Computational Modeling of the Cardiovascular System

Overview

Introduction to Anatomy

CVRTI

Frank B. Sachse, University of Utah

Overview

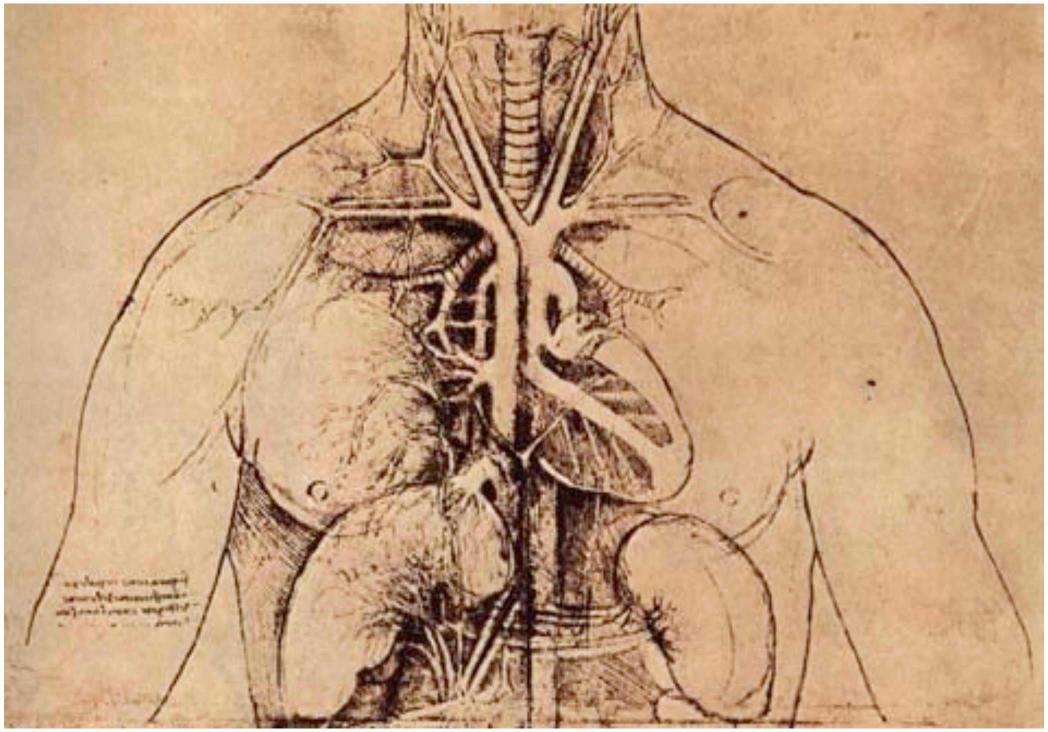
- Overview
  - History
  - Rationale
  - Topics
  - Literature

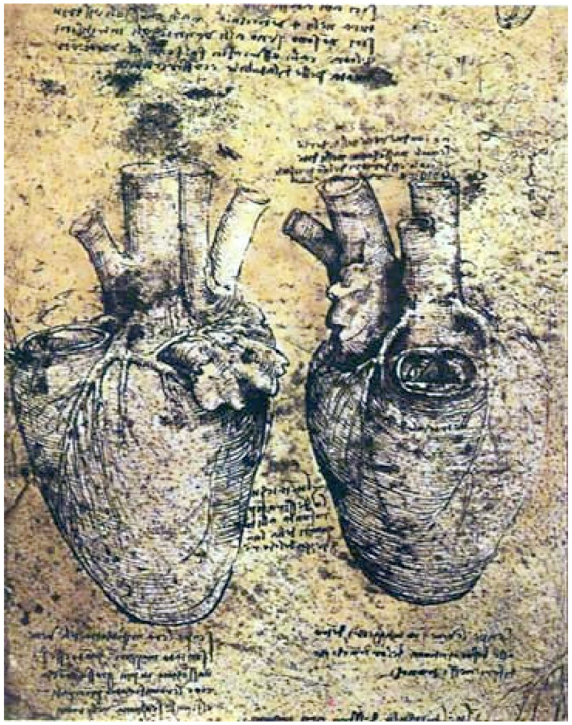
Group work & pause

- Introduction to Anatomy
  - Macroscopic
  - Cellular
  - Molecular
  - Modeling

Group work

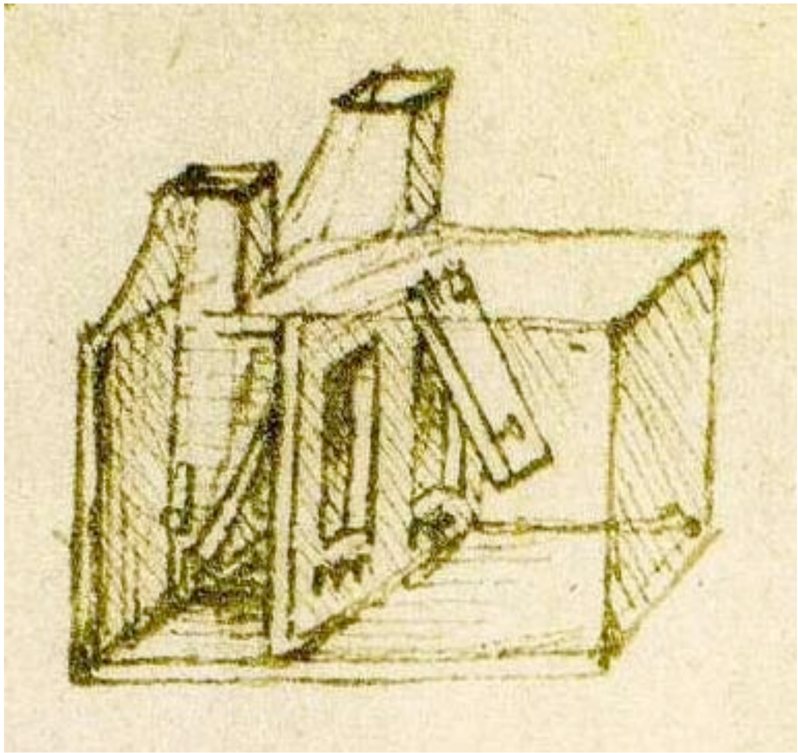
Anatomical Models of the Heart





Leonardo da Vinci (1452-1519), Anatomical Handbooks

Functional Cardiac Model



Leonardo da Vinci, Codex Arundel

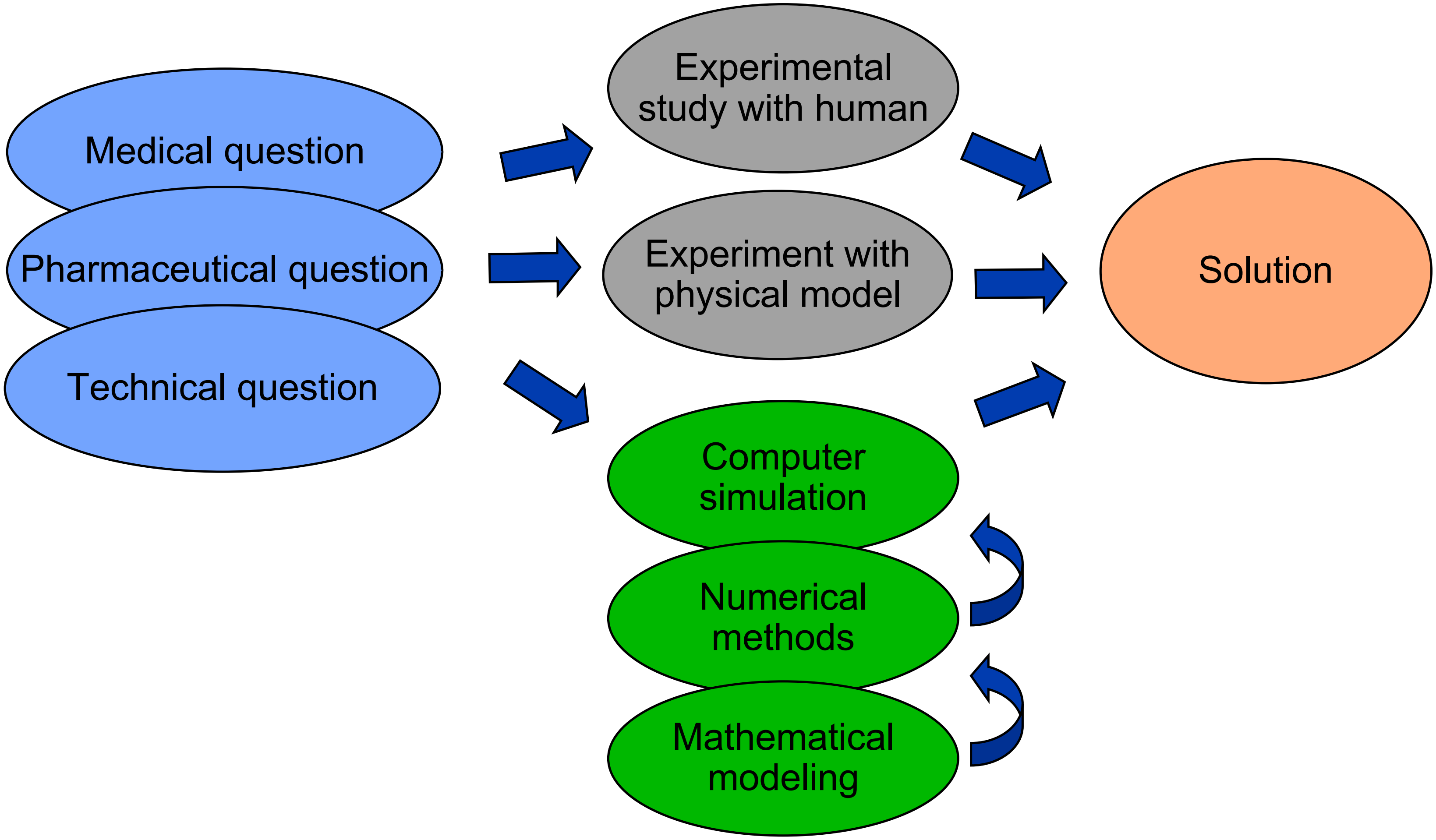
Classification of Lecture

Computational Biology

- Genome
- Proteome
- Cell
- Tissue
- Organ
- Body

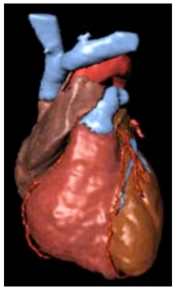
Lecture covers
- Anatomy
- Electrophysiology
- Mechanics

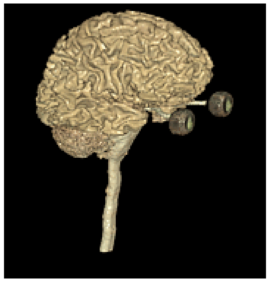
Rationale



CVRTI

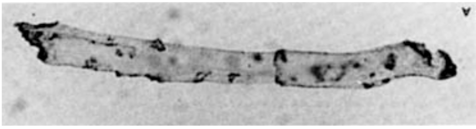
Introduction to Anatomy



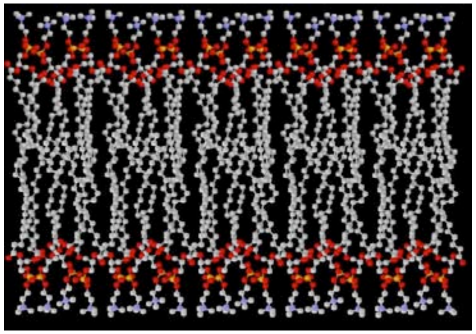


Macroscopic

Cellular



Molecular
- Membrane
- Ion channels
- Sarcomere proteins



Modeling
- Analytical
- Imaging and image processing based

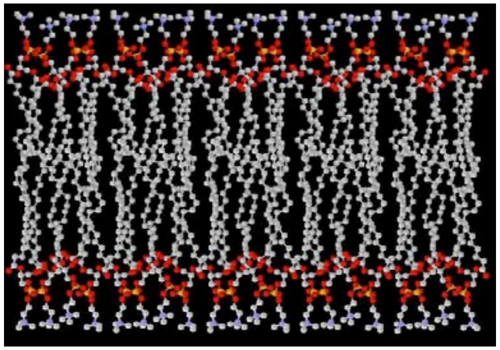
CVRTI

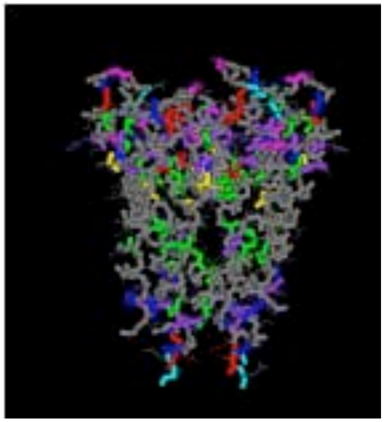
Electrophysiological Modeling of Membranes and Ion Channels

Membrane models
- Experimental studies
- Molecular structure
- Equivalent circuits

Ion channel models
- Experimental studies
- Classification
- Molecular structure
- Hodgkin-type models
- Markovian models

Solving of ordinary differential equations





$$\frac{\partial V_m}{\partial t} = -\frac{1}{C_m}\left(I_m + I_{stim}\right)$$

CVRTI

Electrophysiological Modeling of Cells

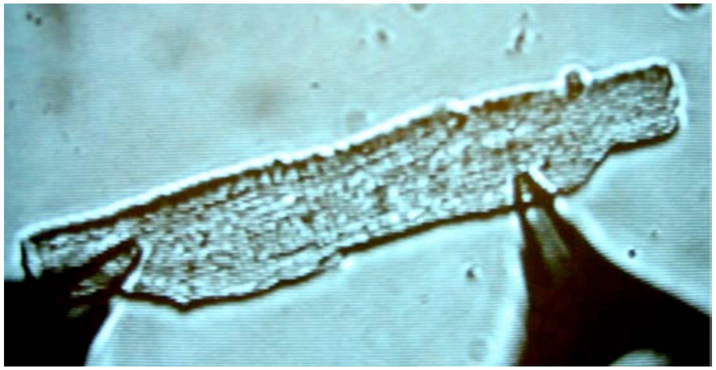
Experimental studies

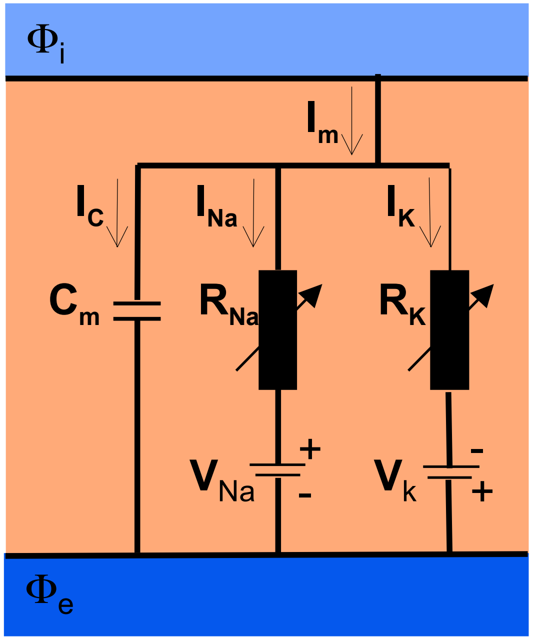
Modeling of membranes

Hodgkin-Huxley membrane model

Modeling of cardiac myocytes

Numerical Methods
- Euler
- Runge-Kutta





CVRTI

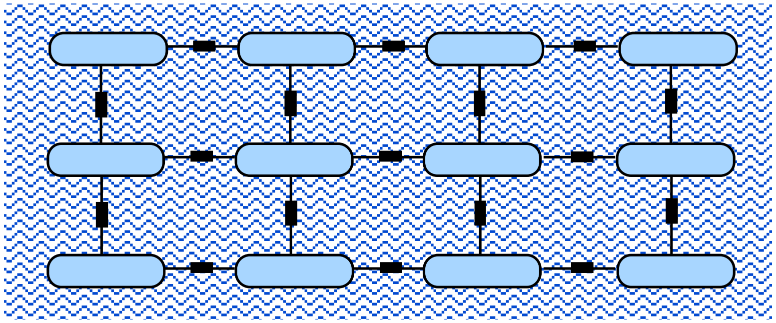
Modeling of Electrical Conduction in Cardiac Tissue

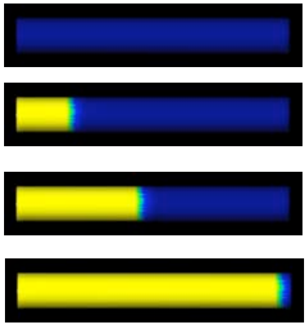
Experimental studies

Gap Junctions

Modeling Approaches
- Cellular automata
- Reaction diffusion equations

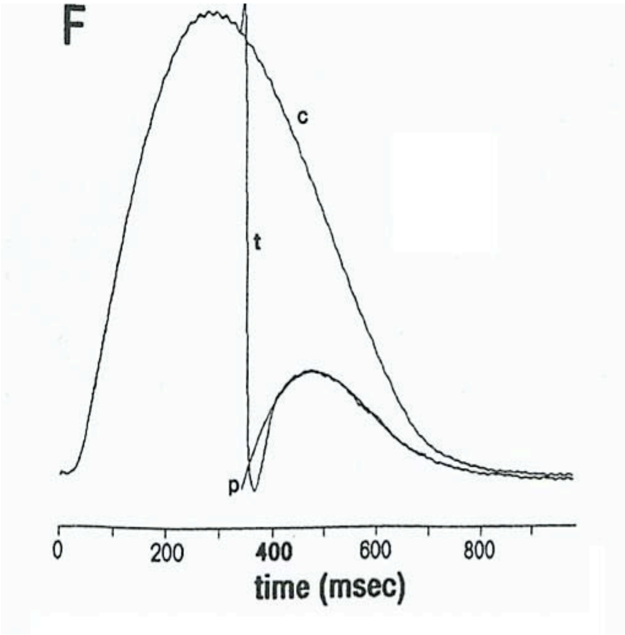
Numerical Methods
- Finite element methods
- Finite difference methods



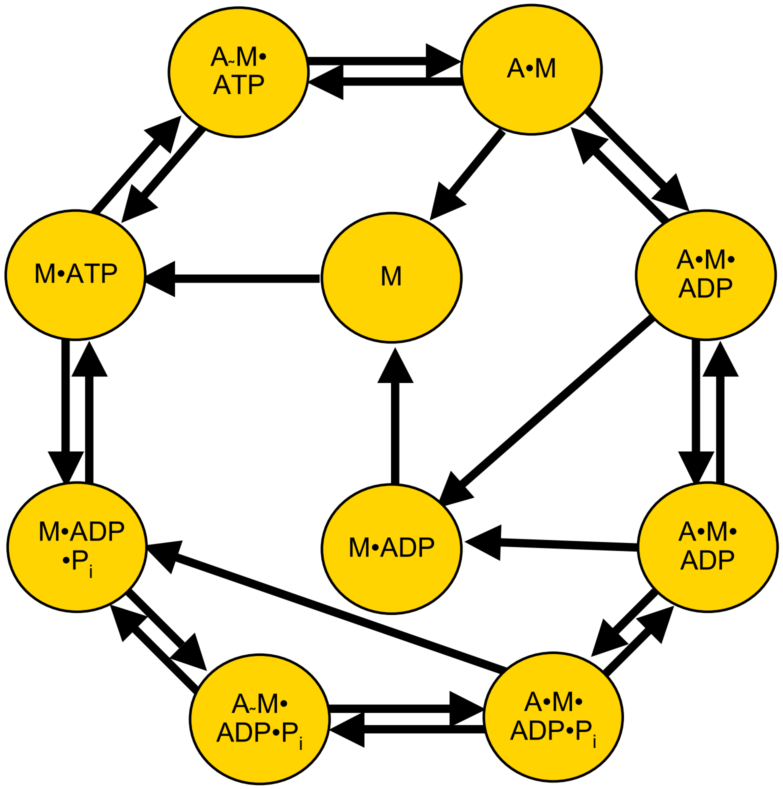


Modeling of Force in Myocytes

Experimental studies approaches



Modeling and numerical



Mechanical Modeling of Tissue

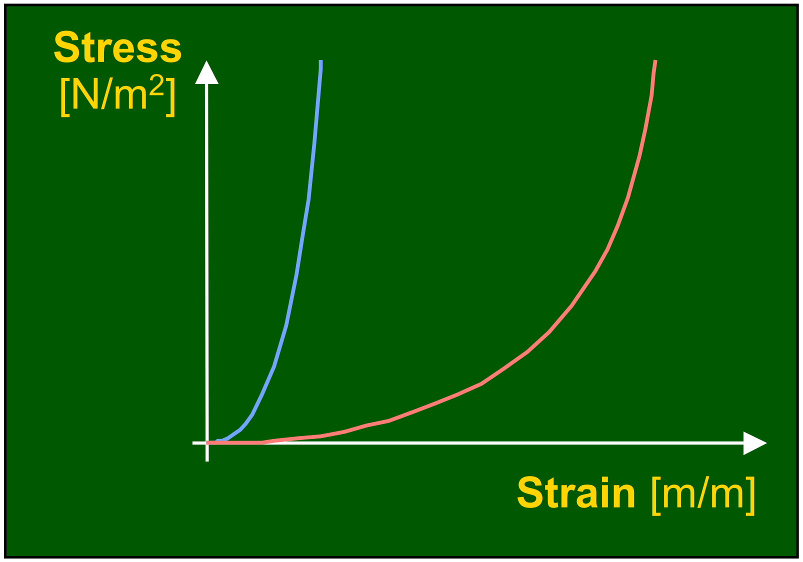
Experimental studies

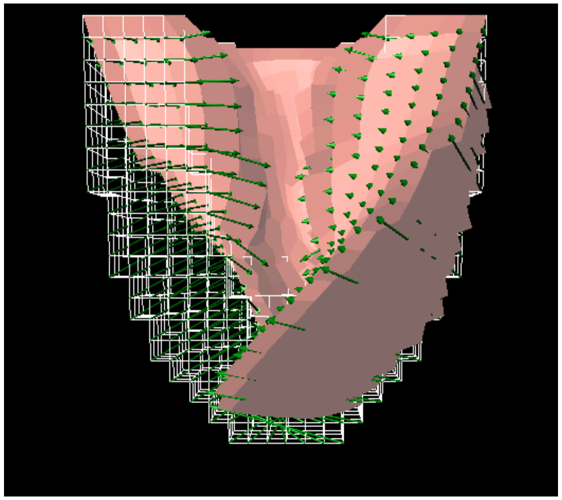
Definitions and physical laws

Strain and stress tensors

Constitutive relationships

Numerical Methods
- Finite element methods
- Finite difference methods



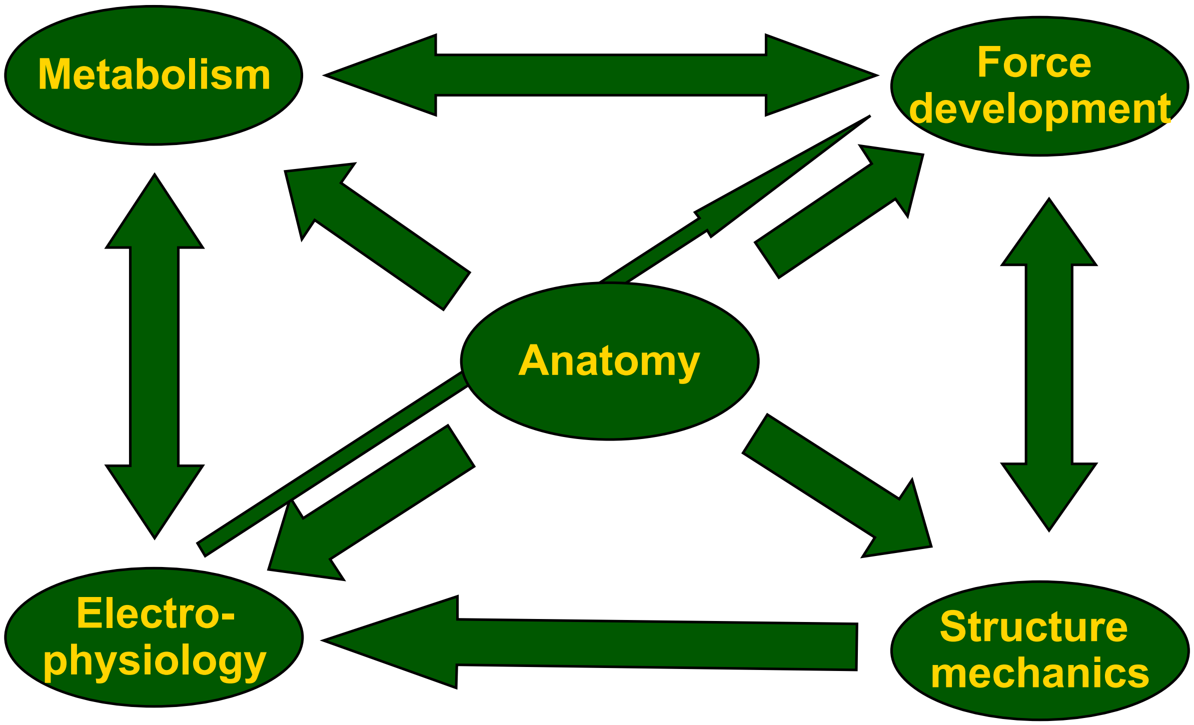


Integration and Coupling of Models

Experimental studies

Modules

Interfaces



Material

Literature

Hille	**Ion Channels of Excitable Membranes** Sinauer Associates
Lodish et al.	**Cell Biology** WH Freemann and Company
Sachse	**Computational Cardiology** LNCS 2966, Springer Press
Malmivuo, Plonsey	**Bioelectromagnetism** Oxford University Press http://butler.cc.tut.fi/~malmivuo/bem/bembook/
Bathe	**Finite Element Procedures** Prentice Hall
Buchanan	**Schaum´s outlines: Finite Element Analysis**

Slides

http://www.cvrti.utah.edu/~fs/lessons/rgi

Grading

50% **Homework**

- 3 assignments
- Work on your project individually
- Ask, if you should get stuck is unclear via email to fs@cvrti.utah.edu
- Send reports with results via email before 1. May 2006 to fs@cvrti.utah.edu
  Include figures and data tables.
  The material should be sufficient to reconstruct results.

50% **Written Exam**

- Date: 23.5.2007

Group Work

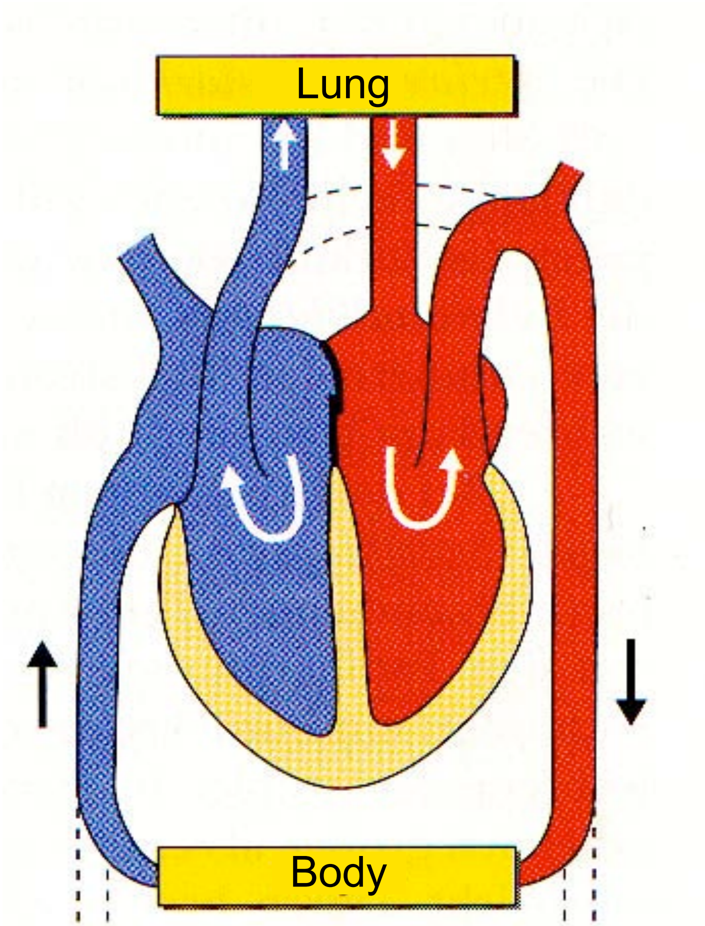
Discuss the role of computational modeling and simulation in other fields.

Which products are developed with help of modeling and simulation?

What is necessary to make modeling and simulation useful?

What are alternatives to modeling and simulation in medicine?

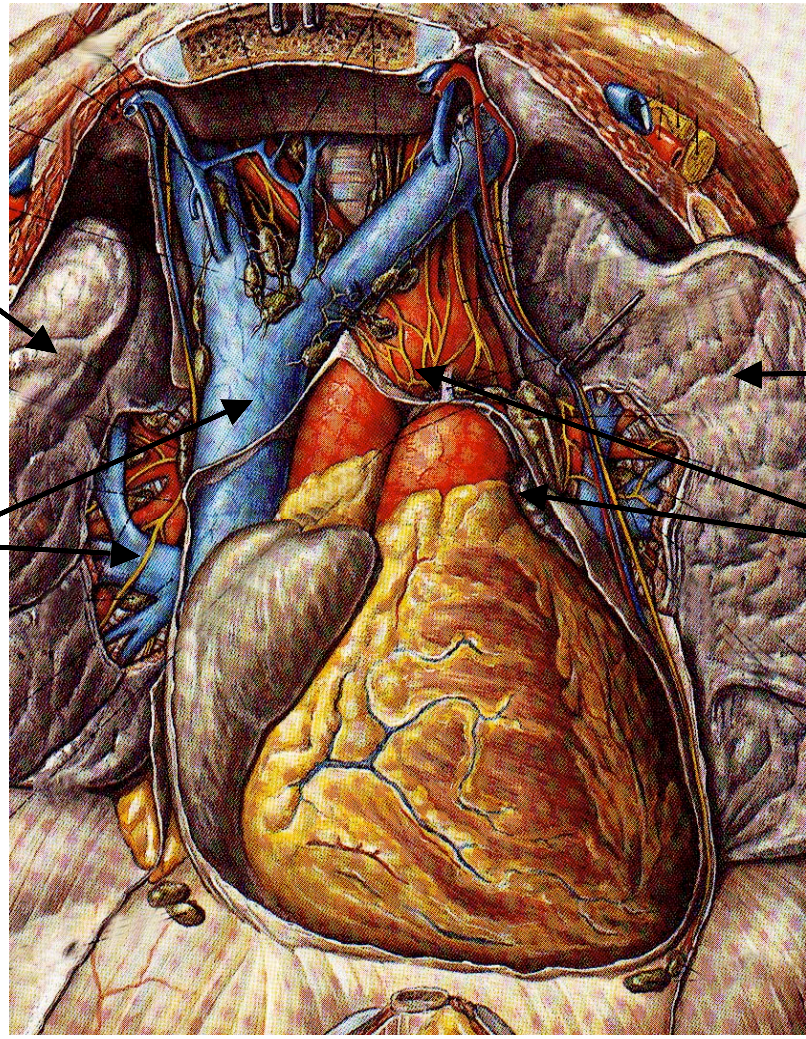
Cardiovascular System



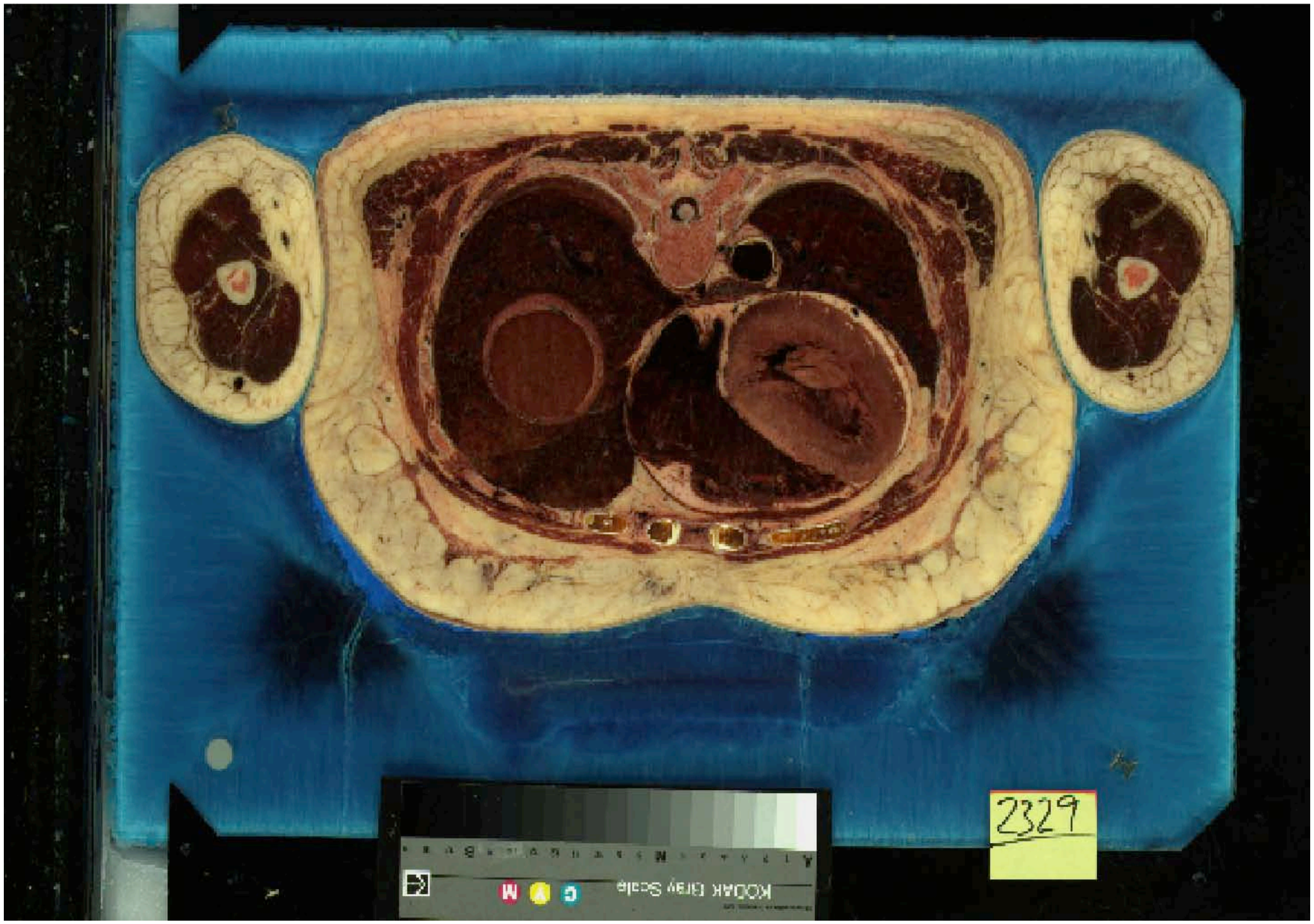
Mammalian heart

- central component of cardiovascular system
- mostly composed of muscle
- connected to blood vessels
- transports blood to/from body and lung
- autonomous function, but modulated by nervous system
- divided in two subsystems, left and right, each consisting of atrium and ventricle

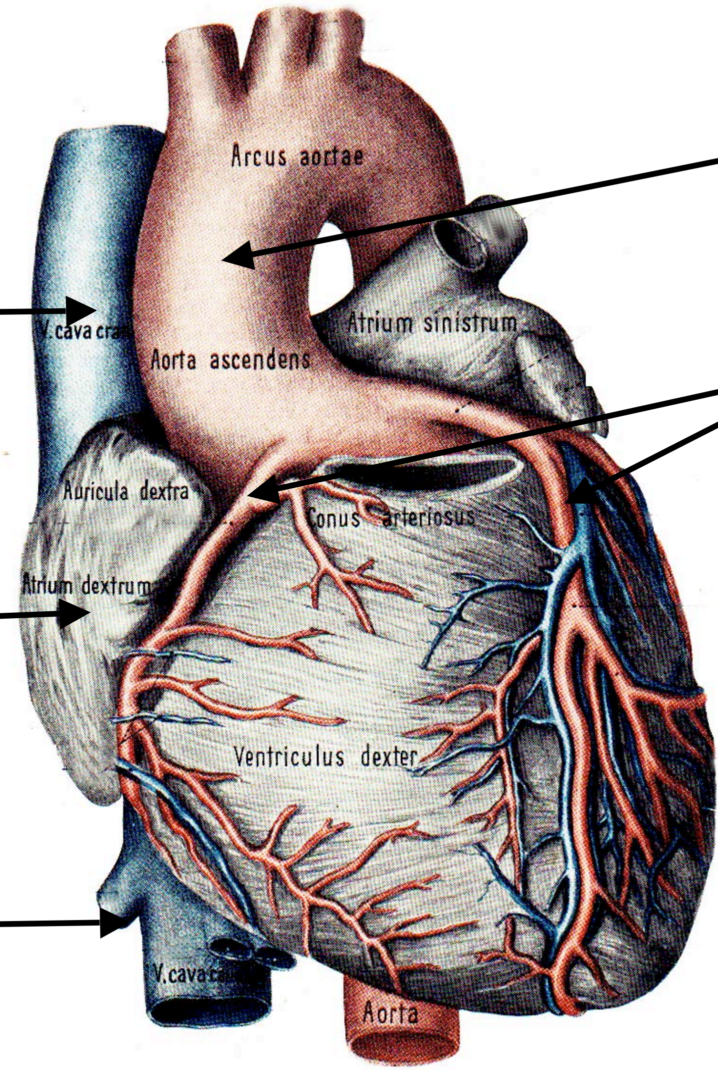
Heart in Thorax



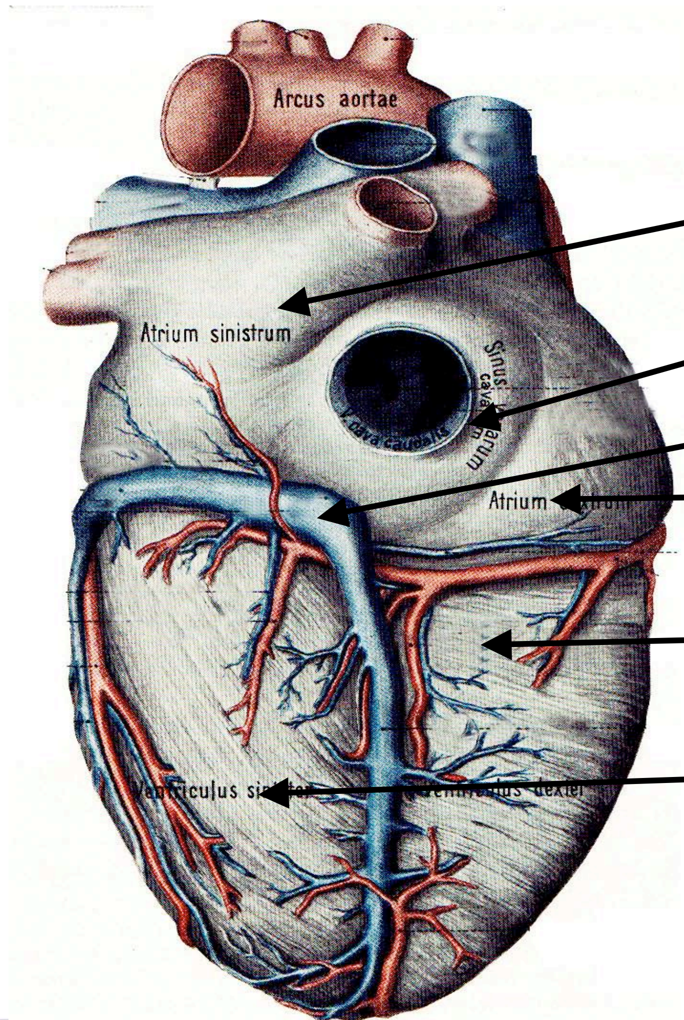
Horizontal Cut Through Thorax



Heart From Right Side



Heart from Dorsal



Left atrium

Vena cava inferior

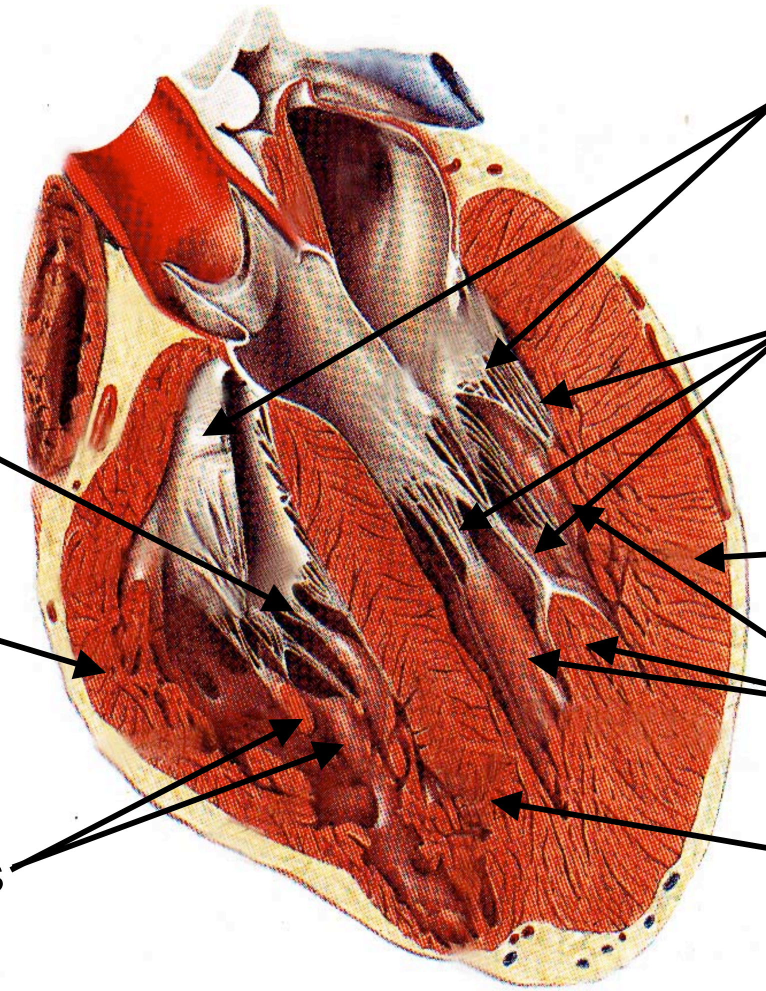
Sinus coronarius

Right atrium

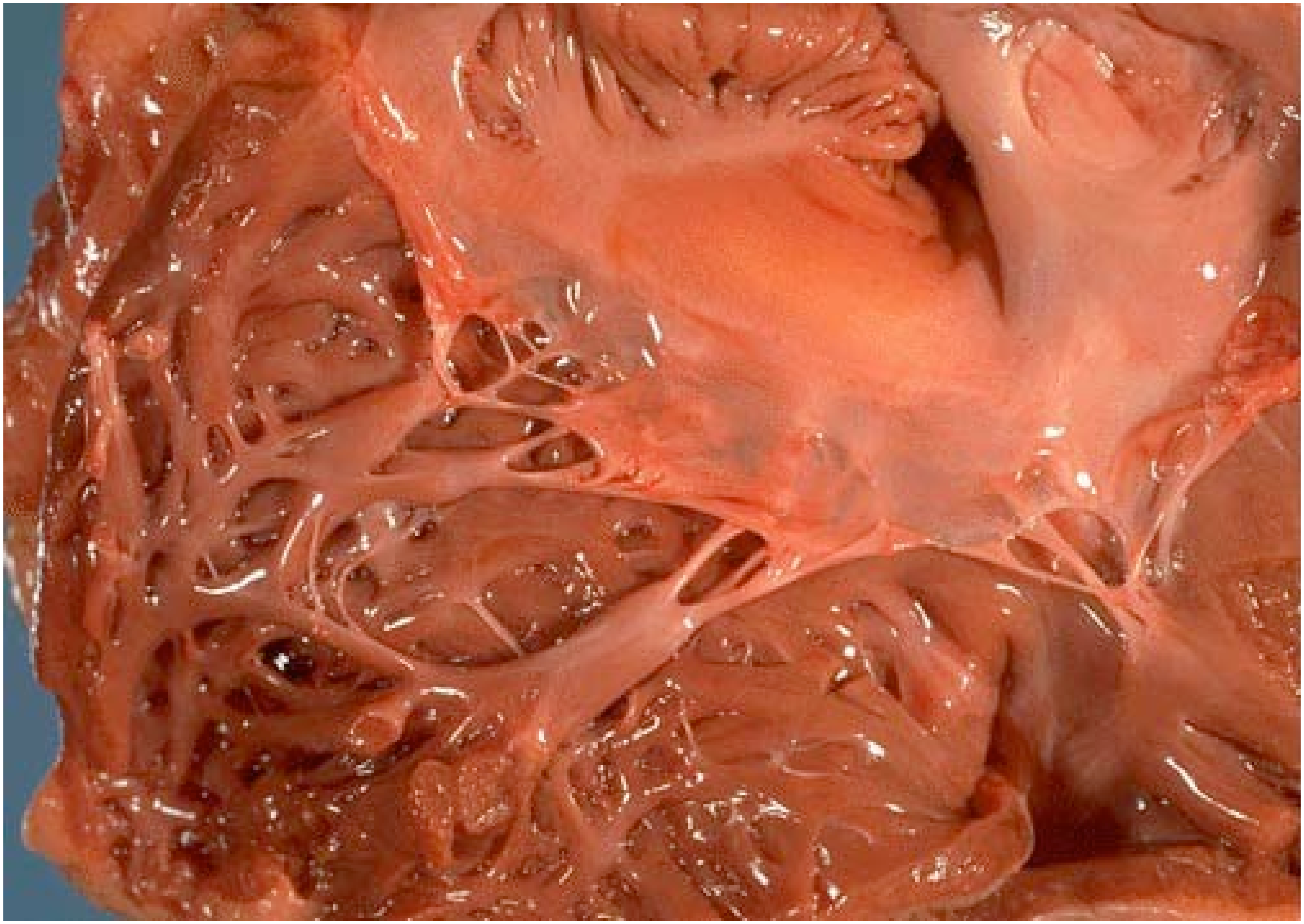
Right ventricle

Left ventricle

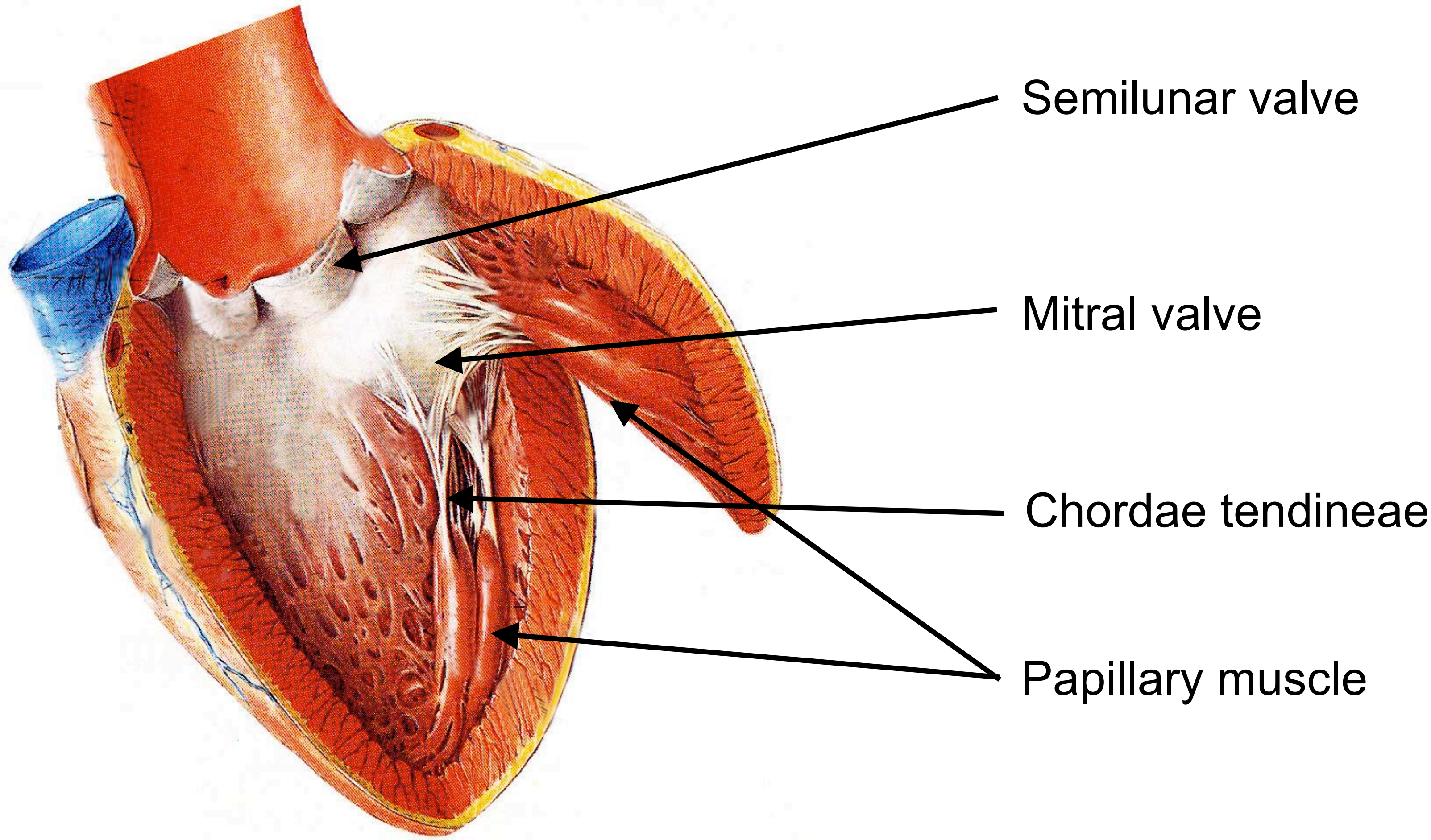
Left and Right Ventricle



Opened Right Ventricle with Valve and Papillary Muscles

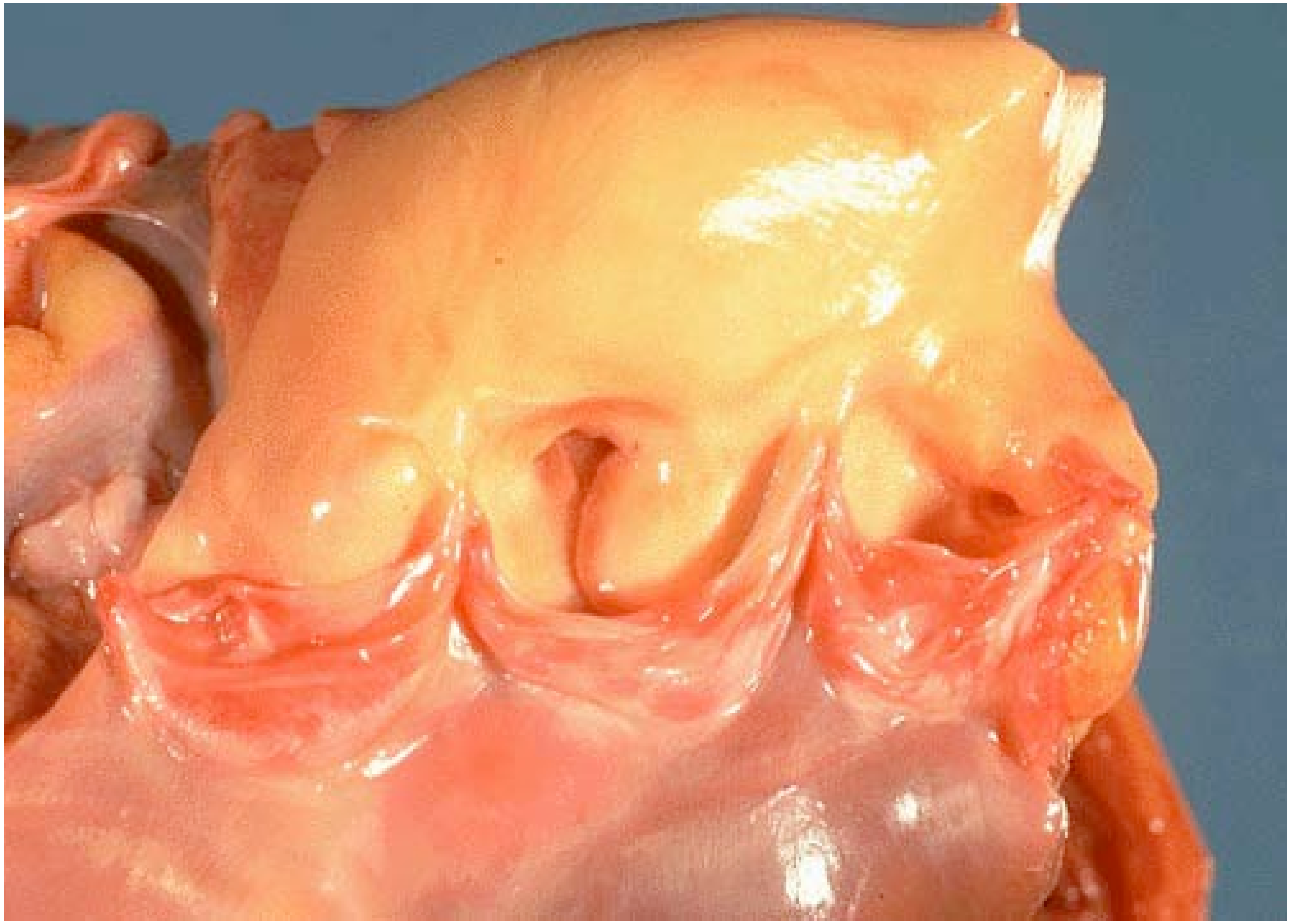


Opened Left Ventricle



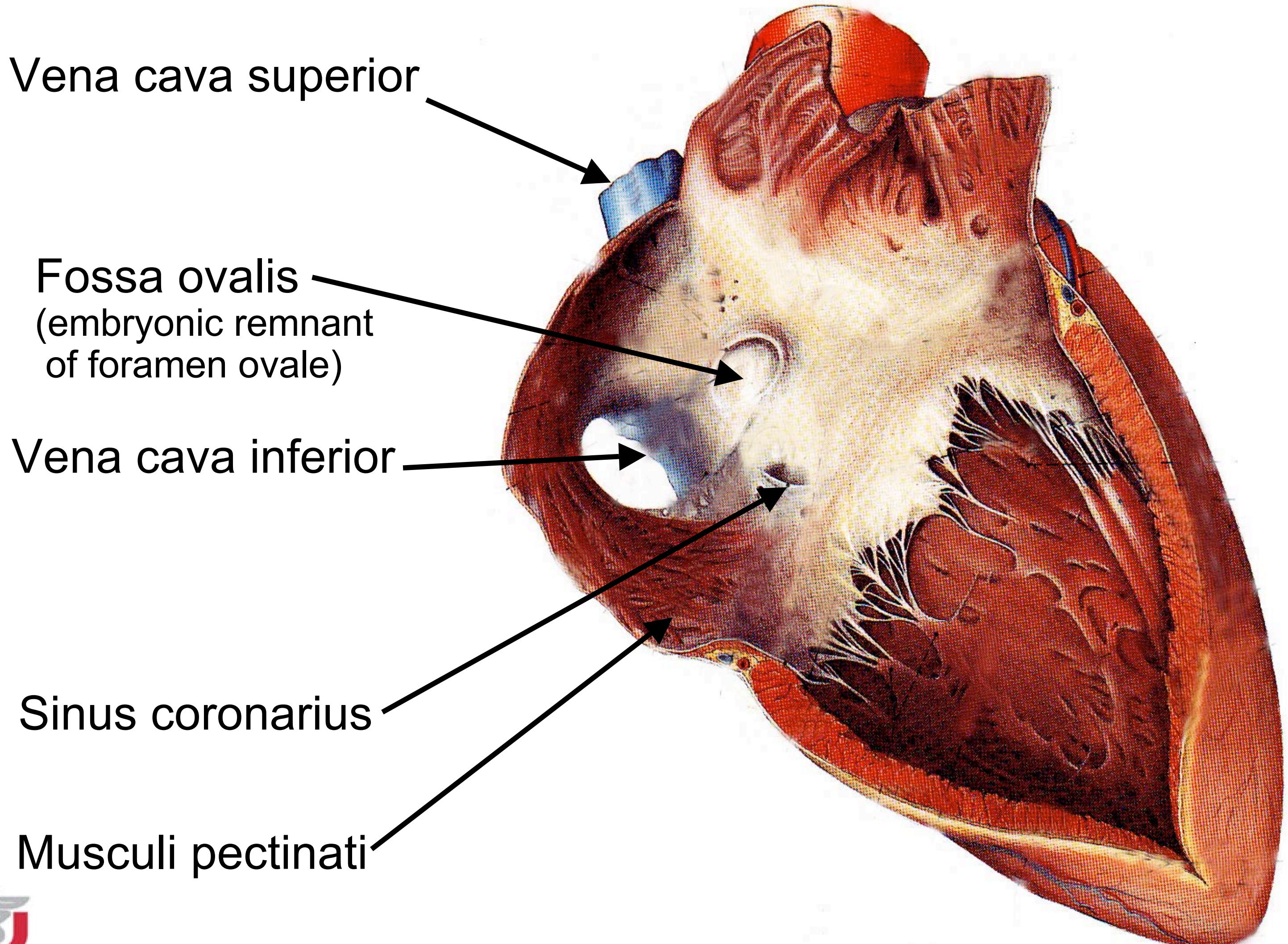
CVRTI

Semilunar Valve

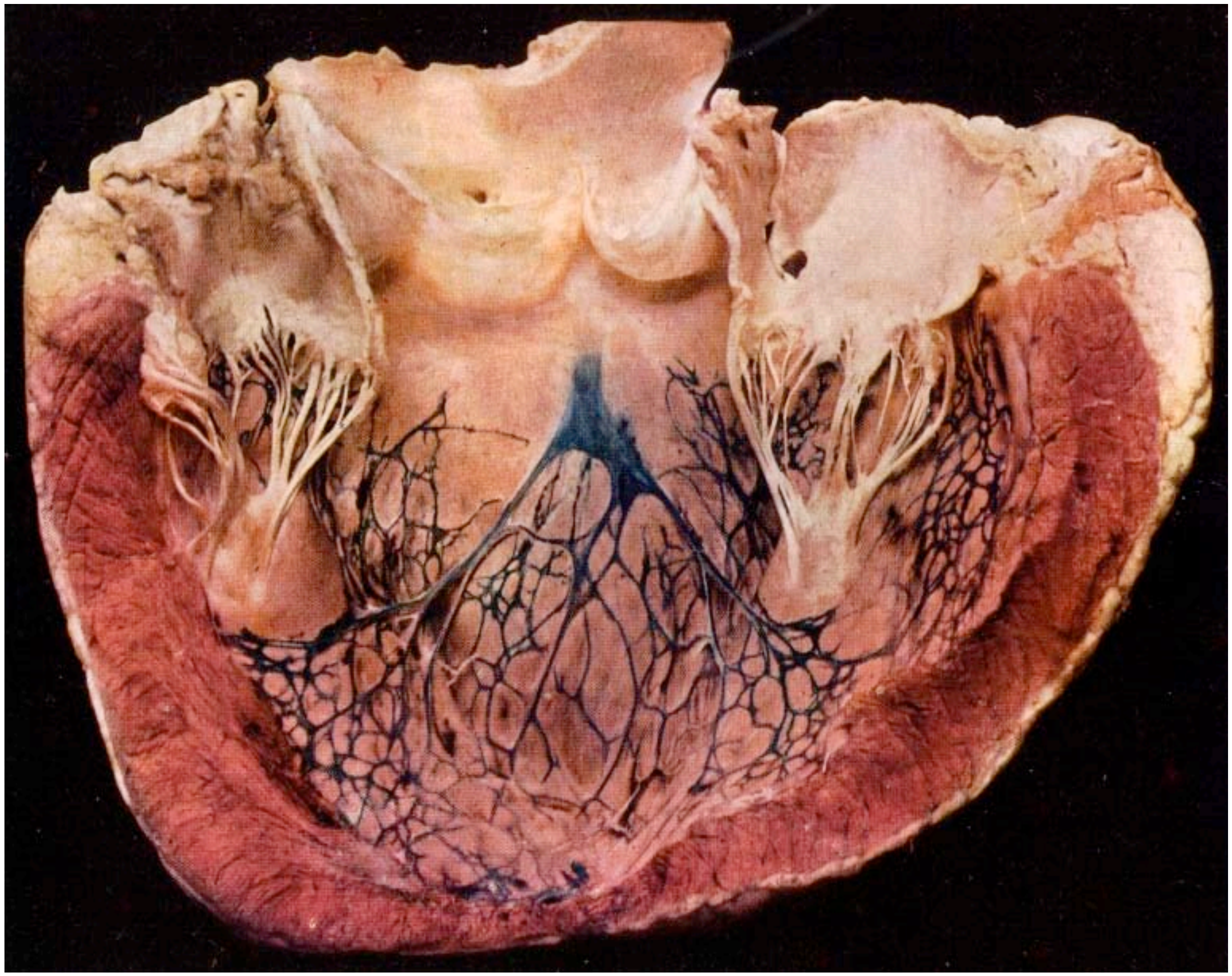


CVRTI

Opened Right Atrium and Ventricle



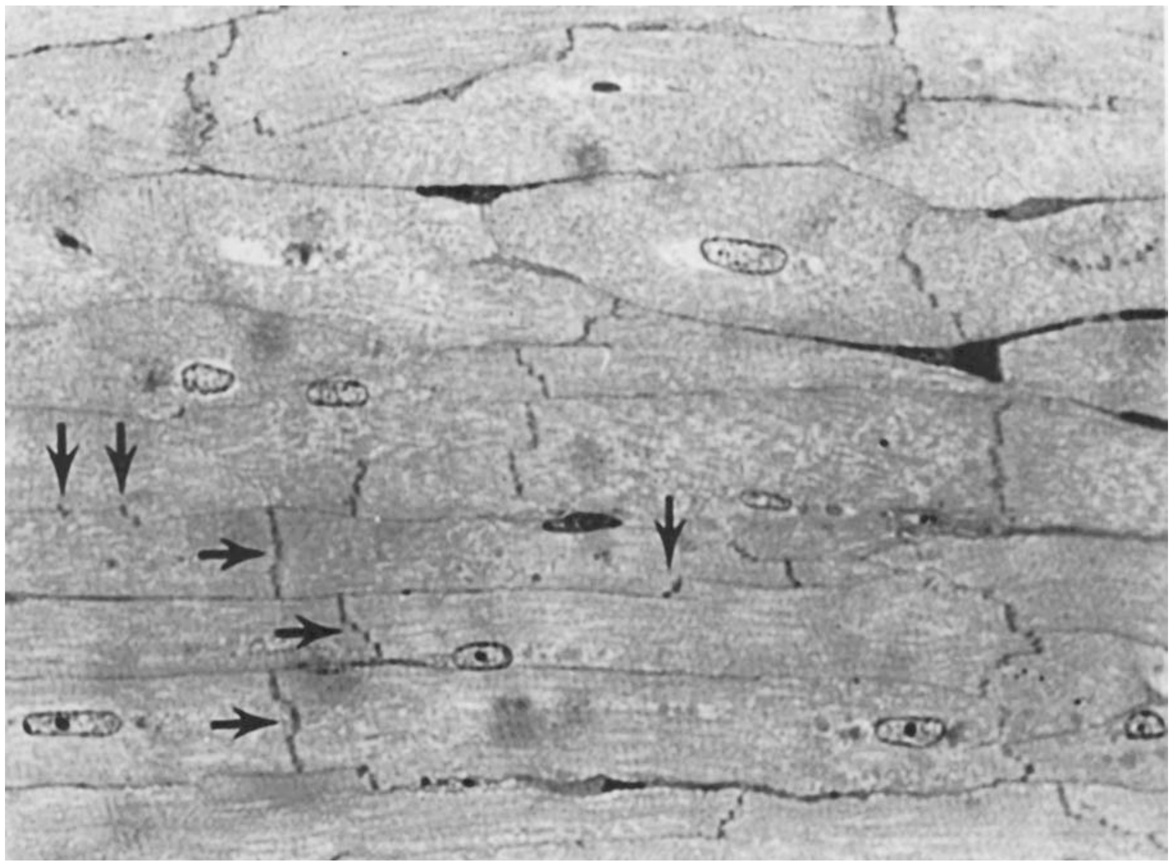
Conduction System in Cow Heart



(Lewis 1925)

Microscopic Anatomy of Cardiac Tissue

Myocytes are connected at intercalated discs { intracellular space via gap junctions / mechanical coupling }



(Saffitz et al. 99)

Microscopic Cellular Anatomy

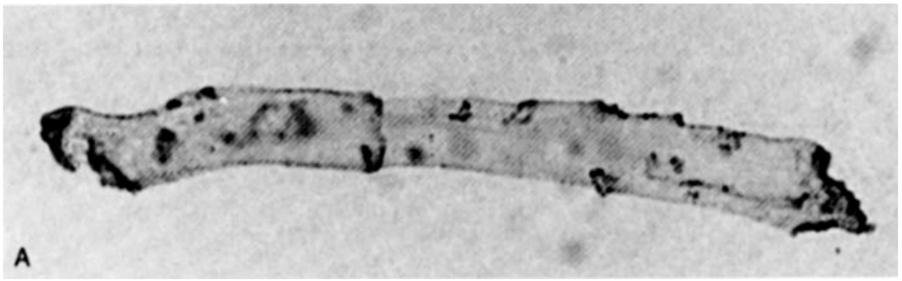
Myocyte of ventricular myocardium

cylinder-shaped

length: 60-120 µm

diameter: 8-15 µm

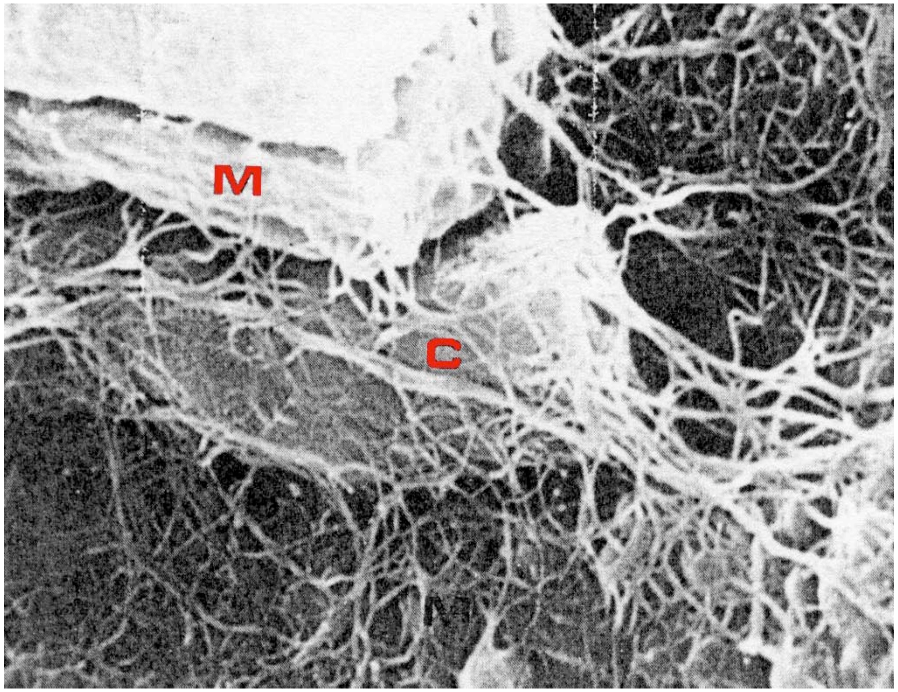
(Hoyt et al. 89)



Myocyte (M) and capillary (C)

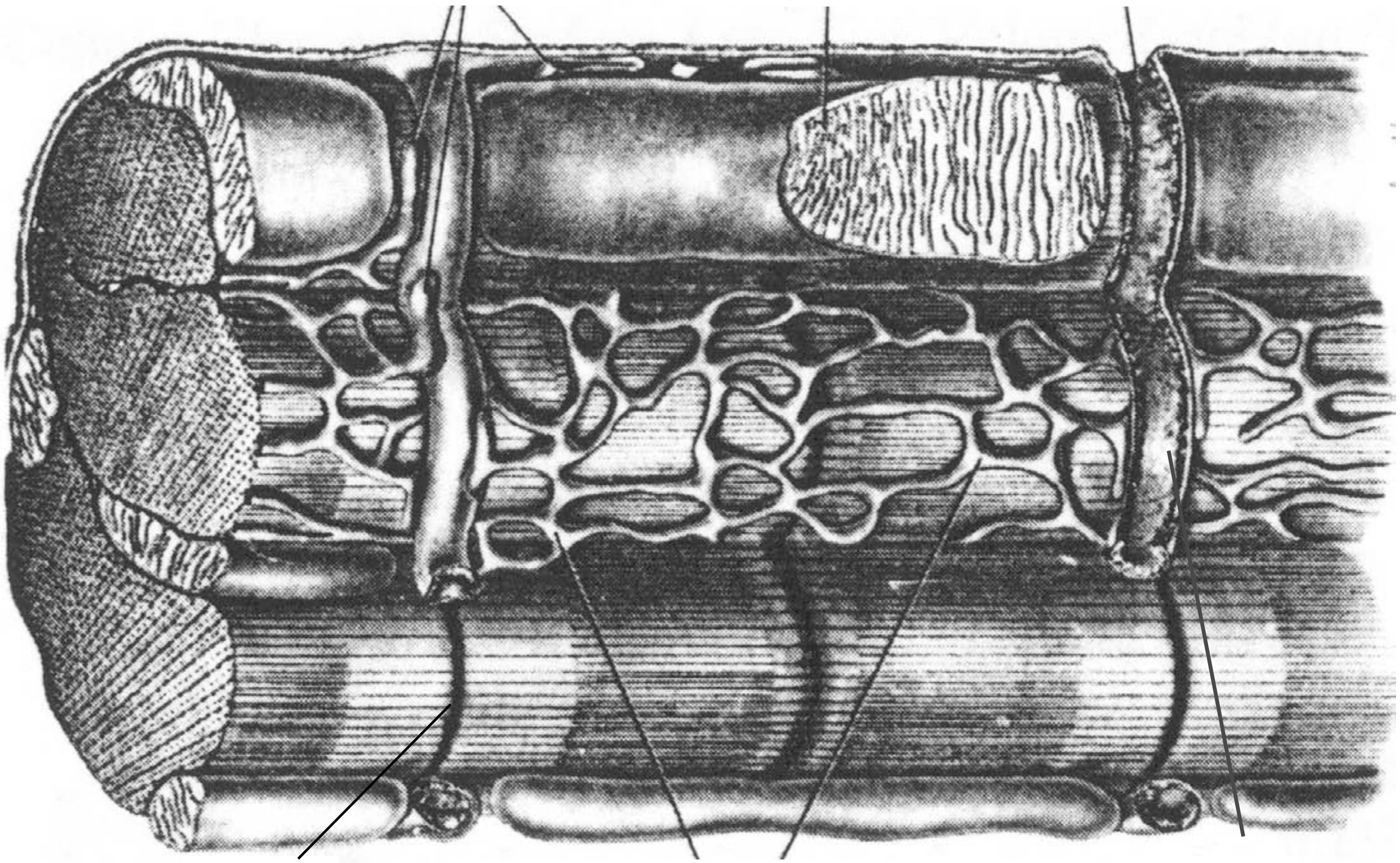
mechanically coupled by fibers of connective tissue (collagen and elastin)

(Caulfield et al. 79)



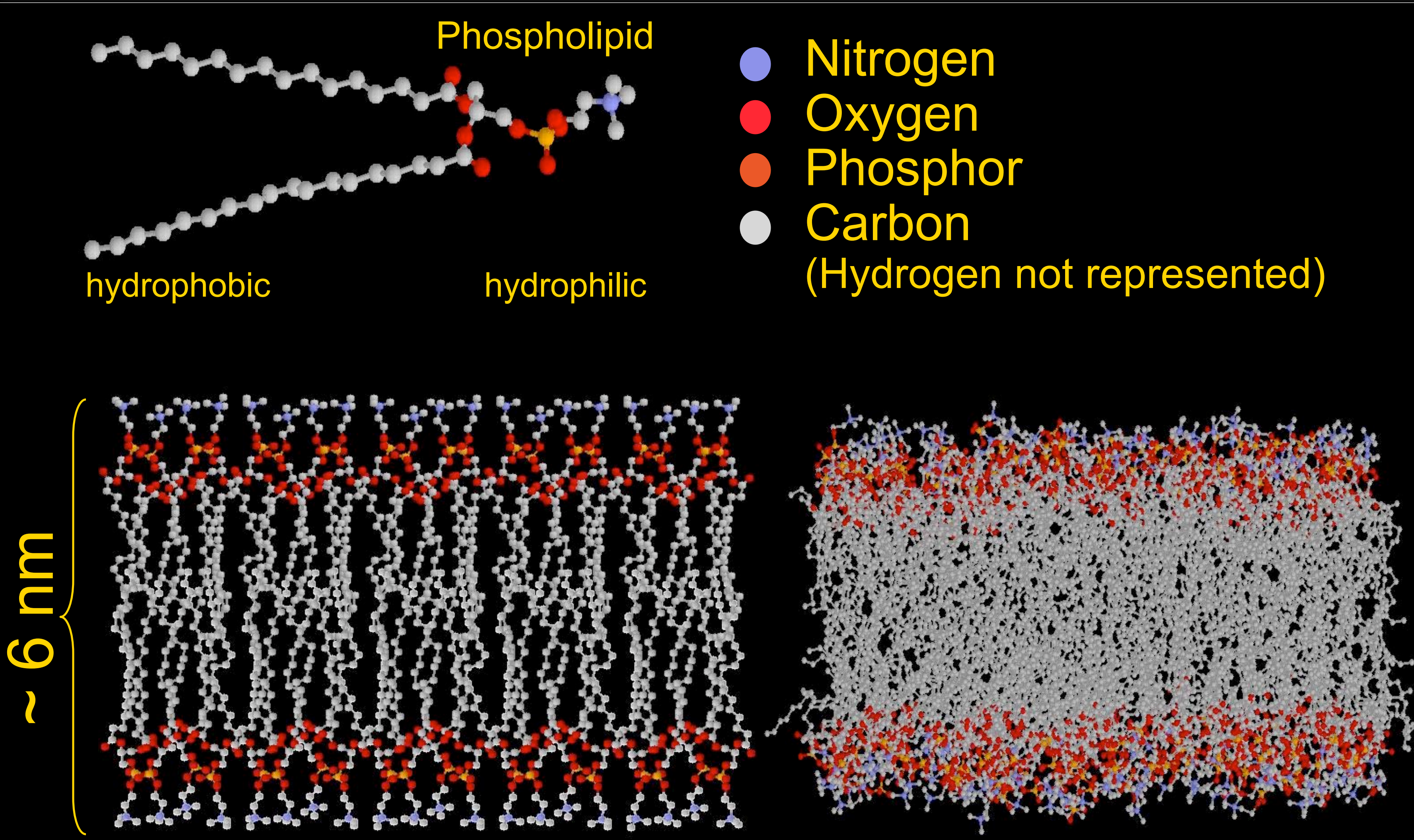
CVRTI

Intracellular Structures of Myocytes: Sarcomere



CVRTI

Molecular Structure of Cell Membrane

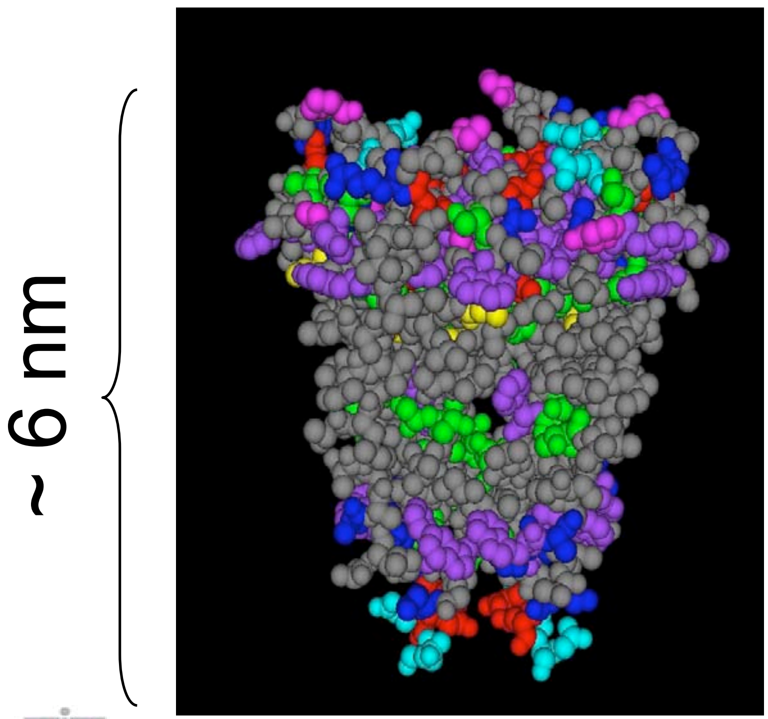


(Structure data from Heller, Schaefer and Schulten, J. Phys. Chem., 1993)

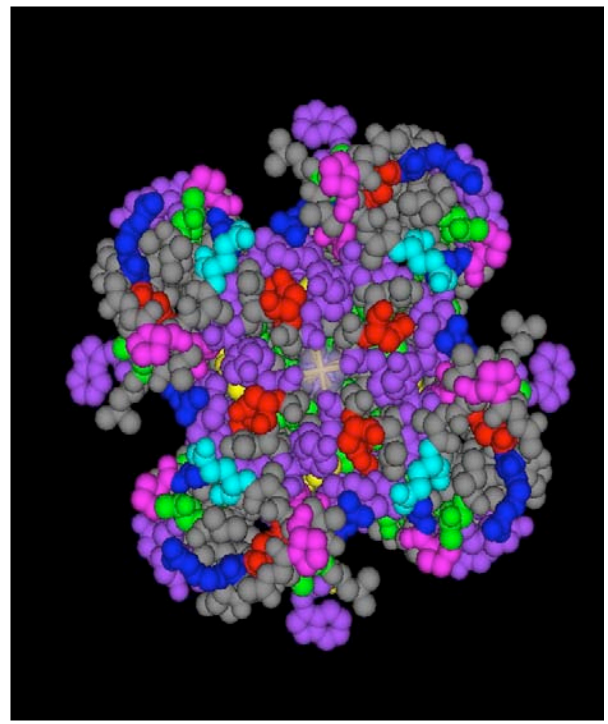
Molecular Structure of Transmembrane Proteins

Transmembrane proteins: connexons, ion channels, pumps, and -exchangers

Example: Molecular structure of potassium channel Kcsa of bacterium streptomyces lividans, color-coded amino acids
Structure data from Molecular Modeling Database, NIH, USA



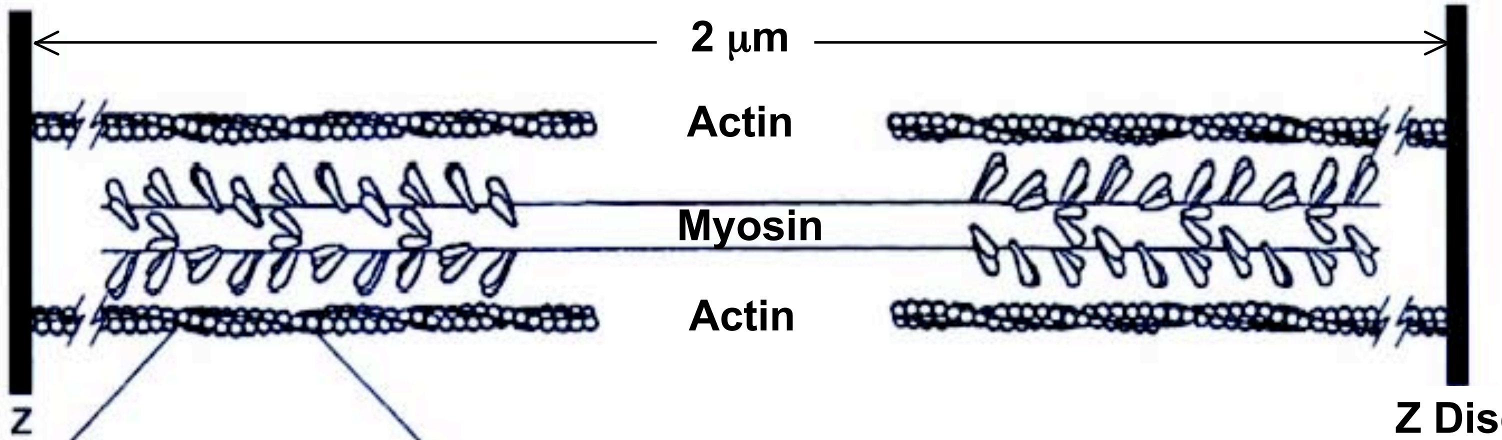
side

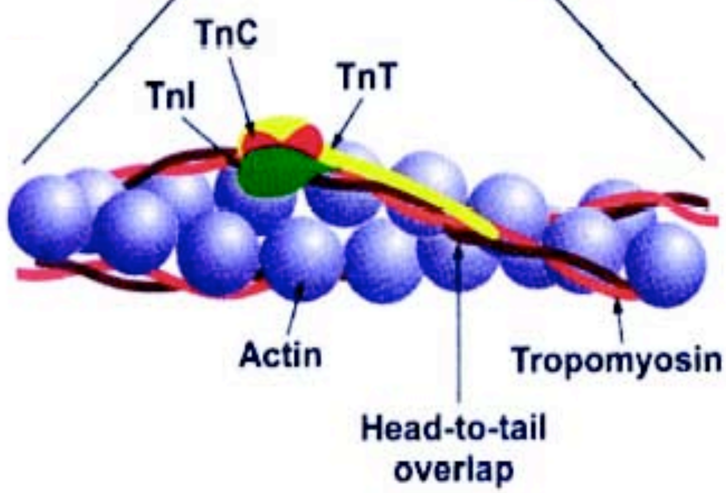


from top

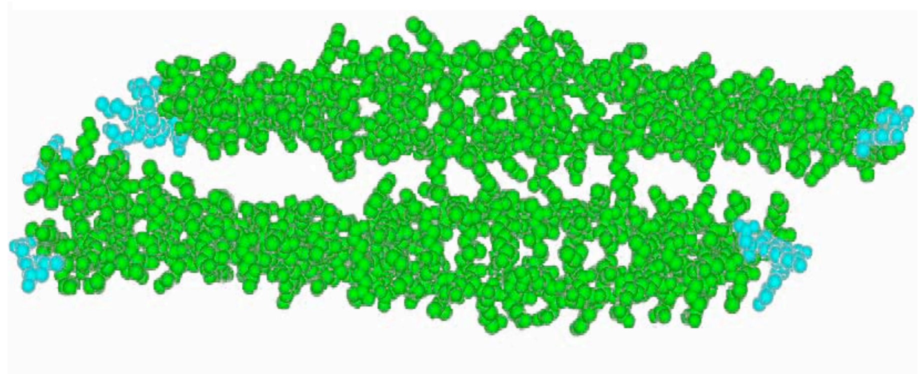
CVRTI

Molecular Structure of Proteins in Sarcomere



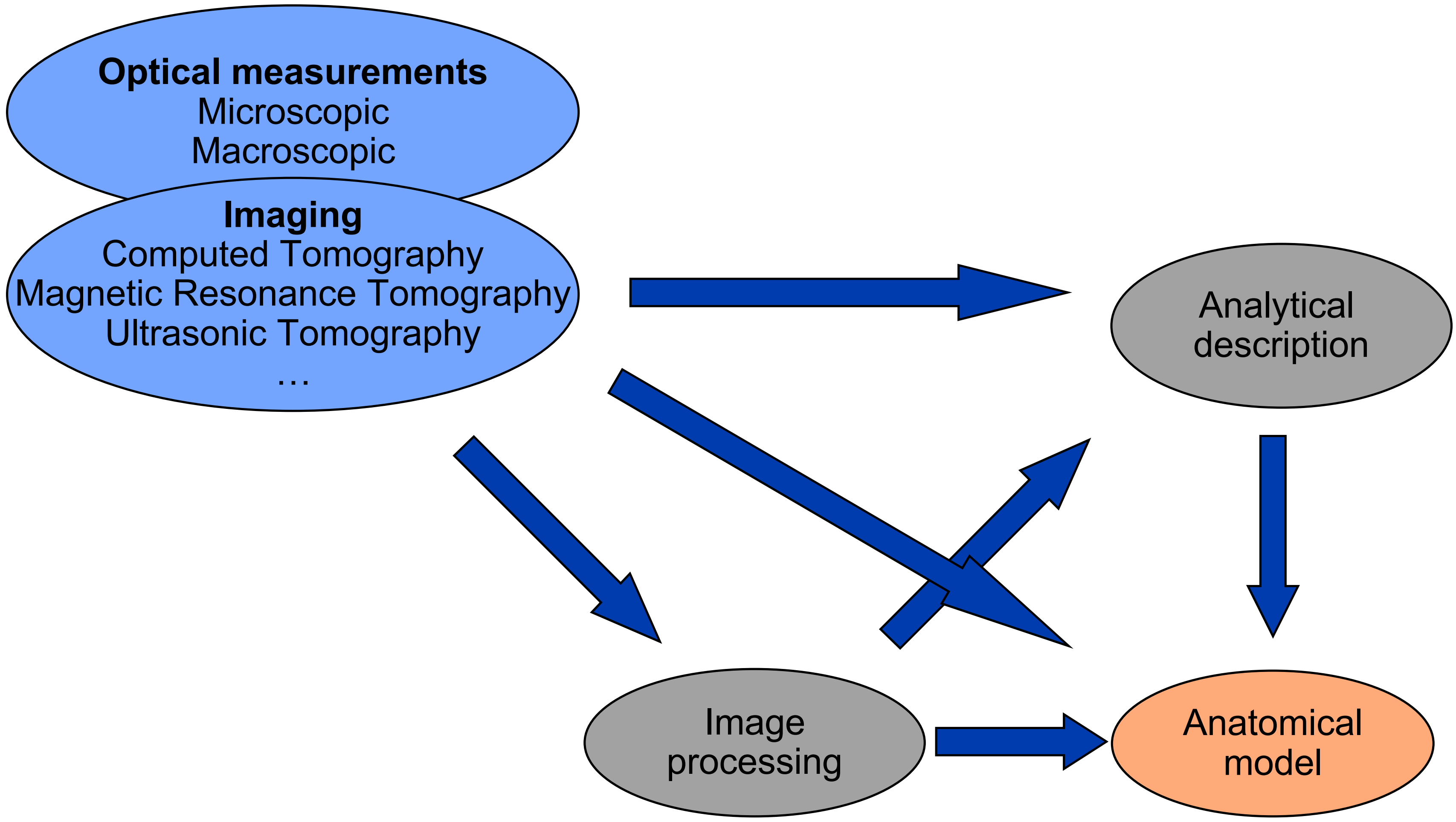


Molecular Structure of Tropomyosin
Structure data for species gallus gallus
from Molecular Modeling Database, NIH, USA



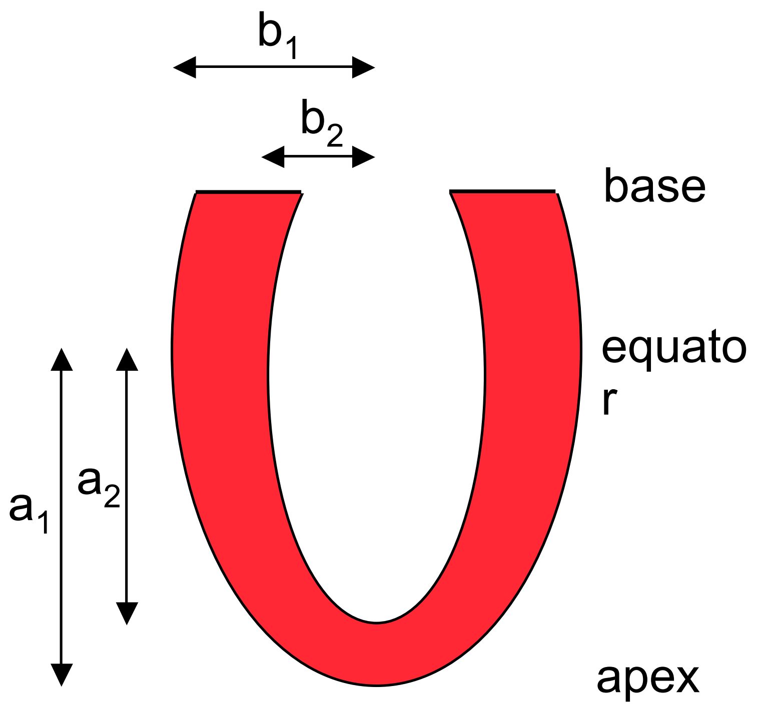
(Gordon, Regnier, and Homsher, News Physiol. Sci., 2001, modified)

Anatomical Modeling



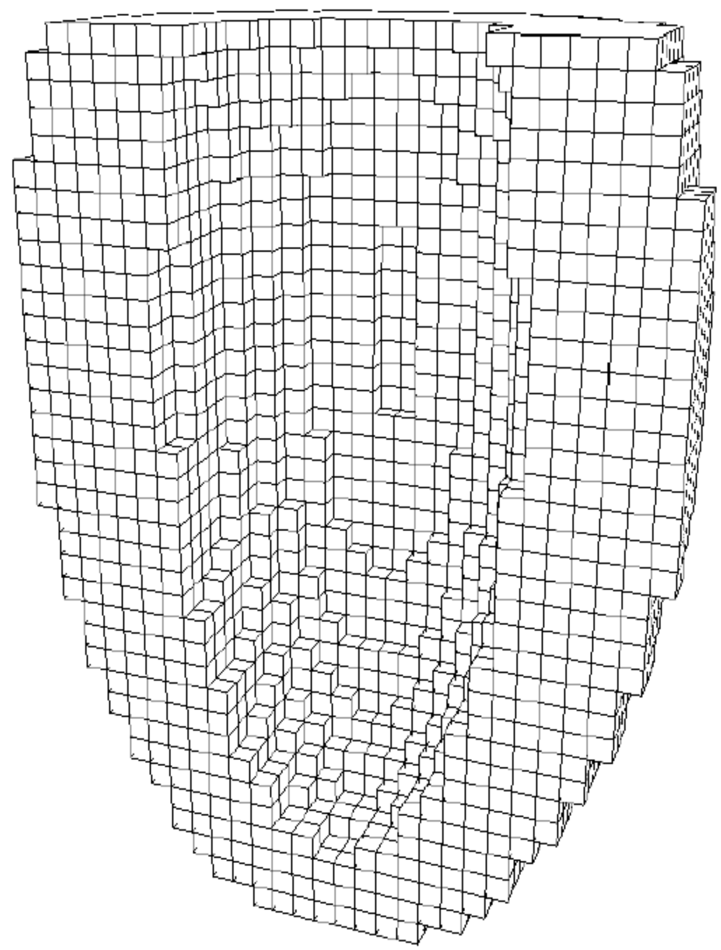
CVRTI

Anatomical Model: Confocal, Truncated Ellipsoids



a_1, a_2: Major axis b_1, b_2: Minor axis

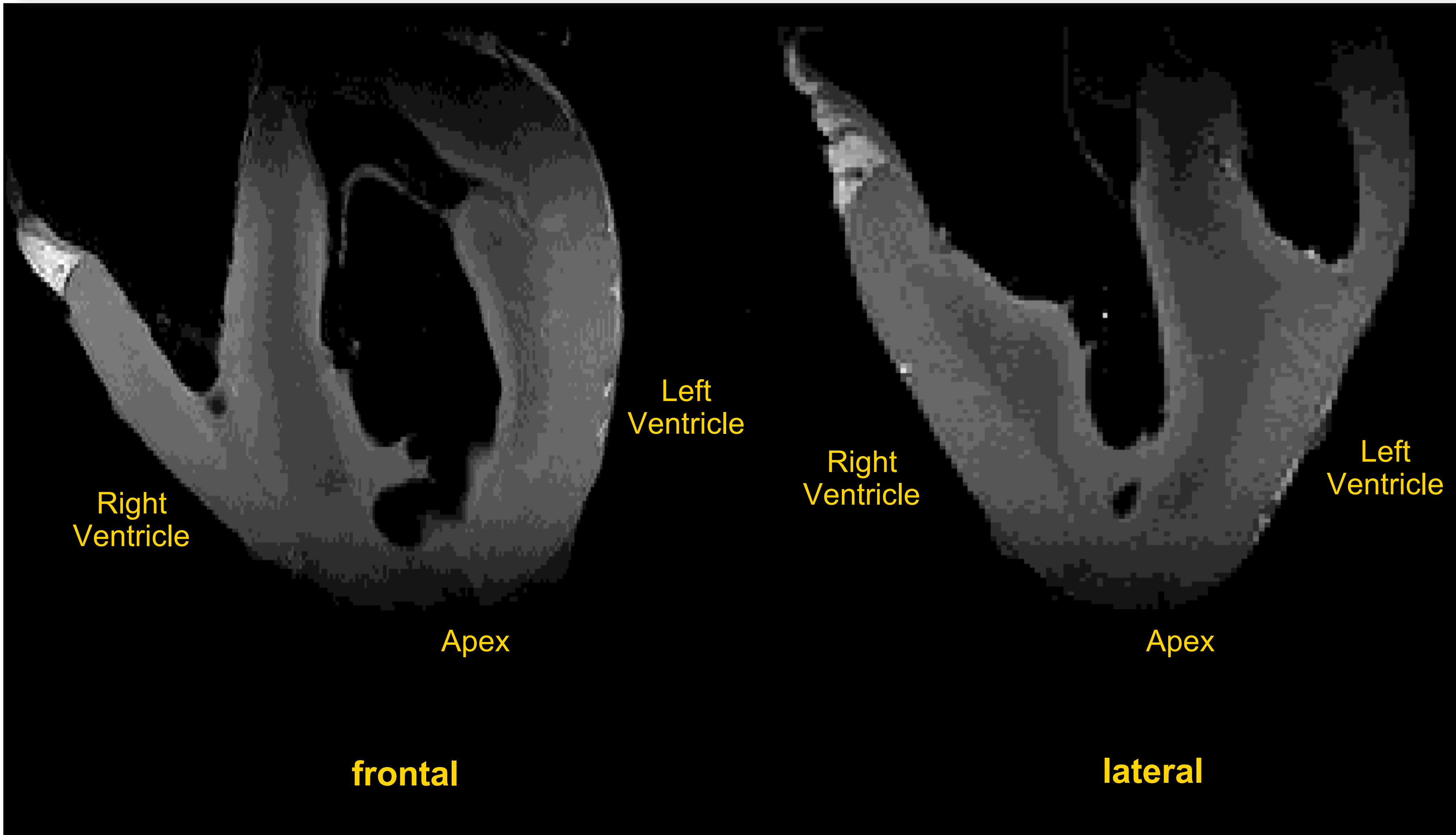
Focus length: $f = \sqrt{a^2 - b^2}$



n x n x m cubic elements

CVRTI

MR-Imaging of Canine Heart



(Sachse, Henriquez, Seemann, Riedel, Werner, Penland, Davis and Hsu, CinC, 2001)

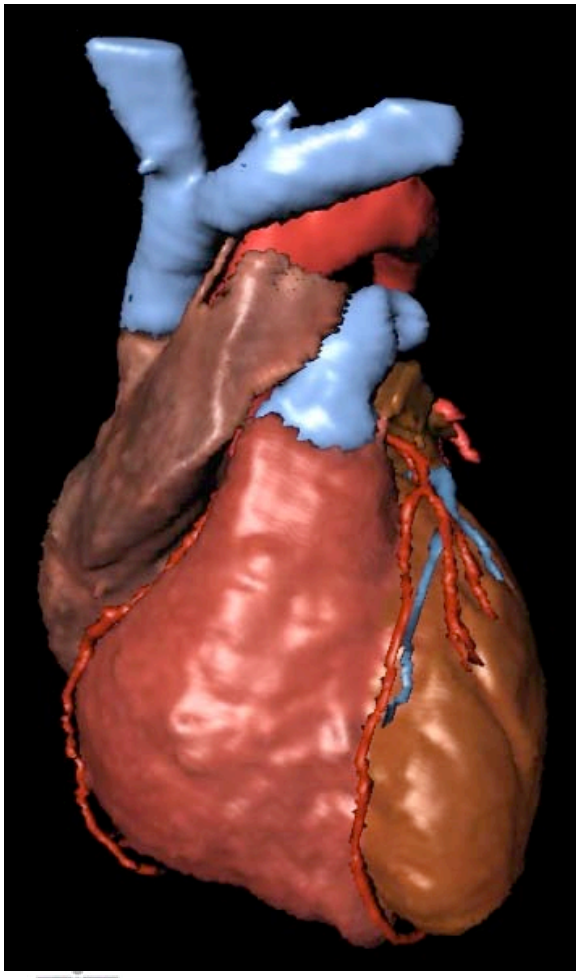
Anatomical Model

View into left ventricle

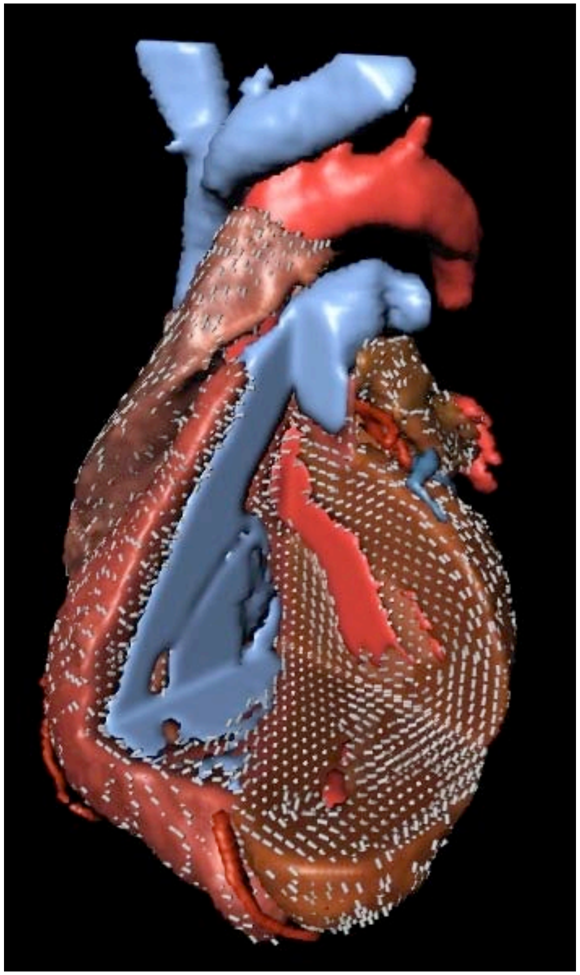
View into right ventricle

Anatomical Model: Visible Man Data Set

Tissue



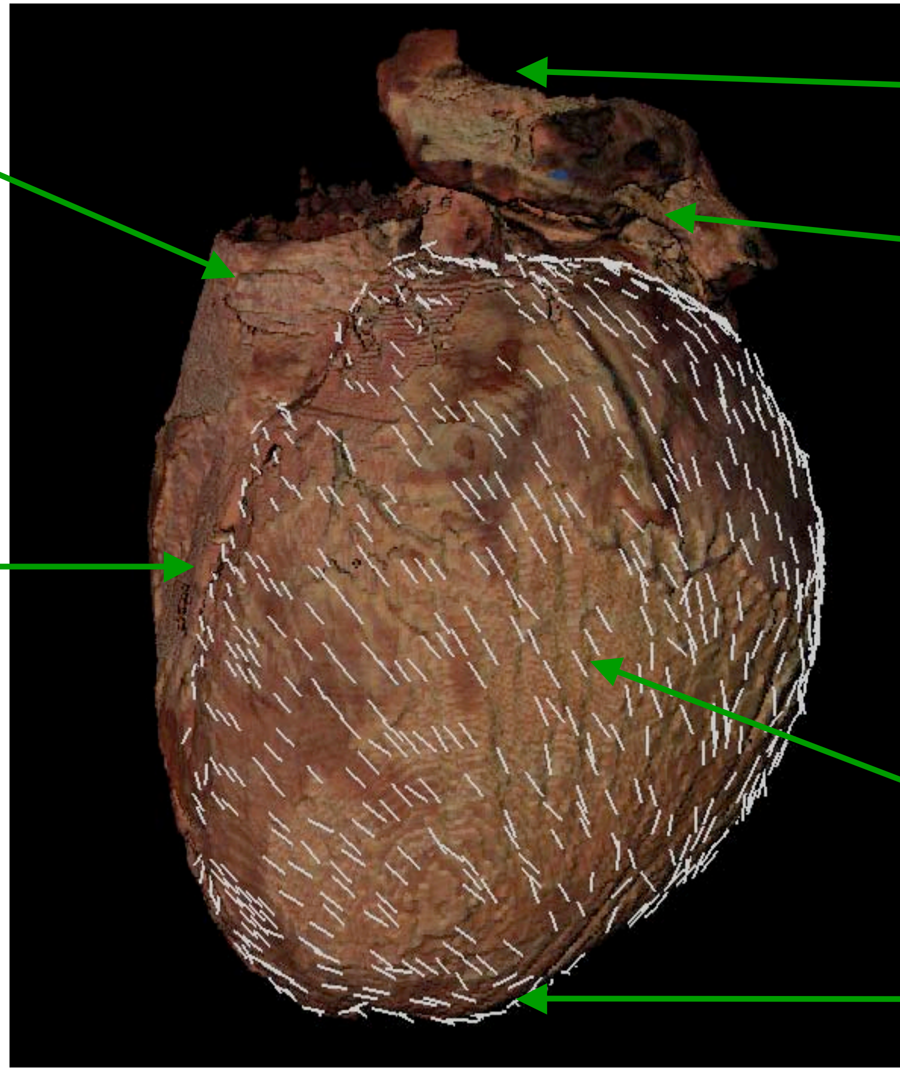
Fiber orientation



Conduction system

CVRTI

Model of Macroscopic Anatomy with Fiber Orientation



CVRTI

Group Work

Anatomical models are frequently used to delineate spatial domains of computational simulations and to assign physical and physiological properties to compartments.

Which level of anatomical detail is necessary in simulations of the cardiovascular system?

Choose 3 examples for simulations and motivate how you would describe spatial domains.