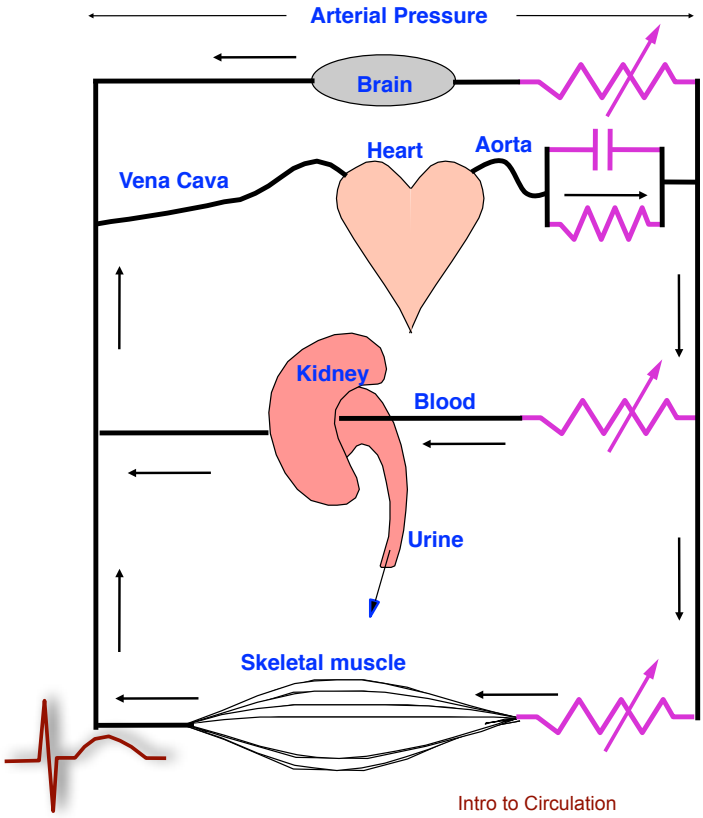
Overview of Circulation

Cardiovascular System Overview

- The plumbing: circulation systems in the body
- The wiring: cardiac electrophysiology
- The pump: the heart as a pump
- The flow: blood and hemodynamics
- The control: brain/hormonal/local, feedback

Cardiovascular System Regulation



- Goal: adequate flow
- Process: pump and flow
- Regulation: parallel circuit with valves
- Sensors?
- Feedback?

Role of the Circulation System

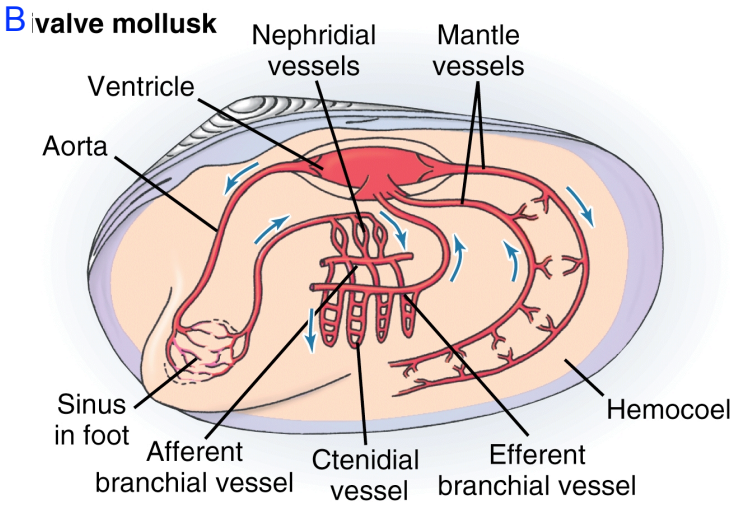
- Transport of Nutrients: O_2, H_2O, glucose, ions, heat, etc.
- Removal of wastes and byproducts: CO_2, pH, urea, nitrates
- Immune system: homeostasis, response to invasion
- Endocrine system: hormone delivery, control and regulation

Function of Circulation System

- Components
  - Propulsion organ (heart)
  - Arterial system
  - Capillaries
  - Venous system
- Movement of blood (roles vary across species)
  - Heart
  - Elastic recoil
  - Venous squeezing (movement and muscles)
  - Paristaltic contractions (smooth muscle)
  - Valves or septa control flow (present in all CV systems)

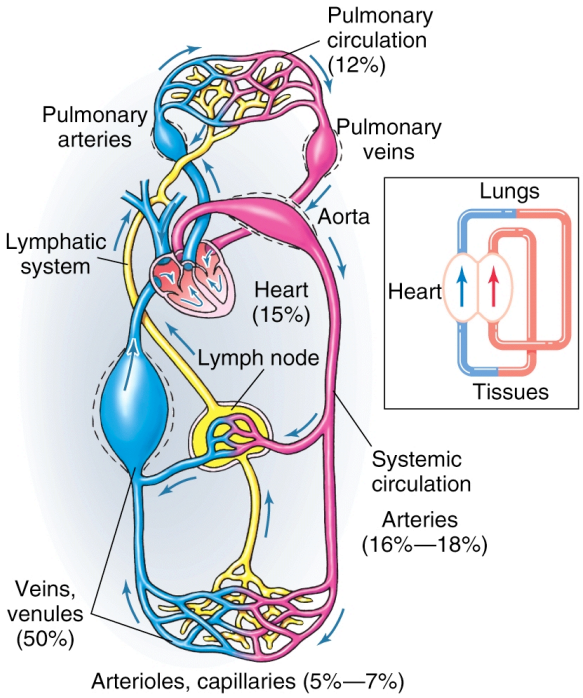
Open Systems

- Blood empties into body space
- Bathes tissues directly, blood in small chambers
- Low pressure system (4-10 mm Hg)
- Typically limited regulation and low oxygen transport (with exceptions)
- Built in Lymph system
- Insects bypass lungs and transport oxygen directly so open circulation does not carry oxygen



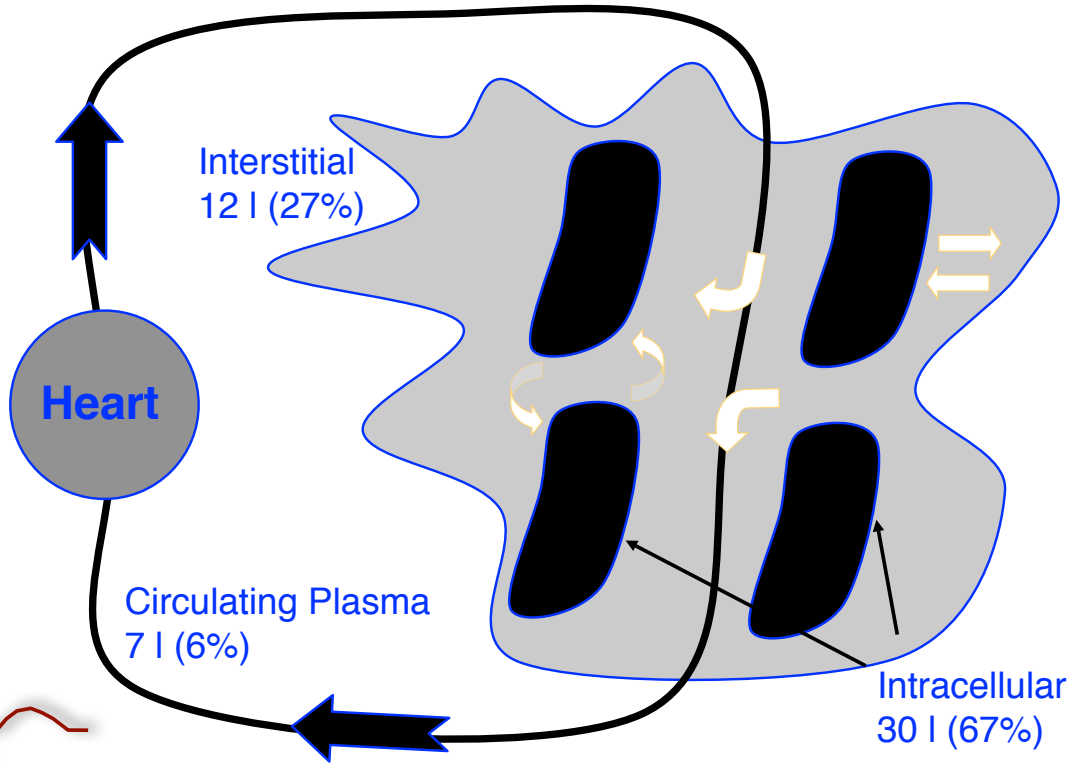
Closed Systems

- Blood stays in vessels, higher pressure than open system
- Separated systemic and pulmonary systems
- Central, peripheral, and microcirculation
- Capillaries provide transport
- Lymph system
- Ultrafiltration occurs (kidneys)
- Lungs have low pressure and hence no filtration
- Many regulation points so wide range of transport rates



- List the advantages and disadvantages of closed and open circulatory systems.
- What situations would favor one system over the other?

Distribution of Fluid in the Body



Roles of Blood

- Capture, transport, and release nutrients e.g., O_2, glucose, minerals
- Store and transmit heat
- Buffer acid/base balance
- Transport water in and out of regions
- Provide substrate and components of the immune system (lymphocytes)

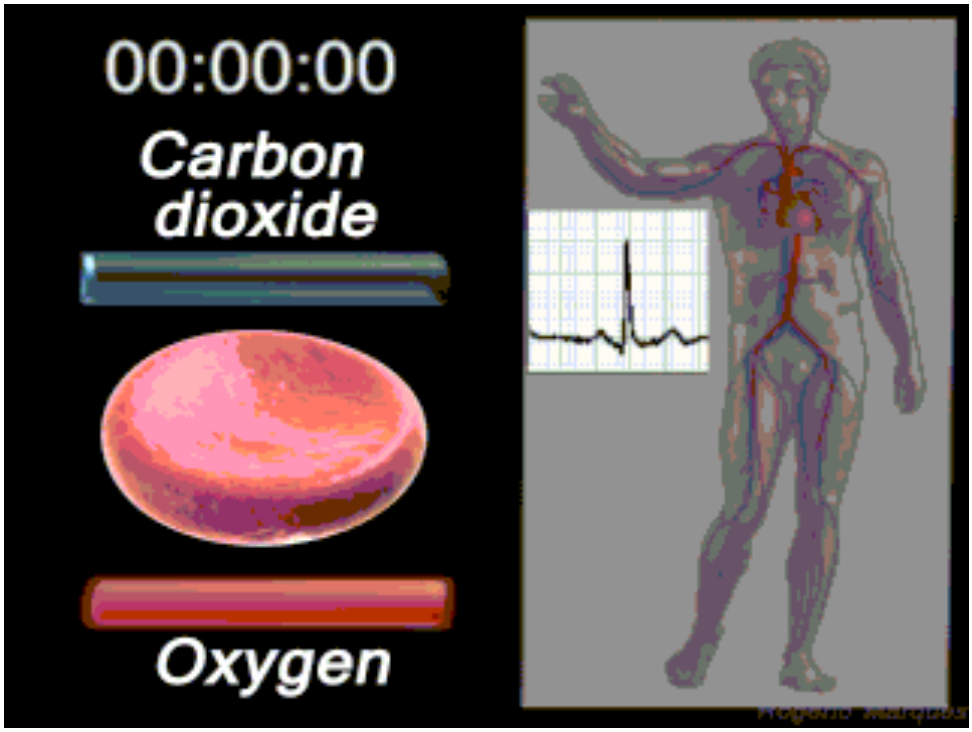
Functional characteristics of Blood

- Composition: RBC, WBC, platelets (40% of volume), plasma proteins, transported substances.
- Production of blood cells (regulation and control)
- Response to injury: coagulation, clotting, self-preserving (regulation and control)
- Hemodynamics (regulation and control)

Note: all these system have regulation and control components so as to maintain homeostasis.

Red Blood Cells (Erythrocytes)

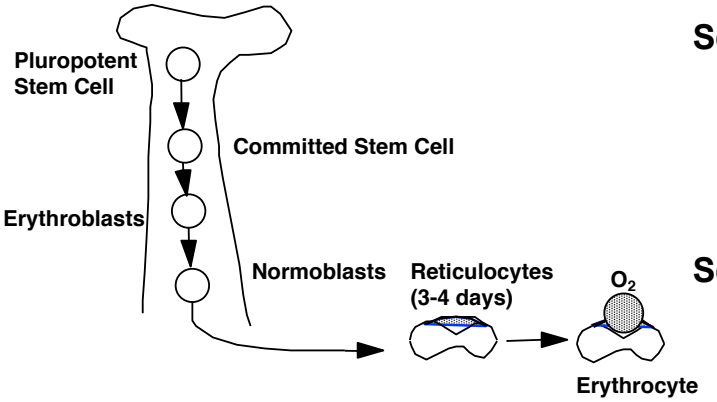
- Function
  - carry oxygen from the lungs to the tissue (increases capacity by 40-50 times!)
  - some buffering of acid/base
- Physical Details
  - 8 μm diameter, 2 μm thick disks
  - deformable
- Amount
  - 5 x 10^6 cell/ml
  - hematocrit (% by volume) = 40-45%



How to Characterize a Physiologic Mechanism (a template)

- Goal: what is the overall purpose of the system (e.g., to control blood pressure, to regulate RBC production)
- Process Steps: the set of steps that produce something (e.g., RBC production)
- Points of Regulation: where can we alter the process?
- Sensor types and locations: the measurement system(s)
- Feedback mechanisms: how do sensors communicate with points of regulation to alter the process?

Production and (possible) Regulation of Erythrocytes

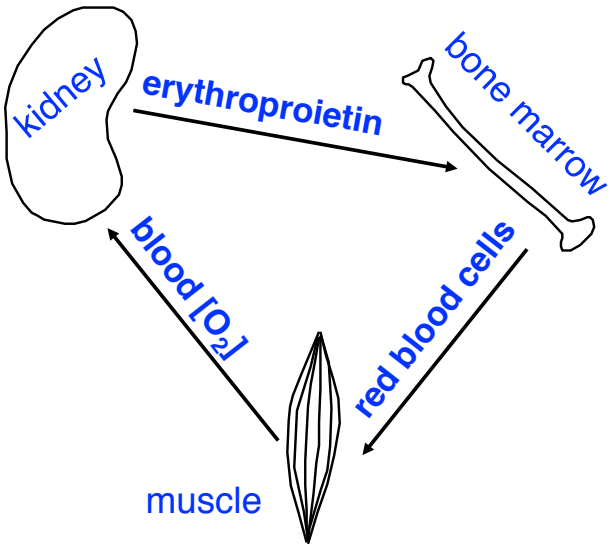


Sensor types:
- RBC concentration?
- stem cell concentration?
- oxygen concentration (hypoxia)?

Sensor locations:
- bone marrow?
- brain?
- kidney?
- liver?
- heart?

Possible regulation points:
- stem cell production?
- cell differentiation and division?
- maturation of RBCs?
- RBC lifetime?

Actual Regulation of Erythrocyte Production

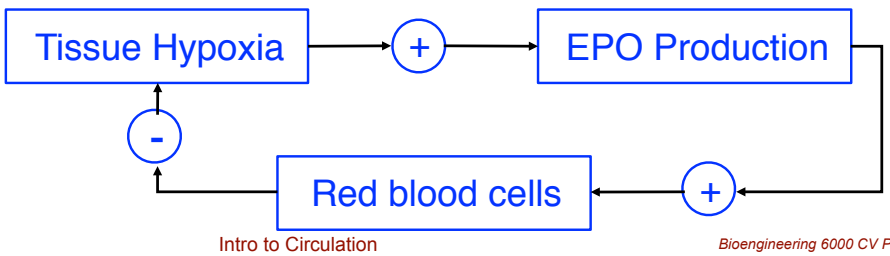


Regulation point:
- maturation of RBCs
- regulated by EPO concentration

Sensor type:
- blood [O_2] levels

Sensor location:
- kidneys

Feedback:
- kidneys sense drop in [O_2], produce EPO, stimulate RBC maturation, increase [O_2].



- If you were to artificially increase the amount of RBC in your body (hematocrit), how would you do it?
- Why would you want more RBC?

Response to Altitude

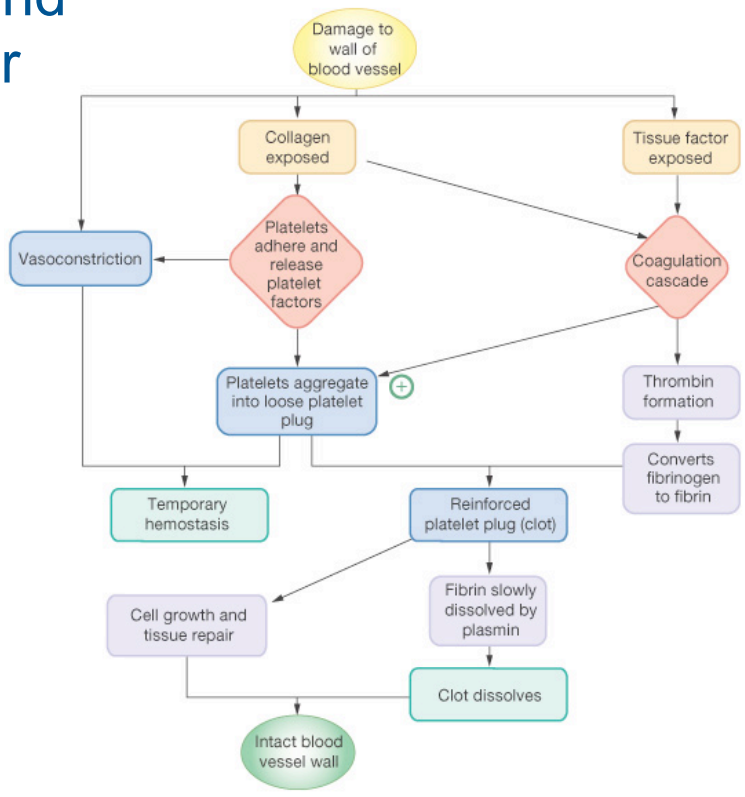
- Drop in arterial O_2 leads to increase in ventilation
  - first 65% above normal
  - later, 300-400% above normal as negative feedback reduced
- Drop in O_2 saturation leads initially to rise in heart rate to bring more blood to the tissues
- To increase hematocrit, blood volume decreases (dehydration) initially and only slowly recovers (2 months). Too high hematocrit increase blood viscosity and reduced cardiac output.
- Concentration of 2,3 diphosphoglycerate (DPG) increase and shifts O_2 dissociation curve.
- Increased ventilation causes loss of CO_2 and alkalosis. Leads to shift in acid/base balance.
- Increase in erythrocyte concentration (sustained): 4-5 fold production in first few days of exposure. Not complete even after a year at (high) altitude.

Homeostasis of Blood

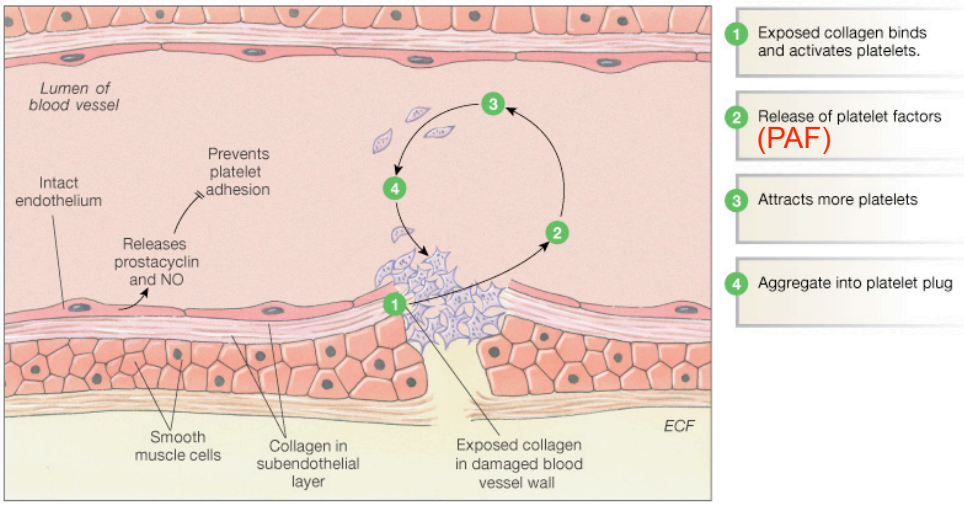
- Response to damage
  - Block off damaged area, reduce pressure (vasoconstriction)
  - Make a patch (platelet aggregation and coagulation)
  - Restore pressure (vasodilation)
  - Restore tissue (cell division and growth)
  - Remove patch (clot retraction/dissolving)

Homeostasis and Tissue Repair

- Vascular Spasm: lasts minutes to hours, CNS mediated
- Platelet plug: within seconds, bind to injured tissue, form plug adequate for small incisions.
- Coagulation: (clotting) complex series of reactions that result in the formation of a fibrinous plug that stops blood loss.
- Clot retraction: platelets interact with fibrin to pull clot together and squeeze out plasma; role unclear but perhaps to promote vessel closure.
- Tissue repair, clot removal by plasmin

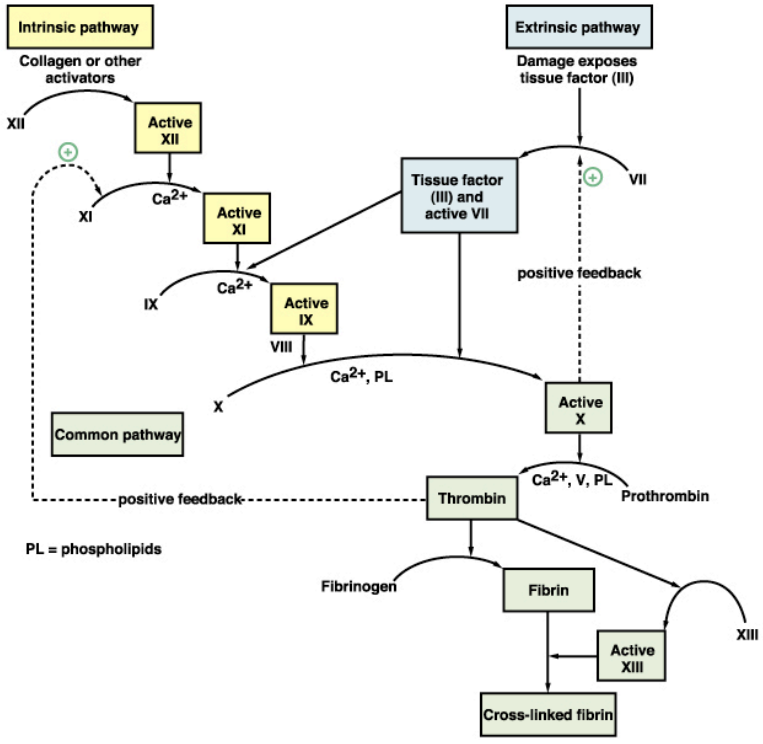


Platelet Aggregation



- Example of positive feedback: what stops it?
  - Selective adhesion of platelets to vessels

Coagulation



Coagulation

- Key steps:
  - initiation of coagulation cascade
  - conversion of soluble fibrinogin into fibrin monomers by thrombin
  - conversion of fibrin monomers into strands and linking into a mesh by activated stabilizing factor
  - clot includes plasmin, which cause eventual dissolving
- Calcium is key ingredient
- Two initiation pathways:
  - extrinsic (tissue trauma)
  - intrinsic (blood trauma)

Regulation of Coagulation

- Physical/mechanical
  - New endothelial cells coat the vessels, reduce stimulus
- Remove pro-coagulants
  - Restored blood flow washes pro-coagulants away (perhaps most important factor)
  - Pro-coagulant substances removed by the liver, spleen, and bone marrow
- Inactivate Thrombin
  - Heparin: secreted by mast cells in lung and liver
  - Thrombin (pro-coagulant) absorbed by fibrin threads
  - Blood protein antithrombin III binds and eventually inactivates thrombin
- Calcium
  - Citrate: removes calcium from the blood for blood doning. (tingling lips during apheresis)

Removal of Clots (thrombus, embolus)

- Goal: produce plasmin, which dissolves clot (digests fibrin and other clotting factors)
- Process Steps: complex, see Berne and Levy or Silverthorn
- Points of regulation:
  - urokinase: released from kidneys, activates plasminogen
  - streptokinase and tissue plasminogen activator (TPA) exogenous drugs that activate plasminogen
- Feedback:
  - complex and multilayered
  - e.g., thrombin production eventually activates plasminogen

- Why is it a good idea to apply compression to a cut?