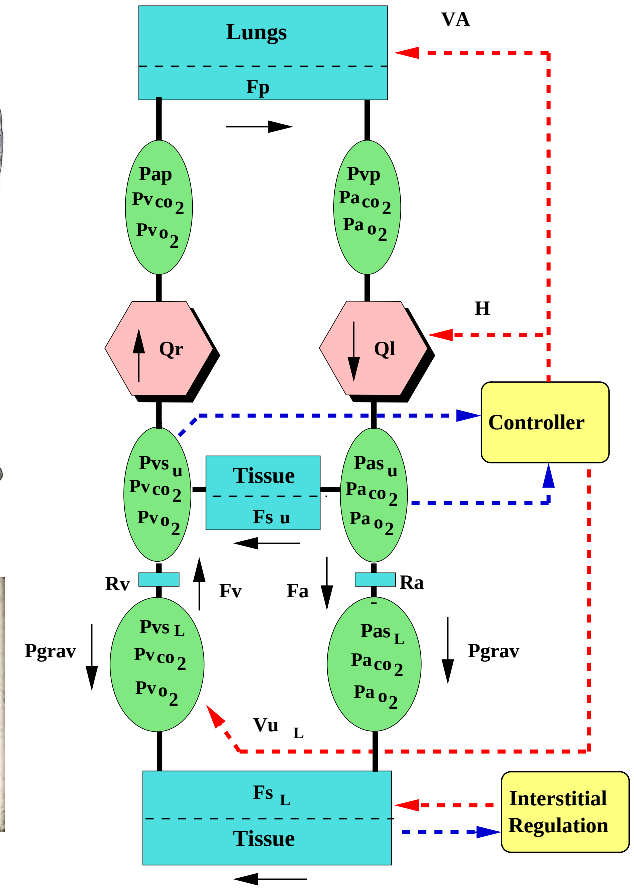
CVR system diagram

- 4 cardiovascular compartments
  - Pulmonary arterial and venous volumes
  - Upper and lower compartment systemic arterial and venous volumes
- 2 respiratory compartments
  - Lung compartment
  - Tissue compartment
  - These compartments act as resistances for blood flow



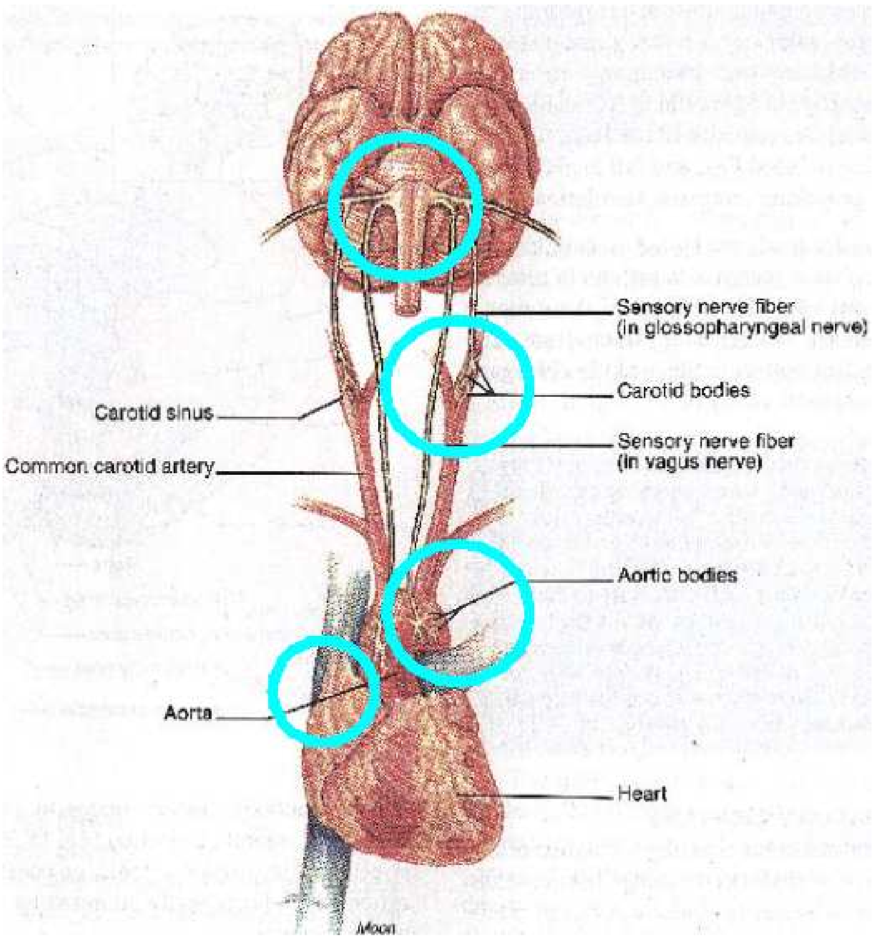






CVR sensory systems

- Sensors for $P_{\mathrm{a,CO_2}}$ in brain
- Control processing center in medulla
- Sensors for $P_{\mathrm{a,CO_2}}$ and $P_{\mathrm{a,O_2}}$ in carotid bodies
- Sensors for P_{as} in aortic and carotid bodies
- Sensors for P_{vs} in veno-atrial region



Control system quantities

Control action

- Heart frequency
- Heart muscle contractility
- Venous tone: capacitance and compliance
- Arterial resistance
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Key controlled quantities

- blood pressure
- cardiac output
- oxygen, carbon-dioxide, and pH

Hypovolemia

- Hypovolemia refers to reduced blood volume which may be due to blood loss, fluid loss due to dialysis and other reasons. Hypovolemia affects blood pressure and other CVS variables.
- When 20 - 40 % of blood volume is lost due to hemorrhage, P_{as} begins to fall, resulting in vasoconstriction and increased heart rate. Shock can begin to set in. When greater than 40% of blood volume is lost, P_{as} may drop severely and organ failure begin.
- Dialysis treatment can cause plasma water depletion and this can result in blood volume reduction of about 15%. This can lead to a sudden, significant decrease in arterial pressure. This is a serious complication of hemodialysis, as the drop in blood pressure can be so severe that it requires quick termination of the treatment.

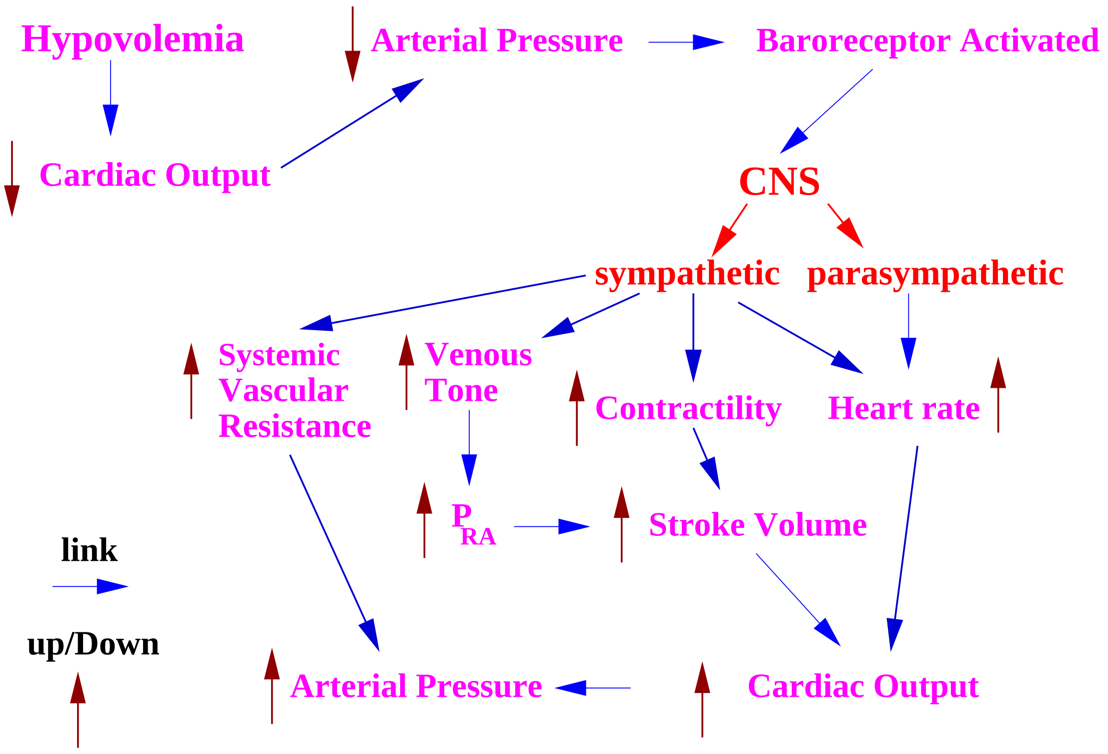
Hemorrhagic Shock

- Hemorrhagic shock is defined as decreased blood and oxygen perfusion of vital organs resulting from blood volume loss.
- Loss of blood sets up the following chain of events:
  1. Reduced volume causes reduction in venous filling pressure;
  2. Reduced filling pressure results in reduced end-diastolic-volume and with Frank-Starling mechanism reduced stroke volume, cardiac output, and blood pressure;
  3. When loss of blood is severe or other conditions intervene the above chain of events can repeat, compensatory mechanisms can be counter productive, resulting in deterioration in system function and perhaps irreversible shock and death.

Compensatory mechanisms II

- Baroreflex firing is reduced due to reduced arterial pressure. This leads to inhibition of the cardioinhibitory area of the vasomotor center via parasympathetic output, as well as increased sympathetic activity from the vasomotor center. This results in increased vasoconstriction, and increased heart rate and contractility which raises cardiac output. Venoconstriction is found in splanchnic and skin tissue thus shifting blood to critical areas.
- Hormonal control also acts to control cardiovascular function including heart rate and vasoconstriction. There are a number of feedback loops involving hormonal mechanisms including circulating catecholamines, the renin-angiotensin system, vasopressin, atrial natriuretic peptide, among others.
- Kidney action.

Baroreflex Compensatory mechanisms



- Baroreflex firing falls due to reduced arterial pressure leading to increased vasoconstriction, increased H, and contractility which raises cardiac output and arterial pressure. Venoconstriction in splanchnic and skin tissue shifts blood to critical areas.

Acute Hemorrhage Treatment Issues

- What fluid should be used in acute hemorrhage treatment? How administered?
  - isotonic vs hypertonic fluids
  - whole blood vs packed blood
  - crystaloid vs non-crystaloid fluids
  - hemoglobin or perflurocarbon-based solutions
- What treatment is best for individuals who have medical conditions?
  - patients that are at risk for myocardial infarction
  - patients with kidney disease
  - patients with diabetes
  - older individuals

Simulations I

- We compare two kinds of infusion during hemorrhage and consider the response of H to reduced blood volume. The heart rate control will act to restore P_{as} by increasing H up to the maximum sustainable rate $H_{e,\max}$ described above. Once $H_{e,\max}$ is reached the system will stabilize around a reduced steady state P_{as} consistent with this fixed control $H_{e,\max}$.

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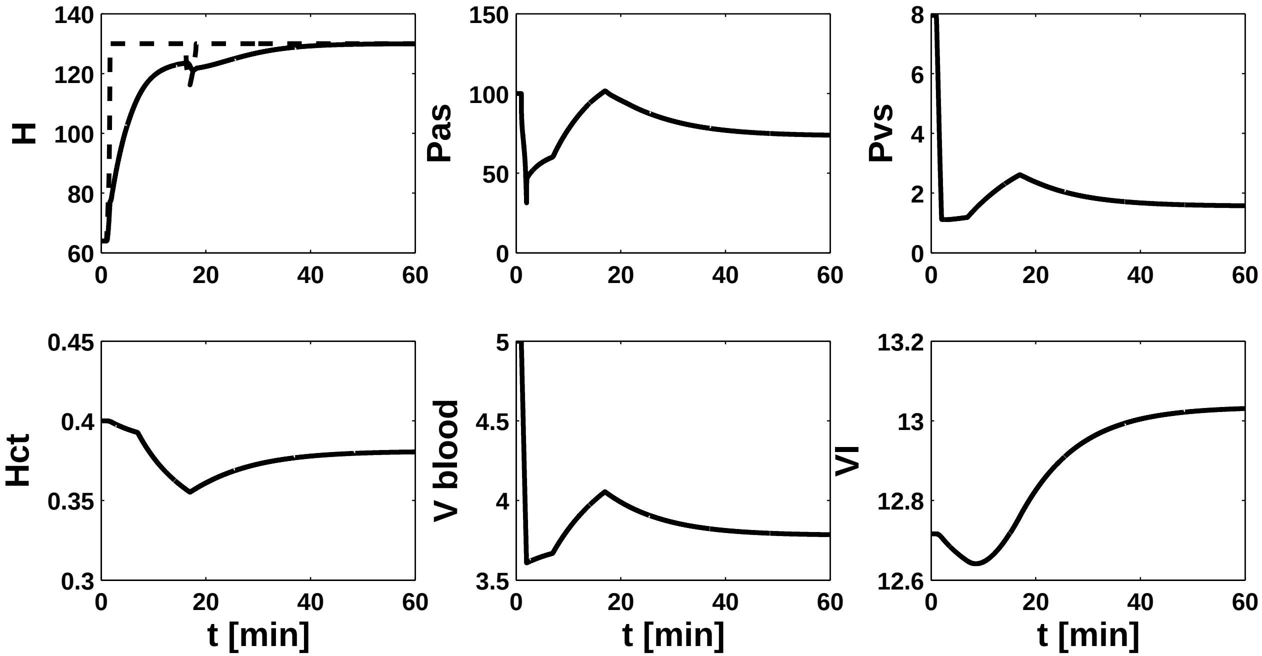
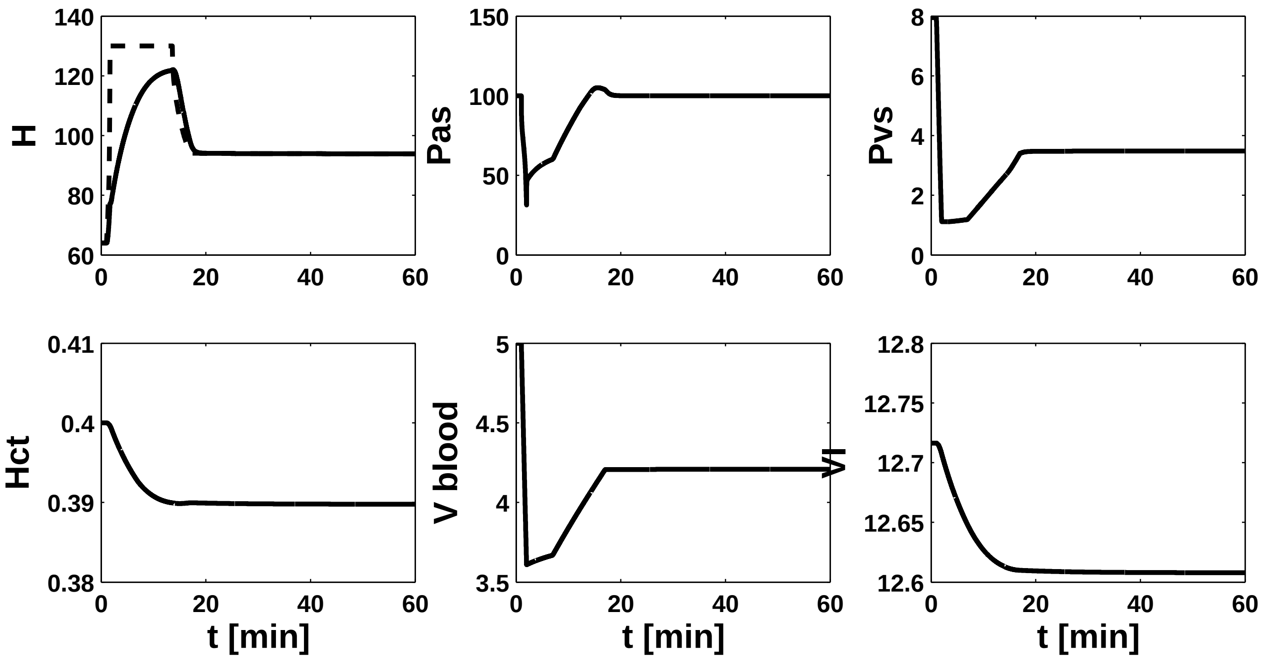
- We consider two different infusions: i) a saline solution and ii) blood or a blood substitute.

Saline infusin simulations II



- Saline infusion does not return the system to the original steady states due to the lack of plasm protein replacement, resulting in osmotic pressure forcing infused fluid into the interstitium.
- There is only a short time interval near the end of the transfusion where H decreases towards normal. As fluid continues to leave the blood vessel compartment, H increases again.

Whole blood simulations III



- Whole blood infused in the blood vessel compartment is able to improve the cardiovascular performance due to the balancing effects on osmotic pressure.
- The saline solution improves the performance of the cardiovascular system for a short time but osmotic pressure effects complicates the stabilization of CVS function.

Our group and collaborators

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