EAE Teaching Course

How to describe LV Function?
From fiber shortening to ejection –
The physiology behind.

Sofia, Bulgaria, 5-7 April 2012

F.E. Rademakers

Content

- Definition
- Anatomy
- Physiology
  - Myofilaments
  - Ventricle
  - Stress - strain
  - Pressure – volume
  - Passive properties

Cardiac 'function' is defined qualitatively:

The ability to work (pump) and keep on working sufficiently.

=

Cardiac performance

Primary goal:

Maintain Cardiac Output

And Perfusion Pressure

by ***developing force*** in the wall to generate *cavity pressure*

and by ***deforming*** the wall to displace *cavity volume*

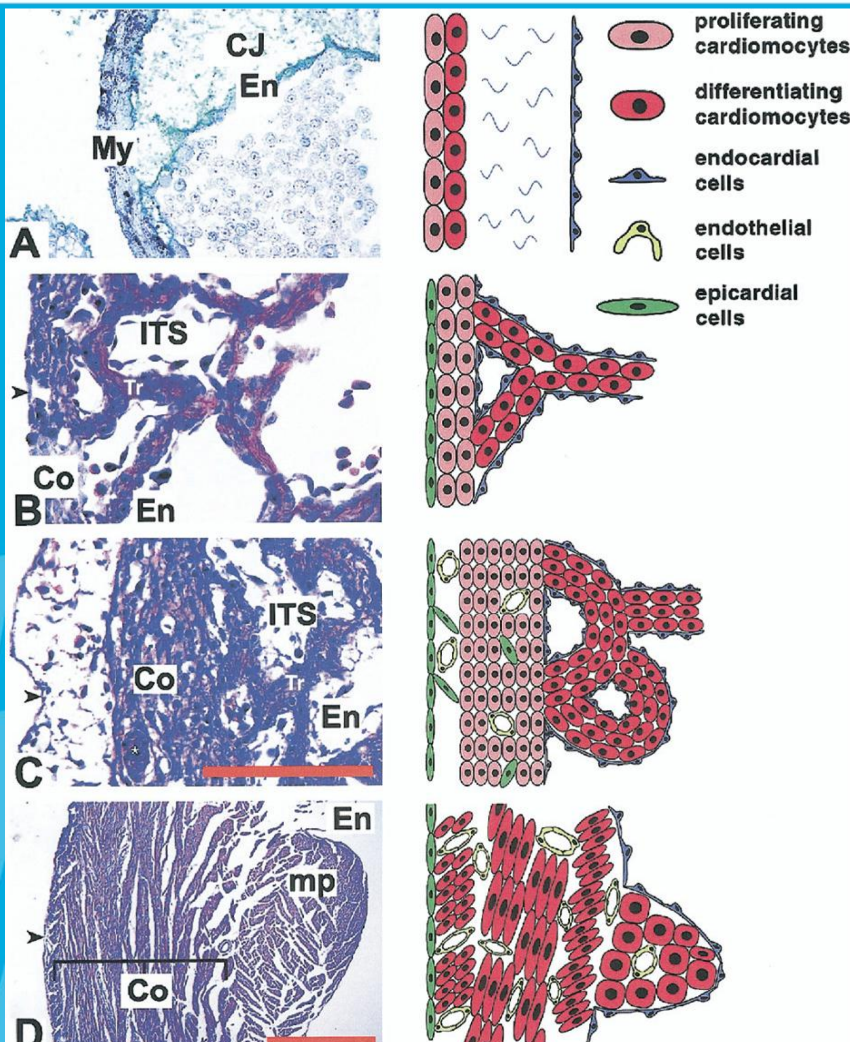
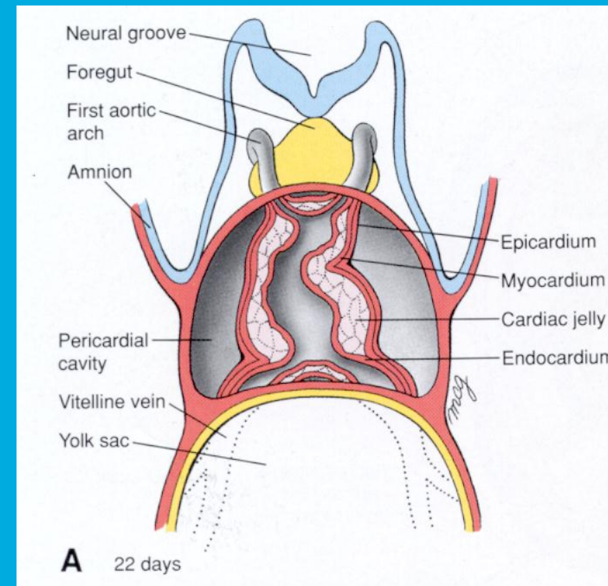
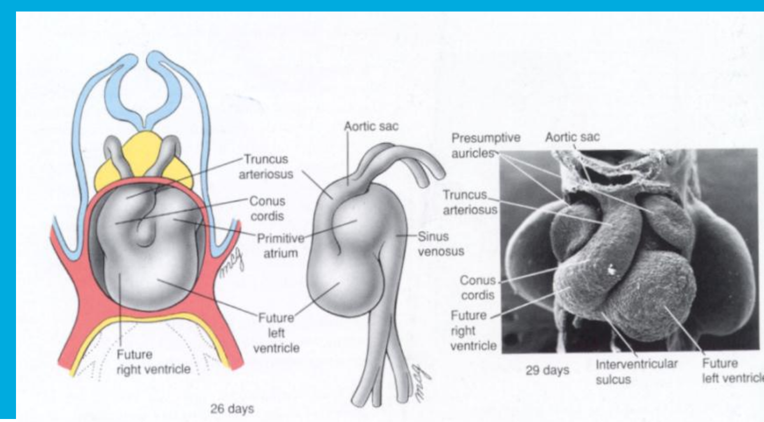


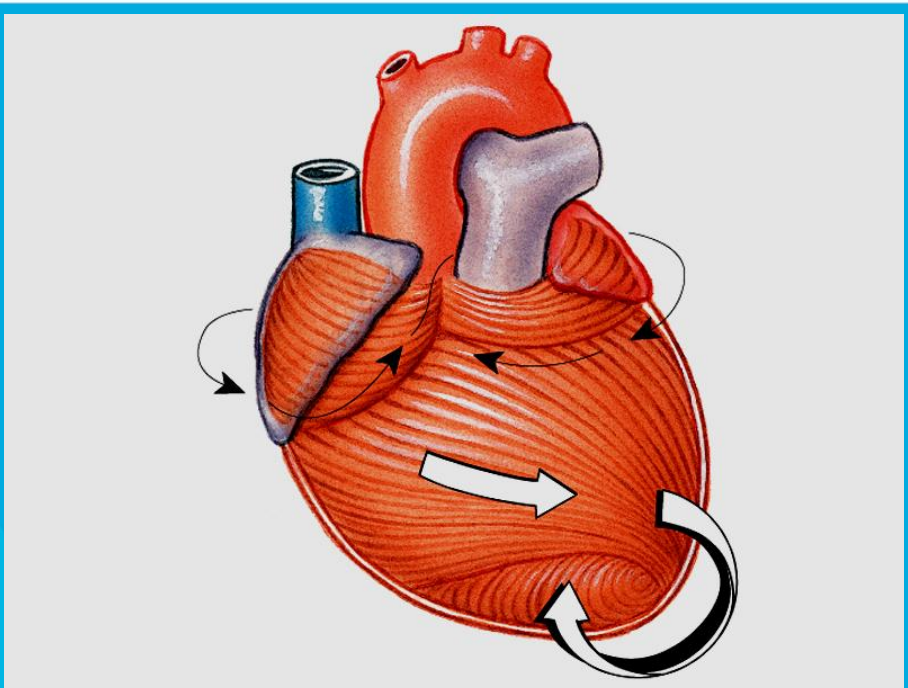
Figure 1. Embryonic development of the left ventricular wall in a chick. (A) The tubular myocardium (My) (2 to 3 cell layers thick) is separated from the endocardium (En) by acellular cardiac jelly (CJ). (B) The inner layers proliferate to form trabeculations (Tr), which are nourished by the blood circulating through the intertrabecular spaces (ITS). The outer layers proliferate and undergo compaction (Co) and are covered by epicardium (arrowhead). (C) By the sixth embryonic day, the compact layer has thickened and is invaded by developing coronaries from the epicardial surface. (D) In the neonatal (day 10) heart, the multilayered compact architecture of the left ventricular wall is clearly appreciated with the innermost layer merging with the papillary muscle (mp). On the right side of each picture is a schematic drawing illustrating the major steps in development of ventricular myoarchitecture. Scale bars = A, B, C, 100 μm; D, 500 μm. Reproduced from Sedmera et al. (20) with permission.

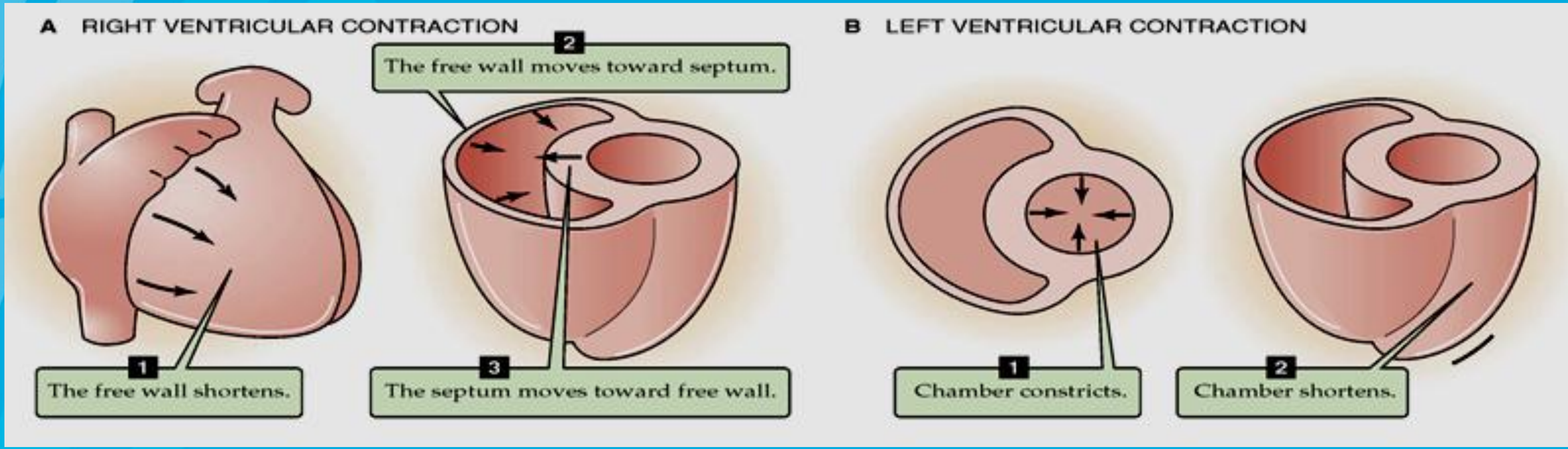




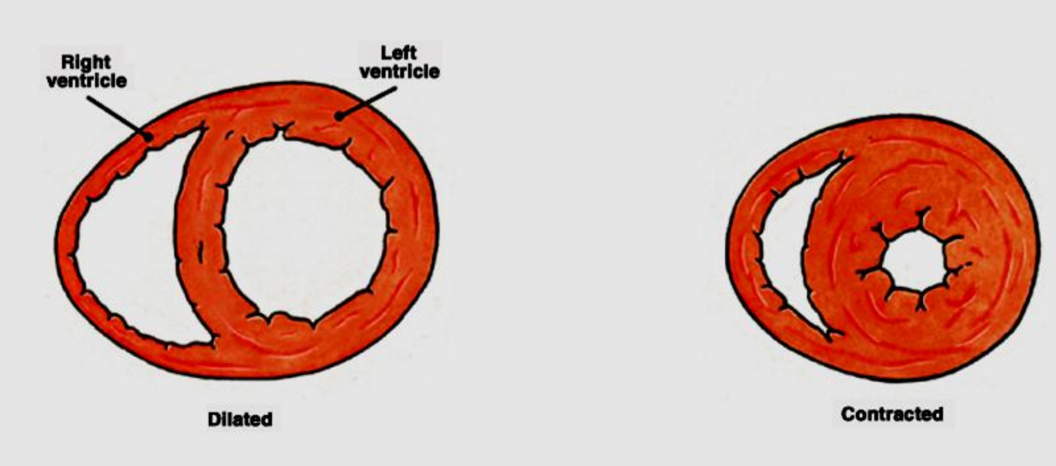
J Am Coll Cardiol 2006;48:1988 –2001

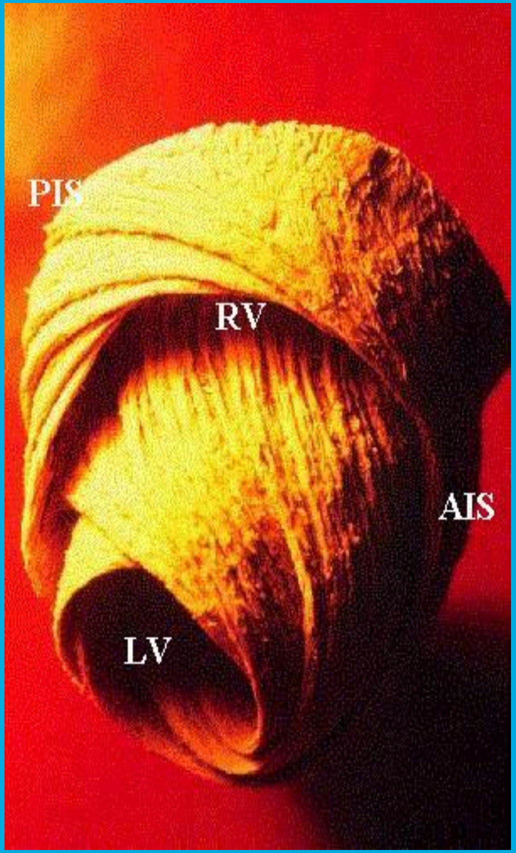
Fiber Architecture

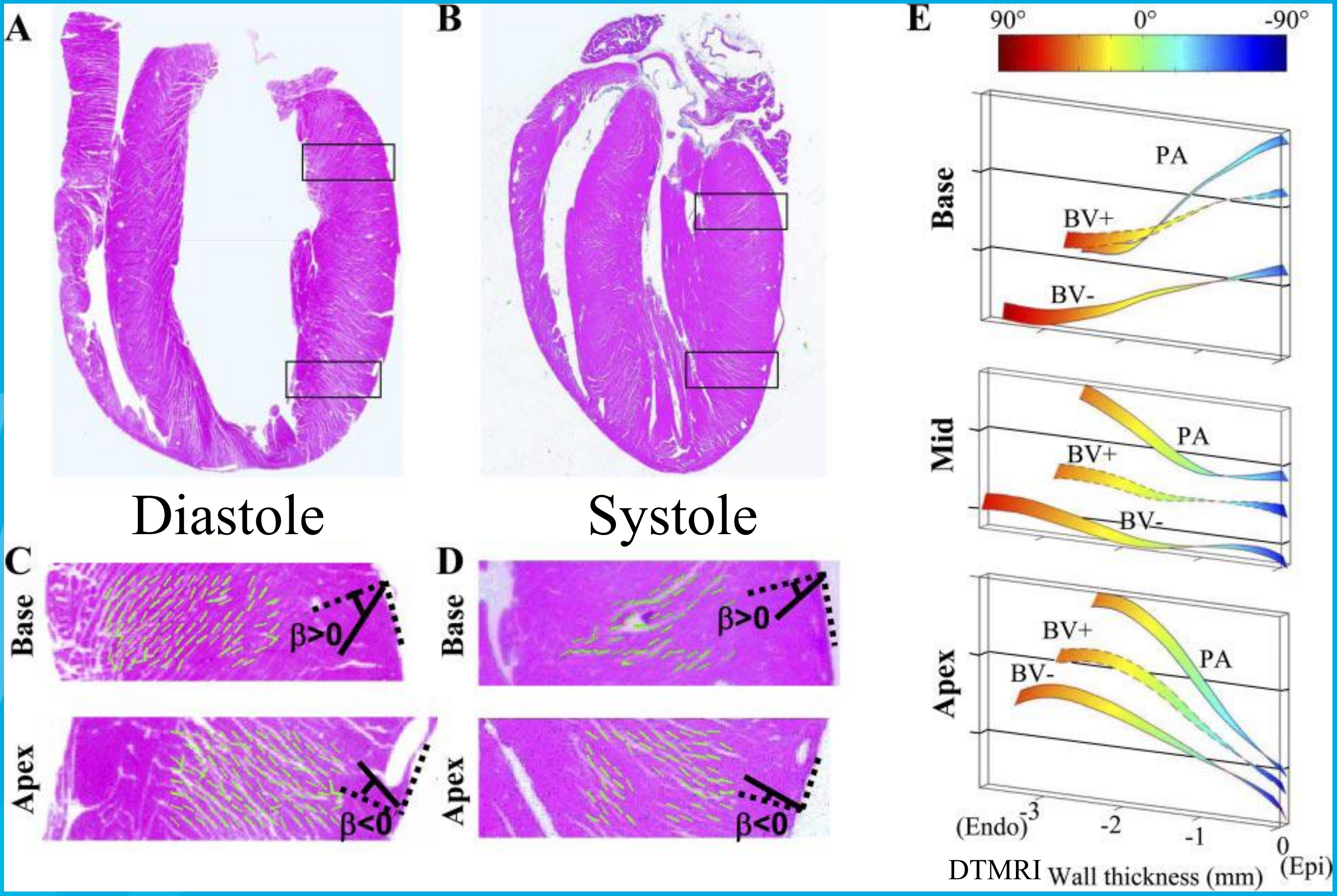




Fiber Architecture

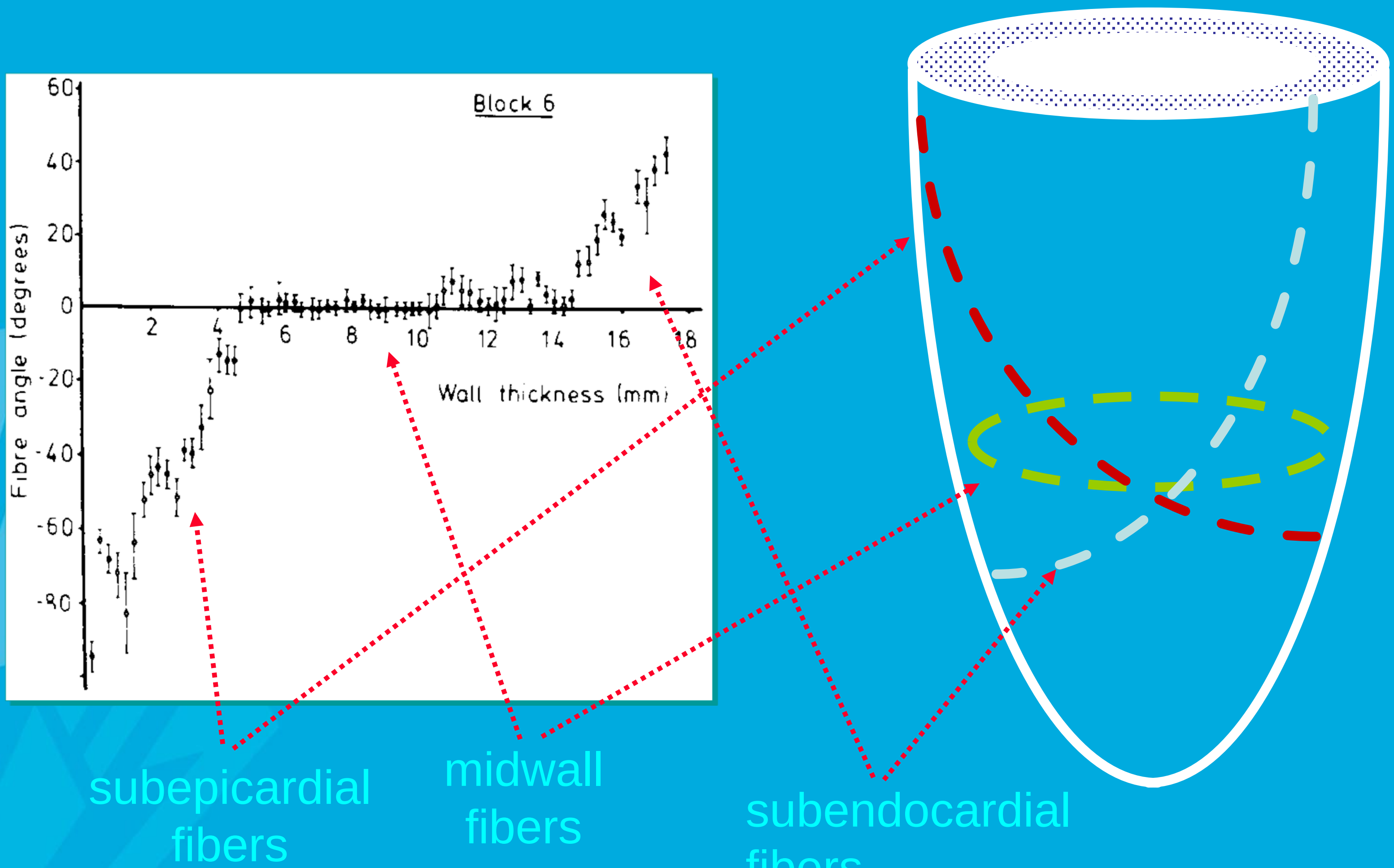






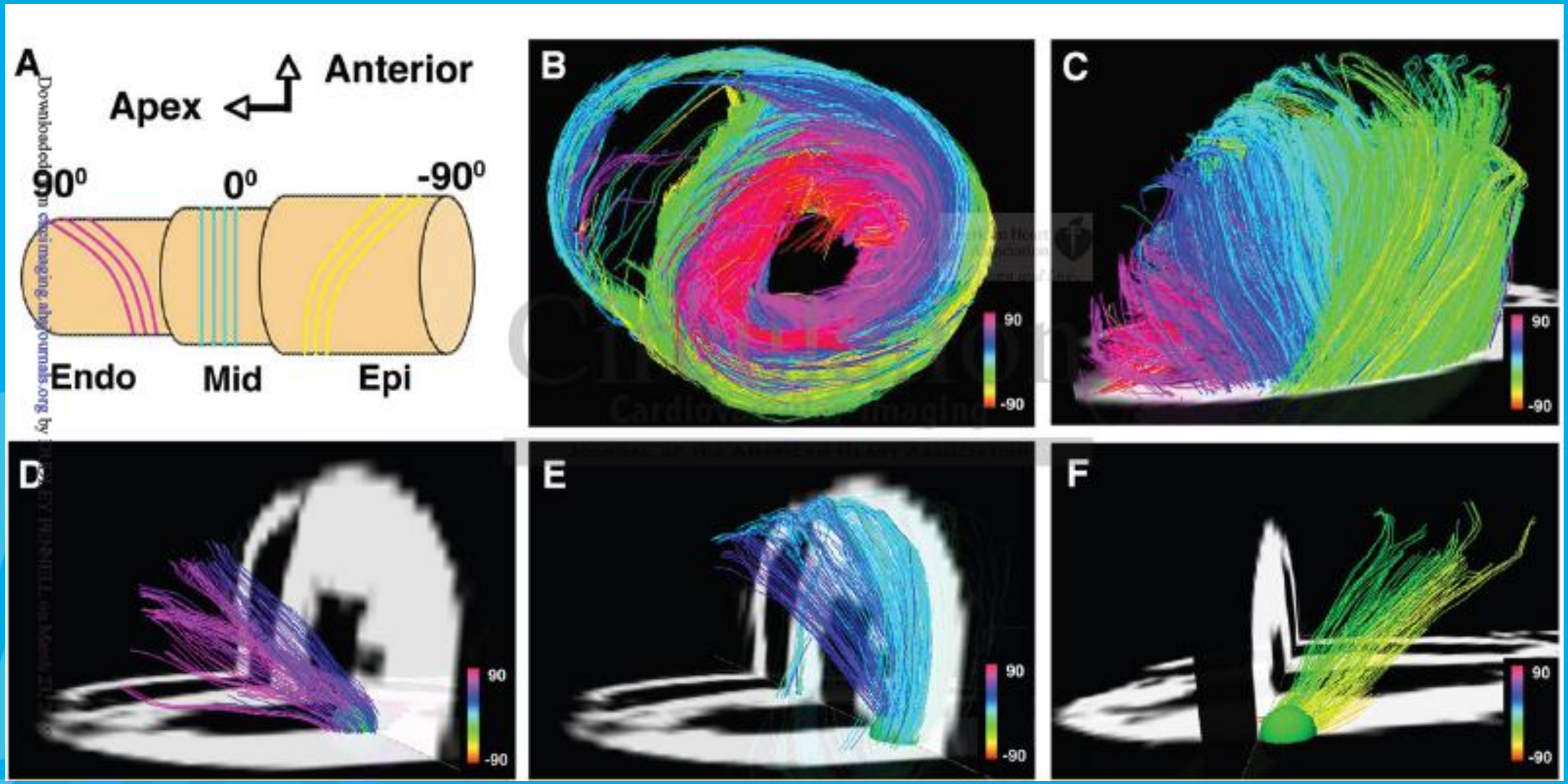
Am J Physiol Heart Circ Physiol 289: H1898–H1907, 2005;

Transmural Fiber Distribution



Greenbaum et al. Br Heart J 1981

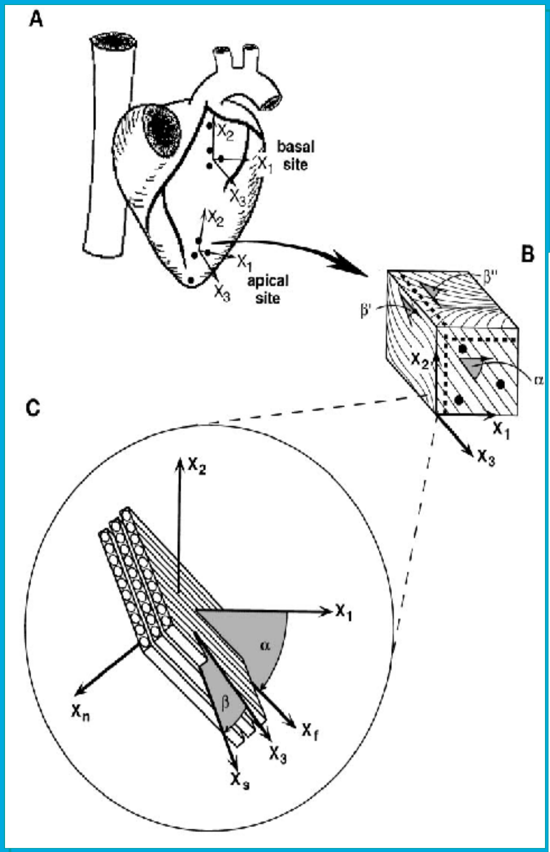
Diffusion Tractography

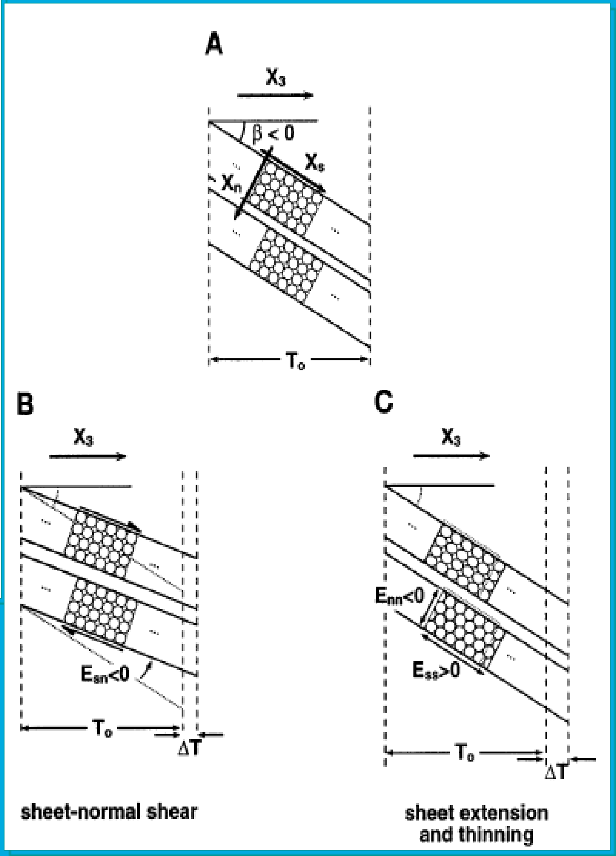


Sosnovik , Circ CV Imaging 2009

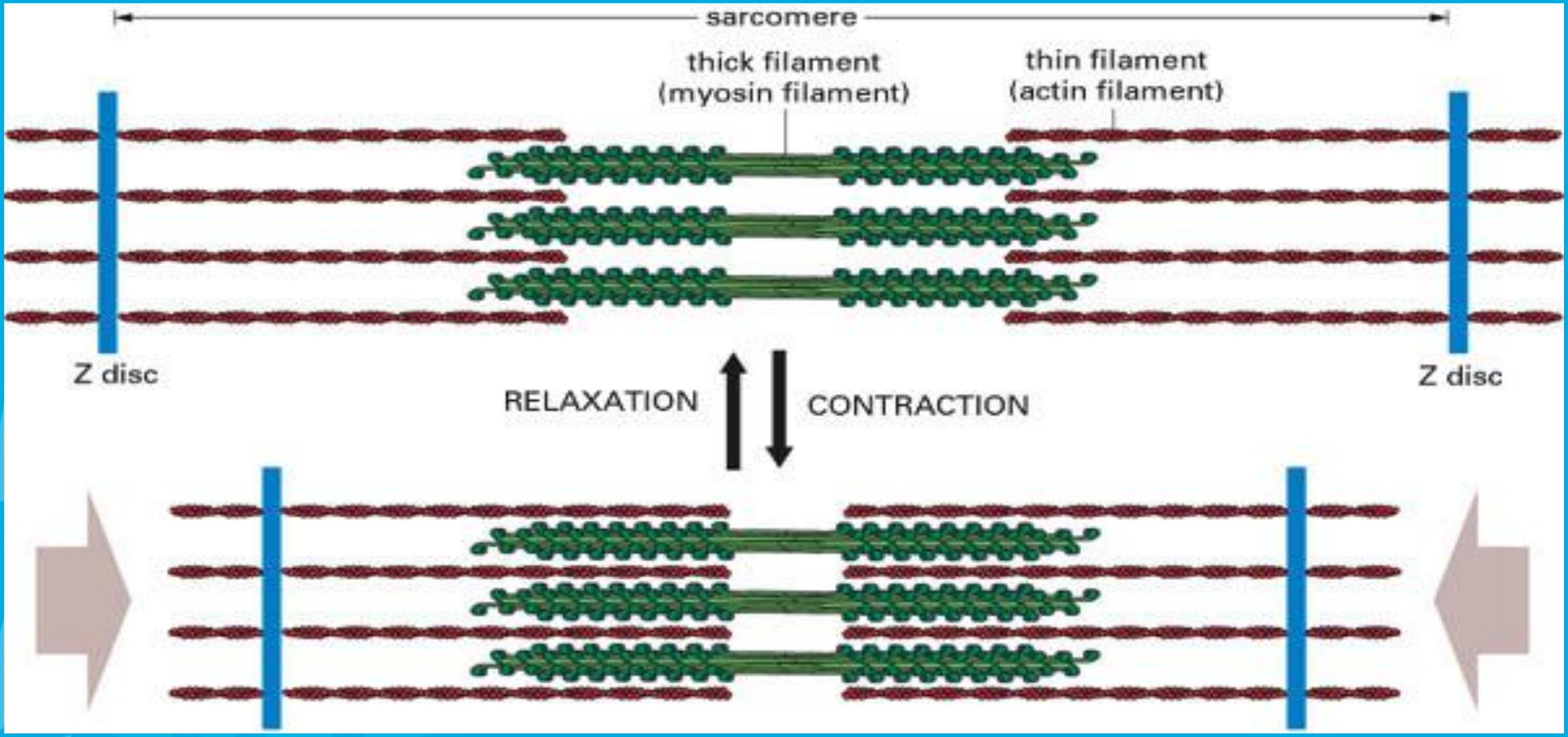
Fiber Architecture

- Laminar sheets
- Packed from base to apex
- Branching
- 4 cells thick
- Cleavage planes
- Tight coupling inside sheets

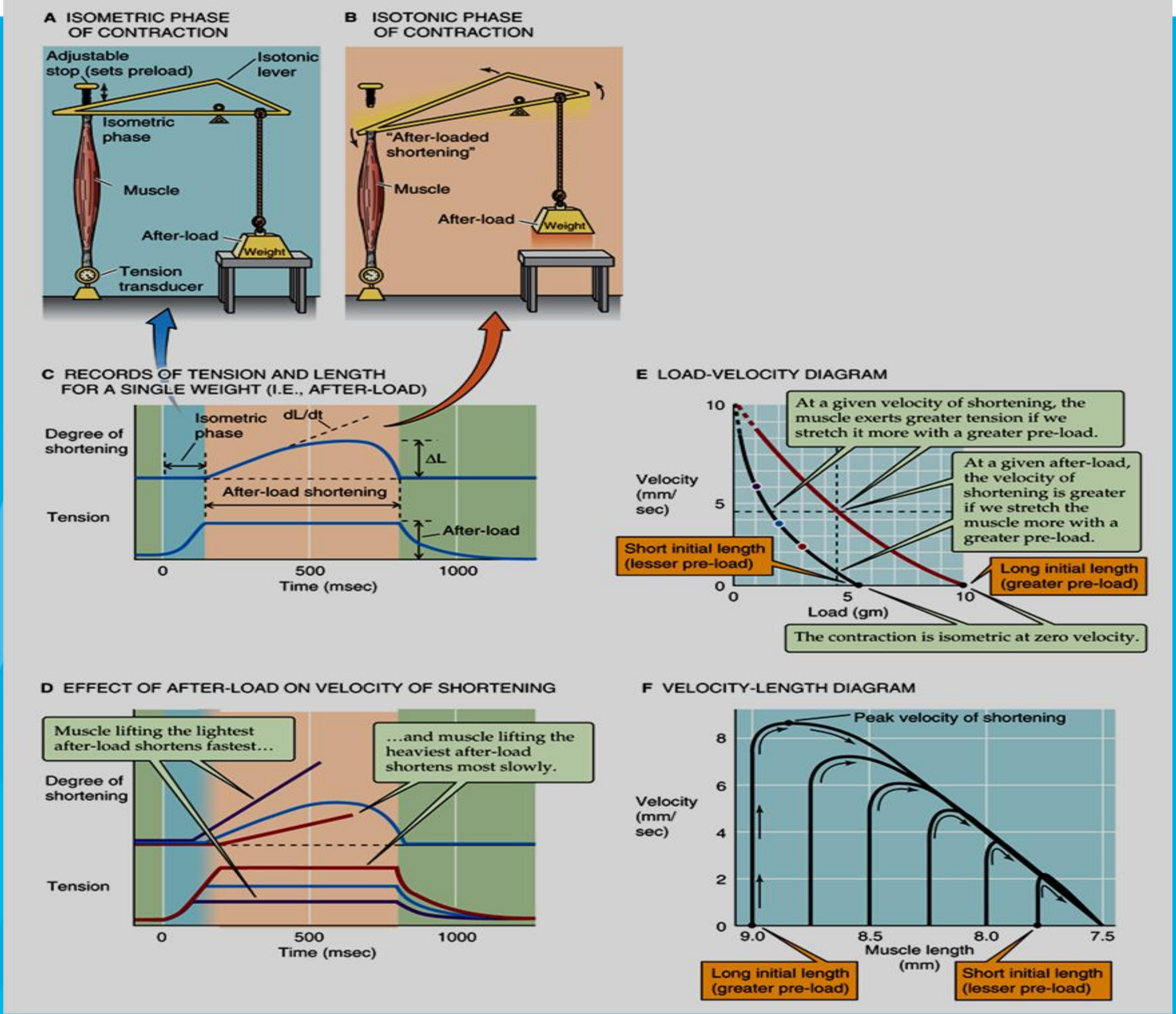


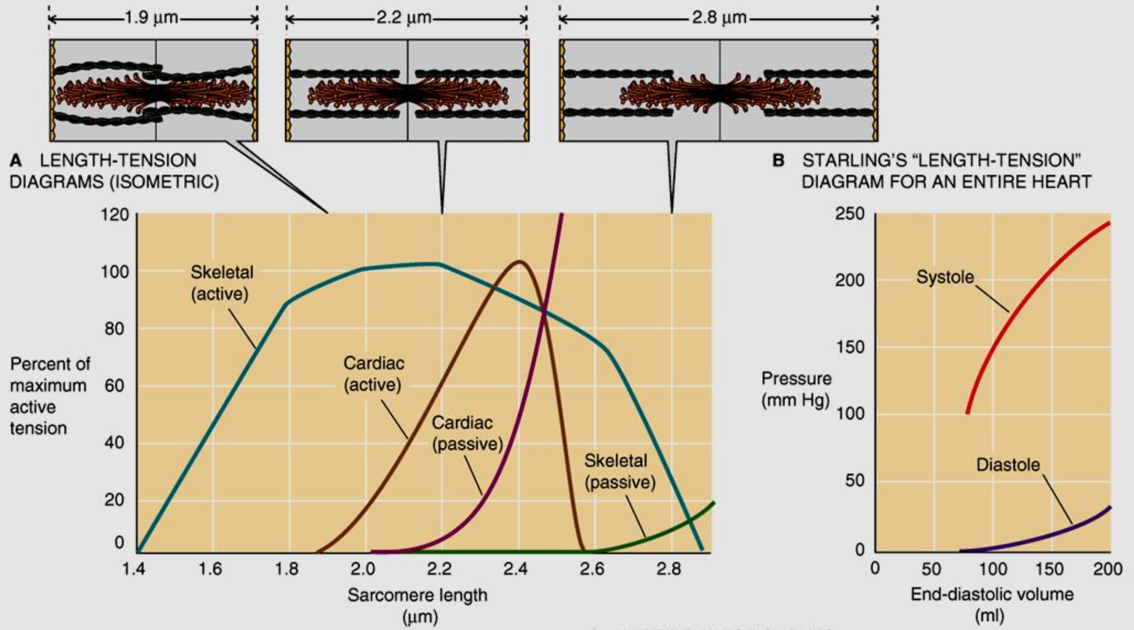


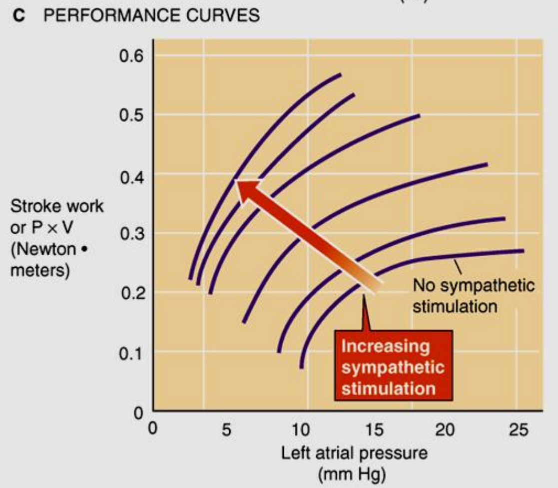
Myofilaments

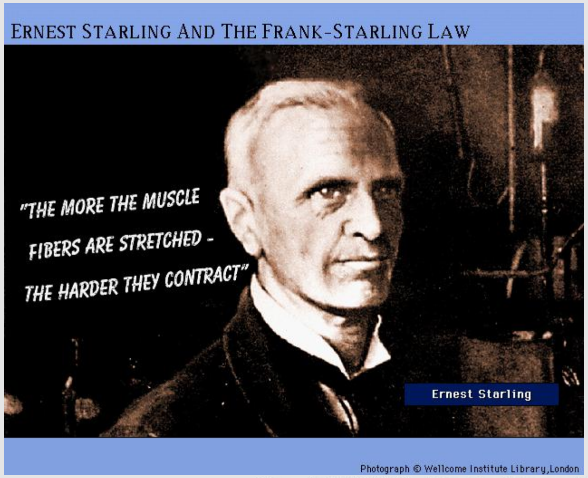


Cardiac physiology

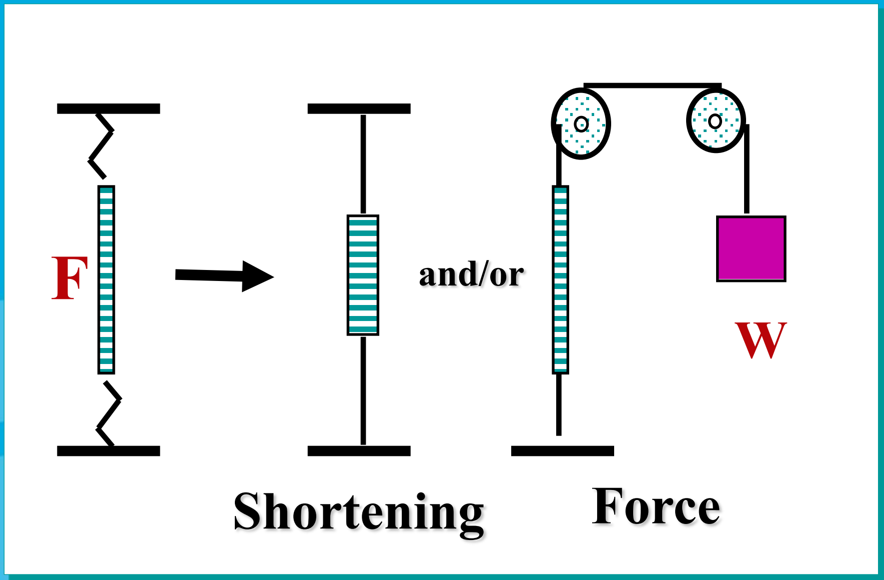


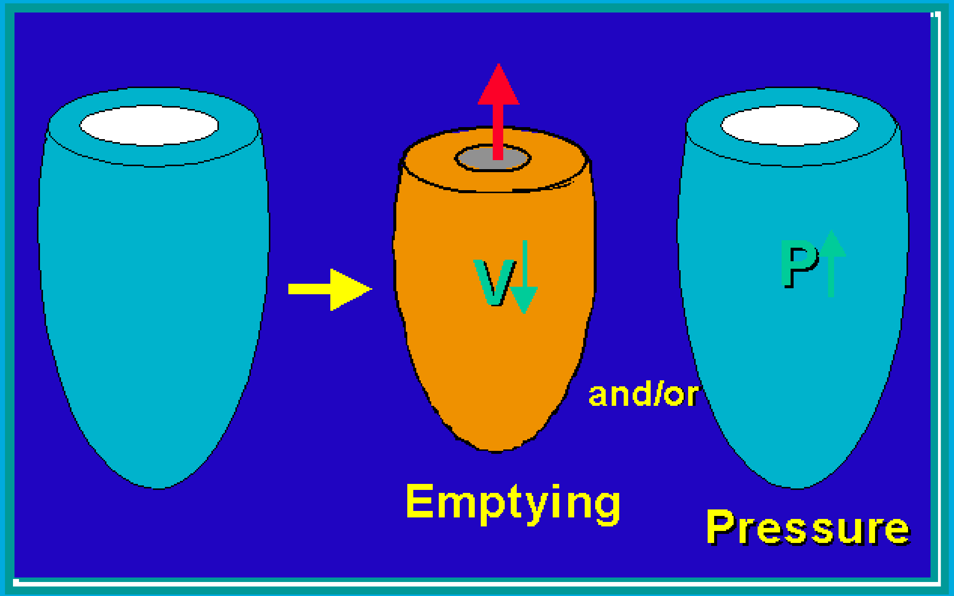

1.9 µm
2.2 µm
2.8 µm
A LENGTH-TENSION DIAGRAMS (ISOMETRIC)
Percent of maximum active tension
Skeletal (active)
Cardiac (active)
Cardiac (passive)
Skeletal (passive)
Sarcomere length (µm)
B STARLING'S "LENGTH-TENSION" DIAGRAM FOR AN ENTIRE HEART
Pressure (mm Hg)
Systole
Diastole
End-diastolic volume (ml)


C PERFORMANCE CURVES
Stroke work or P × V (Newton • meters)
No sympathetic stimulation
Increasing sympathetic stimulation
Left atrial pressure (mm Hg)


Ernest Starling And The Frank-Starling Law
"THE MORE THE MUSCLE FIBERS ARE STRETCHED - THE HARDER THEY CONTRACT"
Ernest Starling
Photograph © Wellcome Institute Library,London

Cardiac Pump

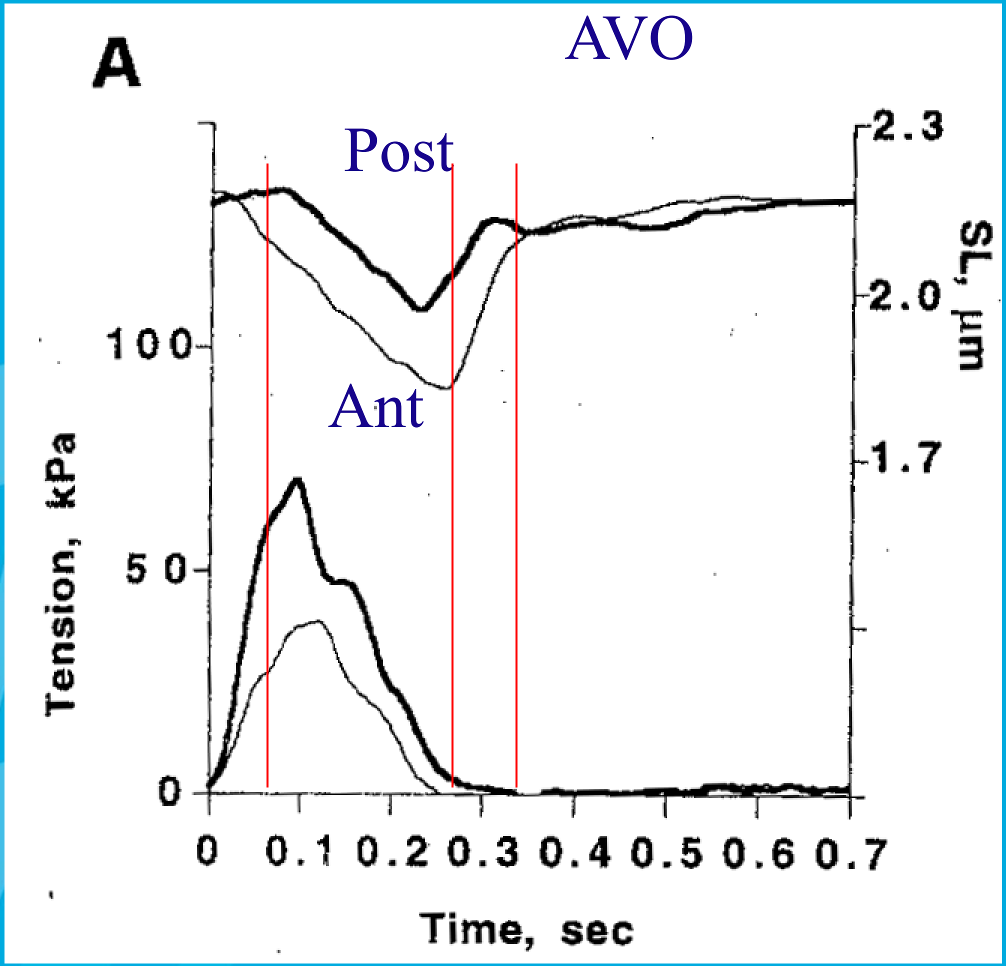


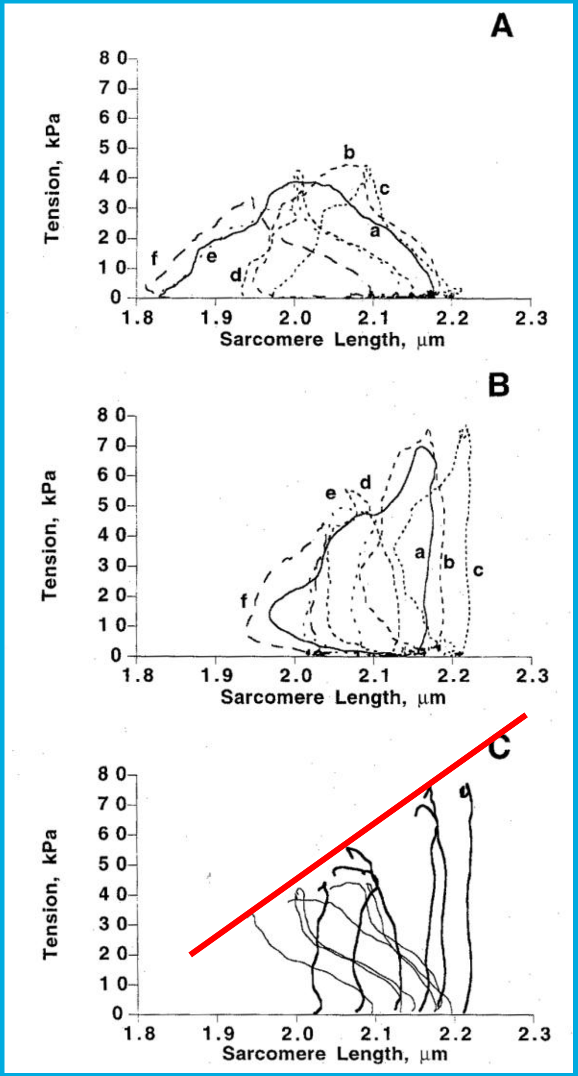


Fiber

Ventricle

Sarcomere Shortening Epicardial





Guccione et al 1997

Ventricular Pump Performance

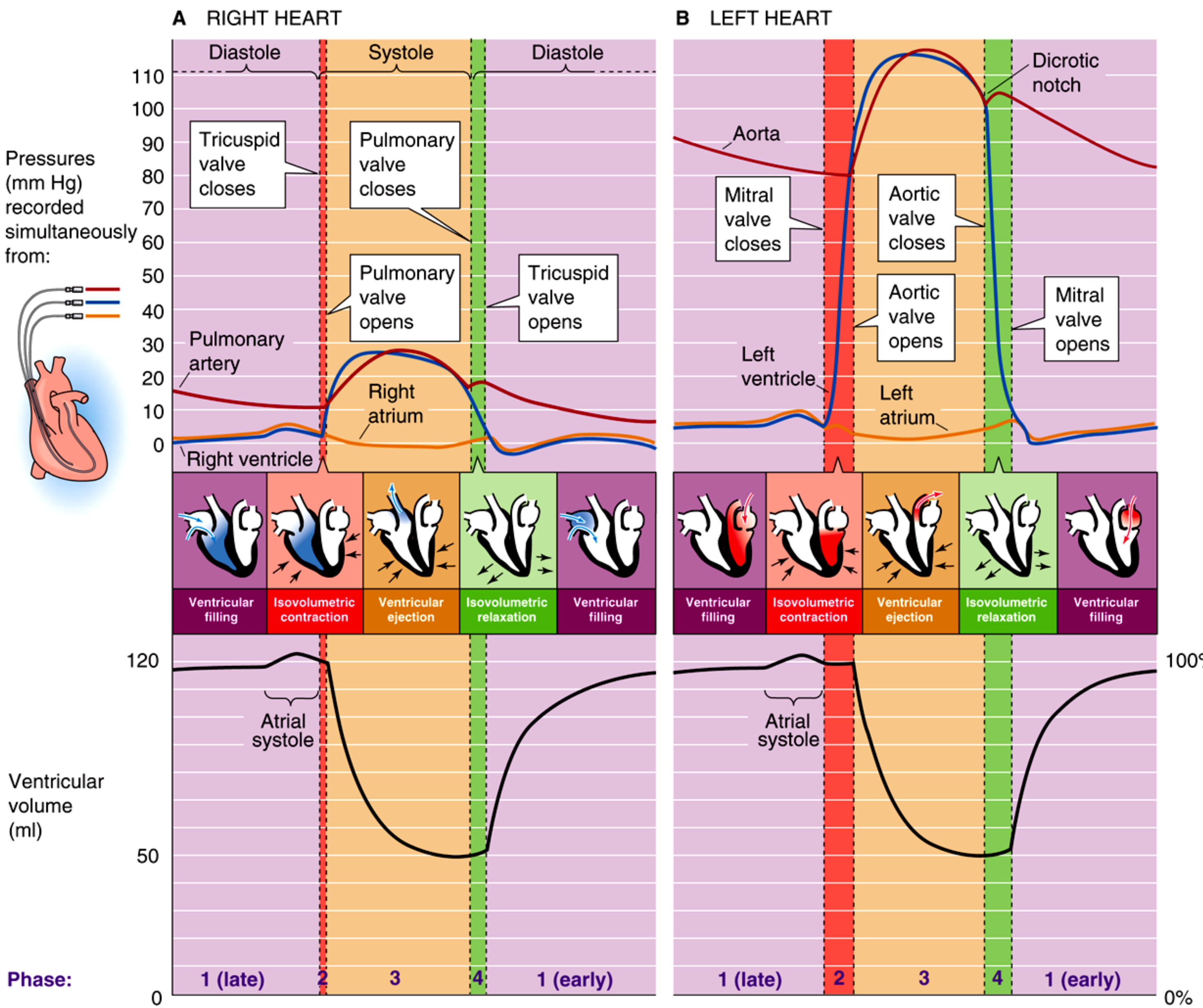
In →

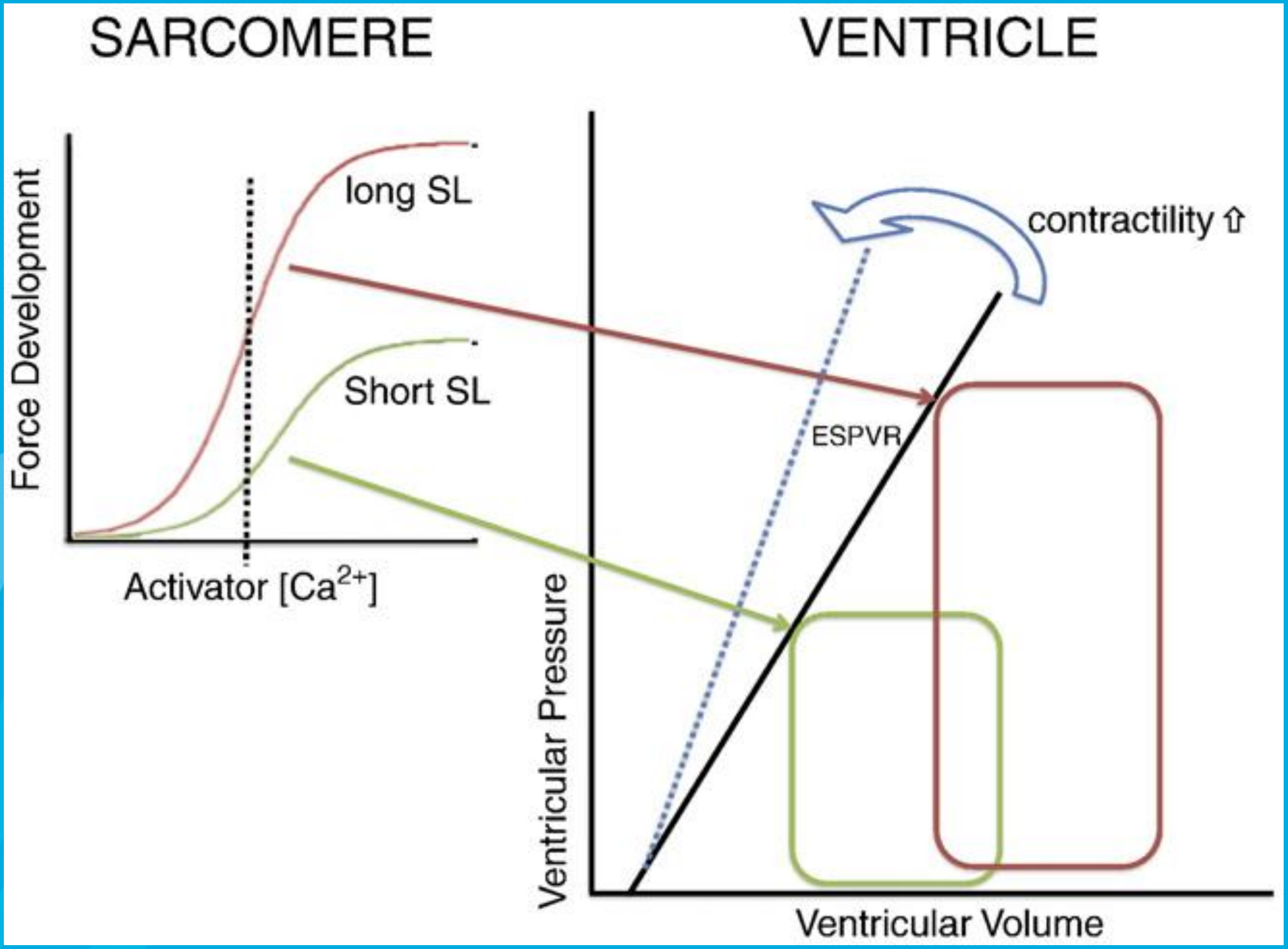
FILLING		EMPTYING		
ED volume	x	EF effective	=	stroke volume
distensibility/ compliance		contractility		
active relaxation		afterload	x	
atrial function		preload		
AV valve		structure	heart rate	
pericardium				

→ Out

diastolic function — systolic function

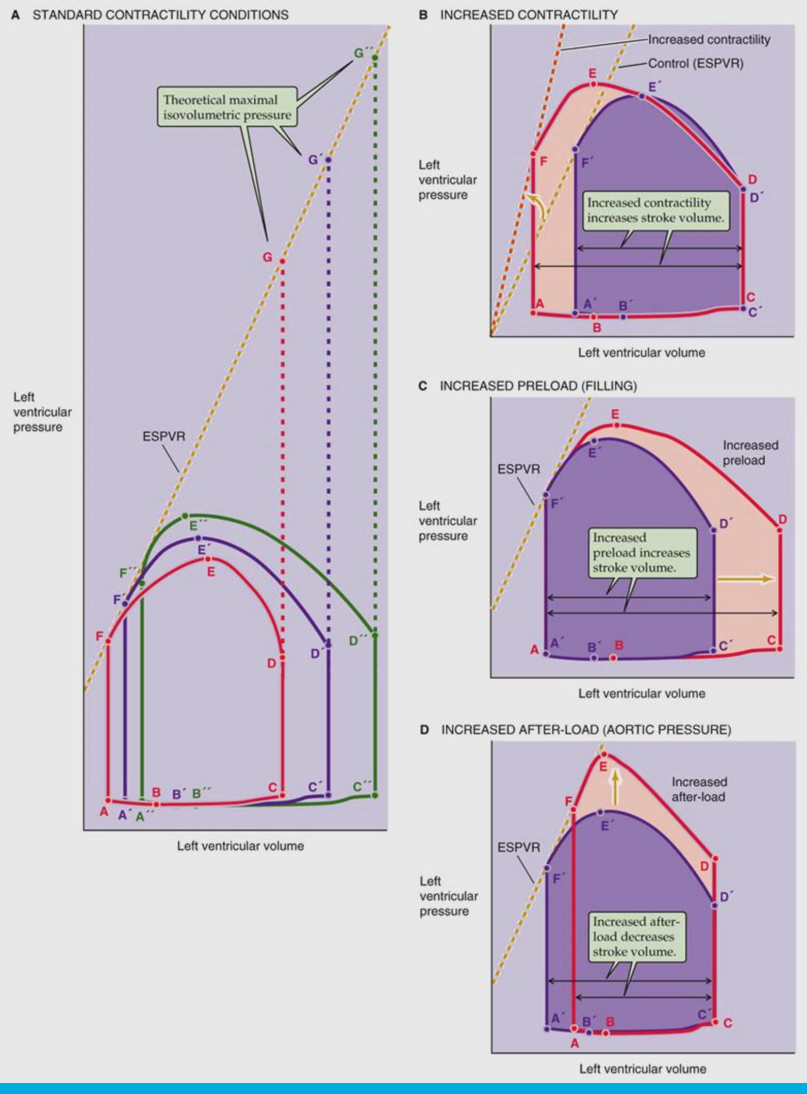
LV Pressure and Volume



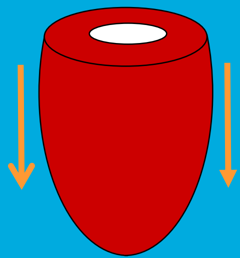


Journal of Molecular and Cellular Cardiology 48 (2010) 851–858

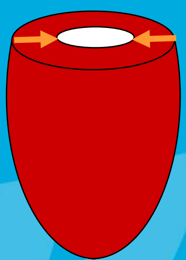
Load Dependence



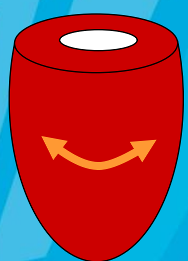
Deformation modes: What?



Longitudinal shortening



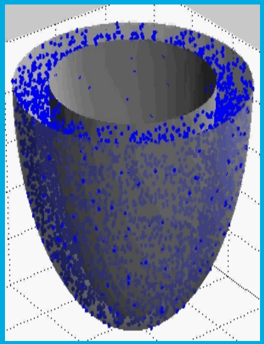
Radial thickening

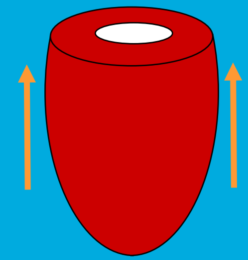


Circumferential shortening

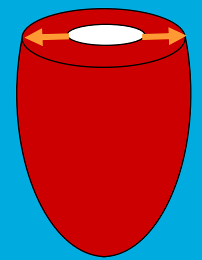
+

Endocardial inward motion for ejection

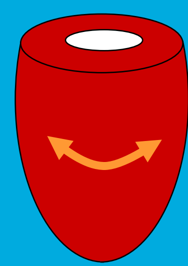




Longitudinal lengthening



Radial thinning



Circumferential lengthening

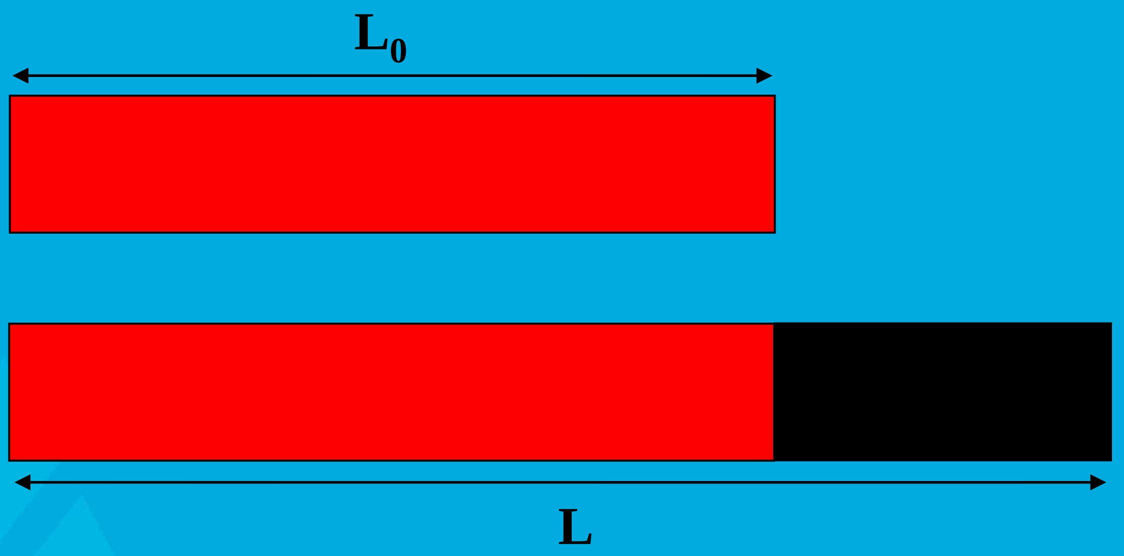
+

Endocardial outward motion for filling

+ Shearing (twisting,…) optimize transmission of fiber force/deformation

Strain: definition

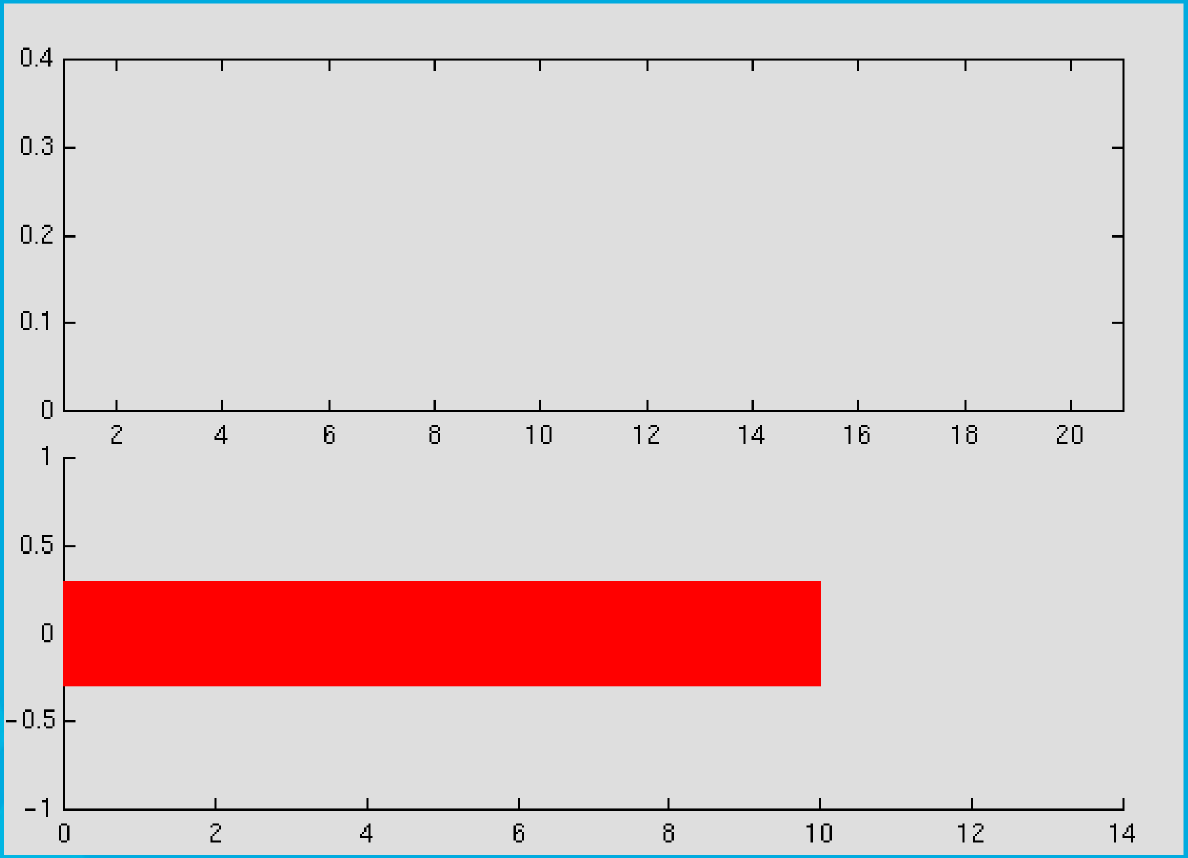
Strain (ε) = the deformation of an object expressed with respect to its original shape



$$\varepsilon = \frac{L - L_0}{L_0}$$

dimensionless

1D Lagrangian strain

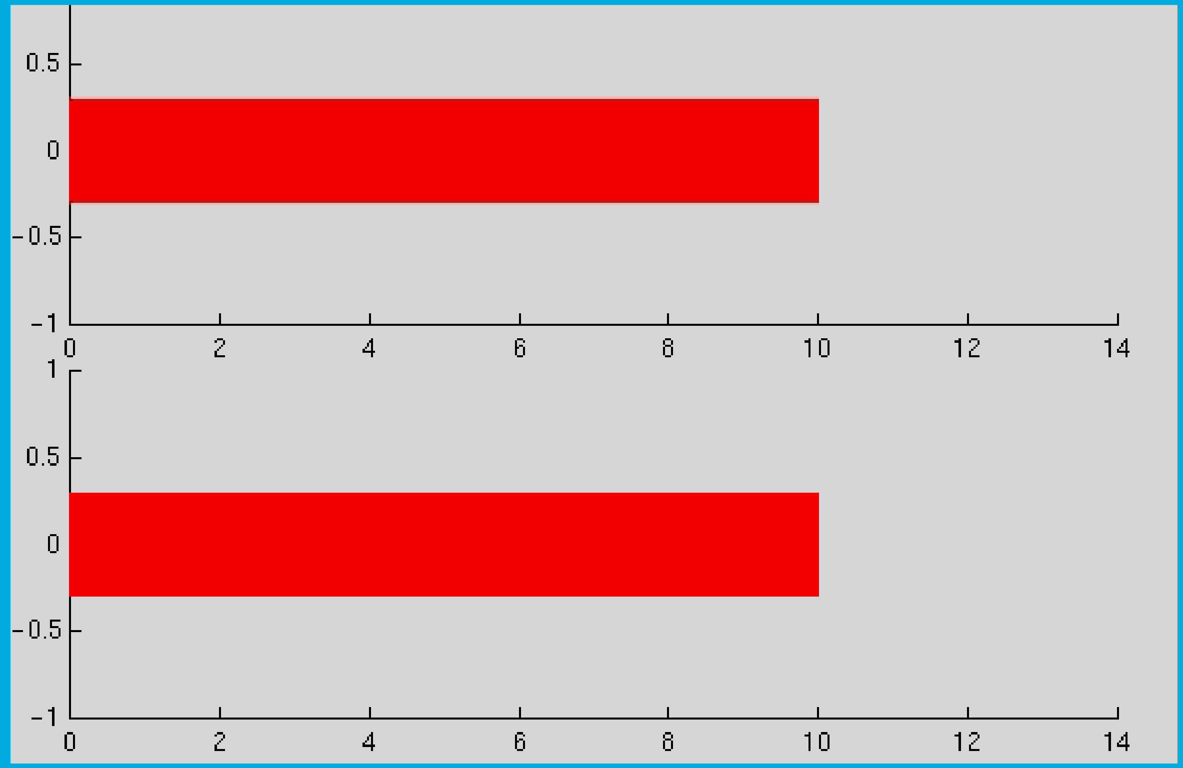


$$\varepsilon(t)=\int_{L_0}^{L}\frac{dL(t)}{L_0}=\frac{L(t)-L_0}{L_0}=\frac{L(t)}{L_0}-1$$

Strain Rate (ε)

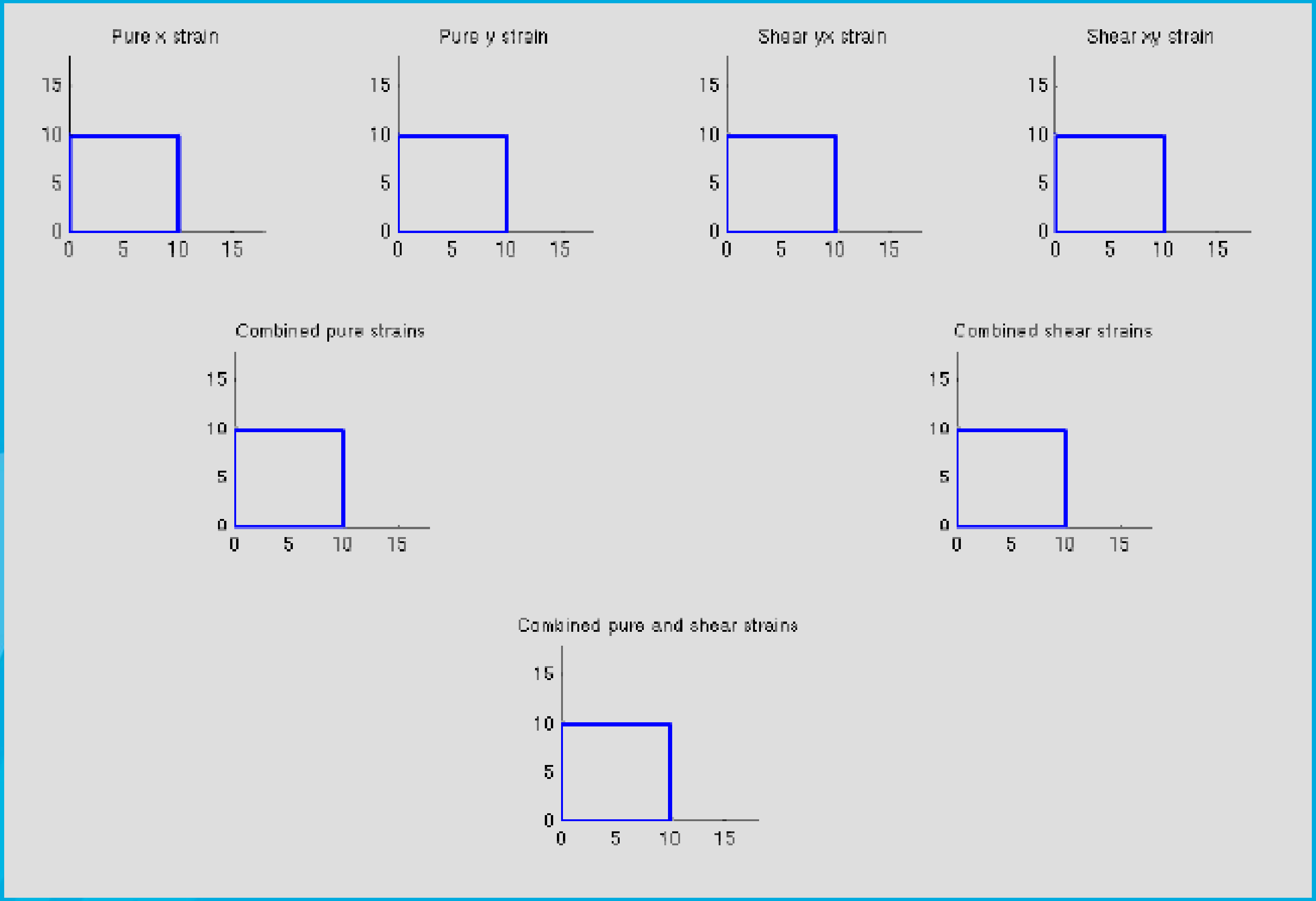
$$\frac{40\%\ \text{strain}}{1\ \text{s}}$$

$$\frac{40\%\ \text{strain}}{2\ \text{s}}$$



⇨ Average Lagrangian strain rate: $0.4\ s^{-1}$ vs. $0.2\ s^{-1}$

2D strain



For a 2D object:

4 independent strains exist

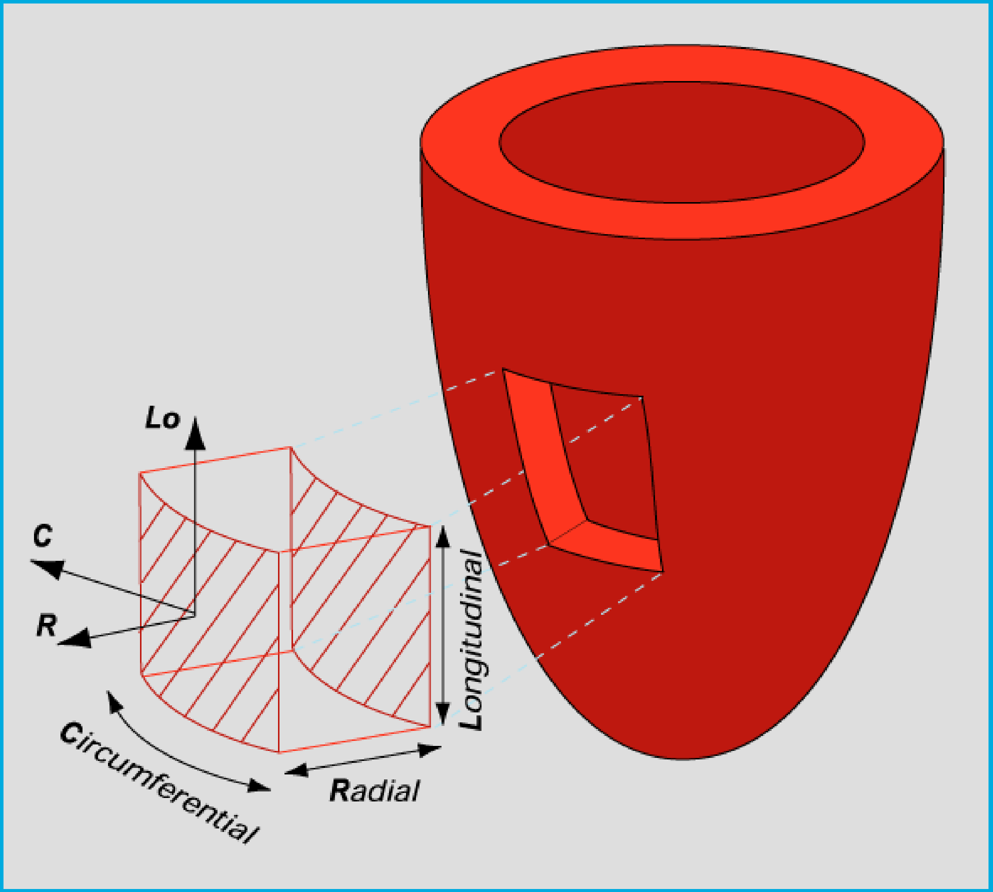
4 independent strain rates exist

Local cardiac coordinates

- Radial
- Longitudinal
- Circumferential

⇩

$$\varepsilon = \begin{bmatrix} \varepsilon_{RR} & \varepsilon_{RC} & \varepsilon_{RL} \\ \varepsilon_{CR} & \varepsilon_{CC} & \varepsilon_{CL} \\ \varepsilon_{LR} & \varepsilon_{LC} & \varepsilon_{LL} \end{bmatrix}$$



Facilitates physical interpretation and mathematics of the strain values
(e.g. RR = wall thickening; CC/LL = circumferential/longitudinal shortening)

Two components to function

Boundary conditions

Ventricular wall

-Perfusion
-Activation

- Fiber structure
- Tissue Elasticity
- Geometry
  (thickness & shape)

- Segment Interaction

Interaction with cardiovascular system

pressure/volume loading

- Venous return
- Valvular function
- Arterial impedance

Intrinsic 'function'

Fiber mechanics

Fiber force development

Myocyte Shortening

Ventricular 'function'

Regional
Myocardial mechanics

Global
Pump performance

Wall stress ⟷ **Ventricular Pressure**

Wall deformation shortening/lengthening thickening/thinning ⟷ **Ventricular Volume Ejection/Filling**

Stress / **Force**

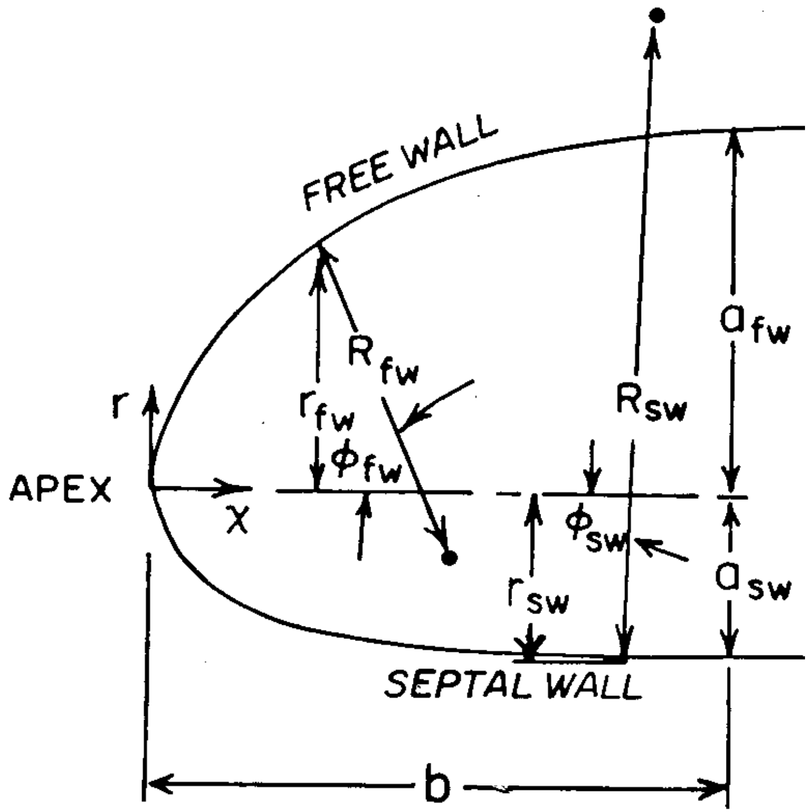
Deformation / **Strain**

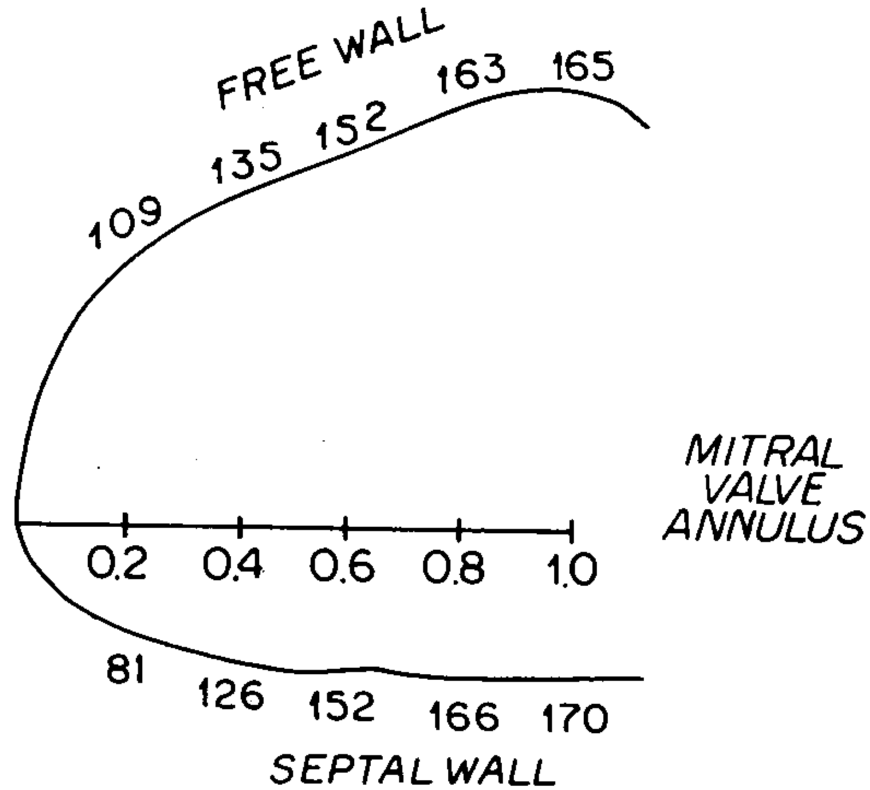
MVI/SRI

To understand the mechanics, we need to combine these two components

Non-uniform systolic stress in the LV wall

Radius of curvature greater in septum

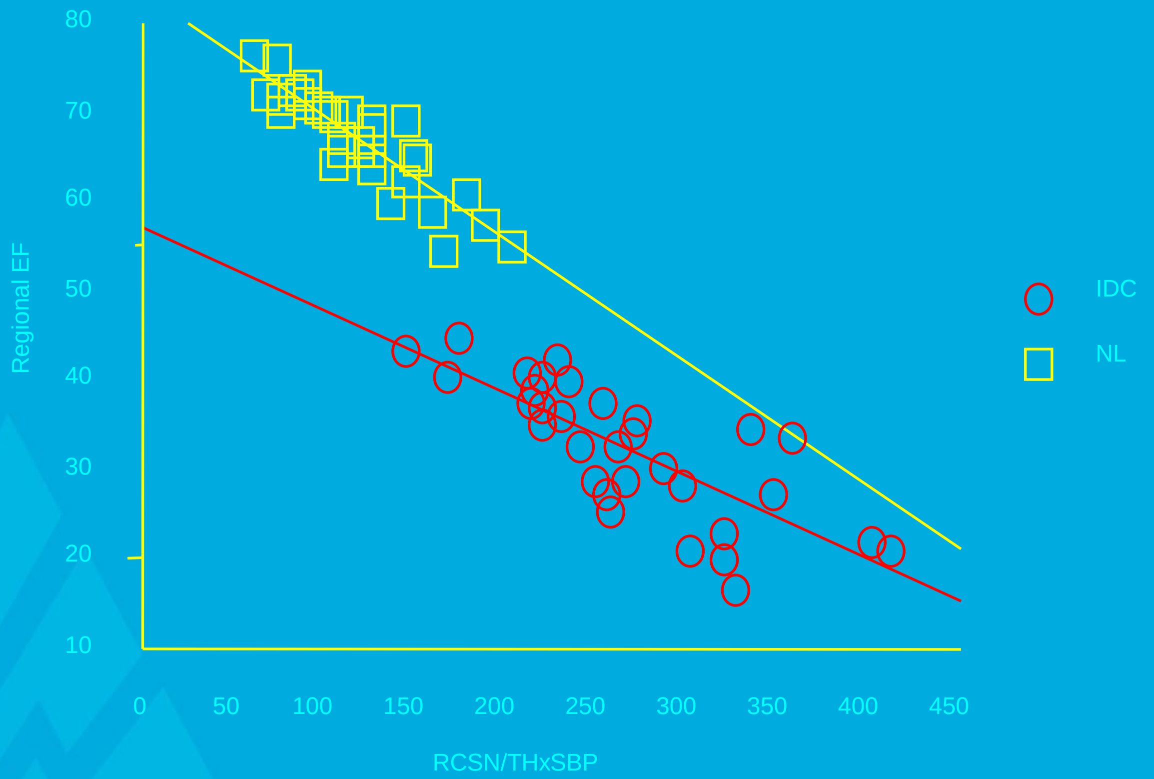




From echocardiography and cuff brachial BP in 9 subjects

Heng MK et al, Am Heart J 1985; 110: 84

Stress-Strain



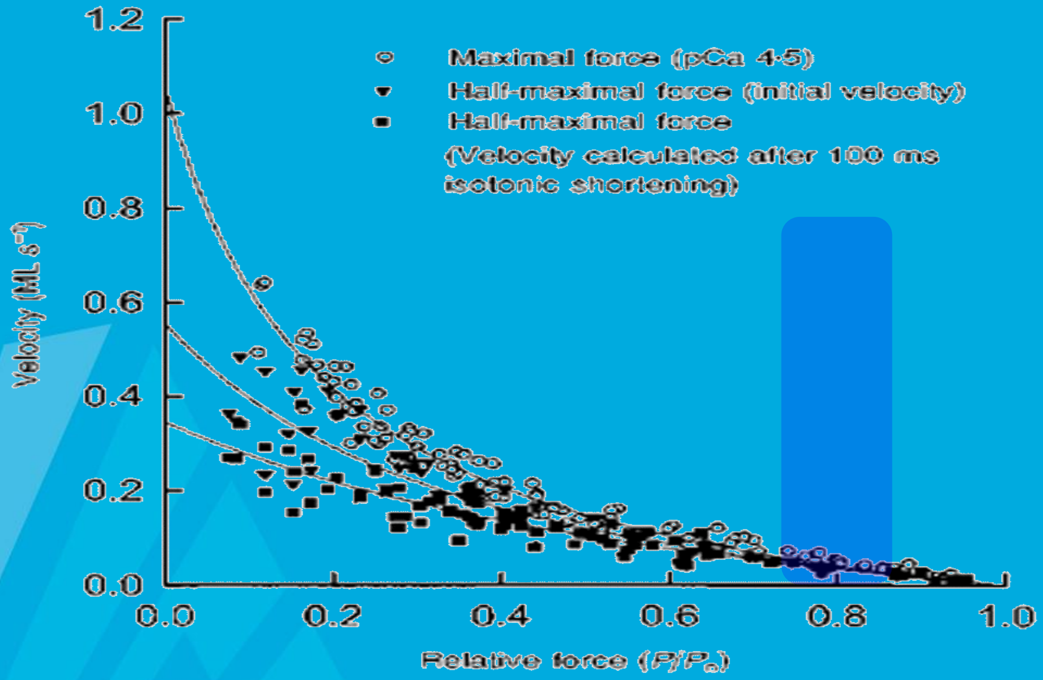
REF = 57.377 - .094 * RCSN/THxSBP; R^2 = .606 (IDC)

REF = 83.396 - .139 * RCSN/THxSBP; R^2 = .795 (NL)

Strain Rate Load dependence

- **Radial/Circumferential strain rate**

➢ Dependent on myocardial contractility

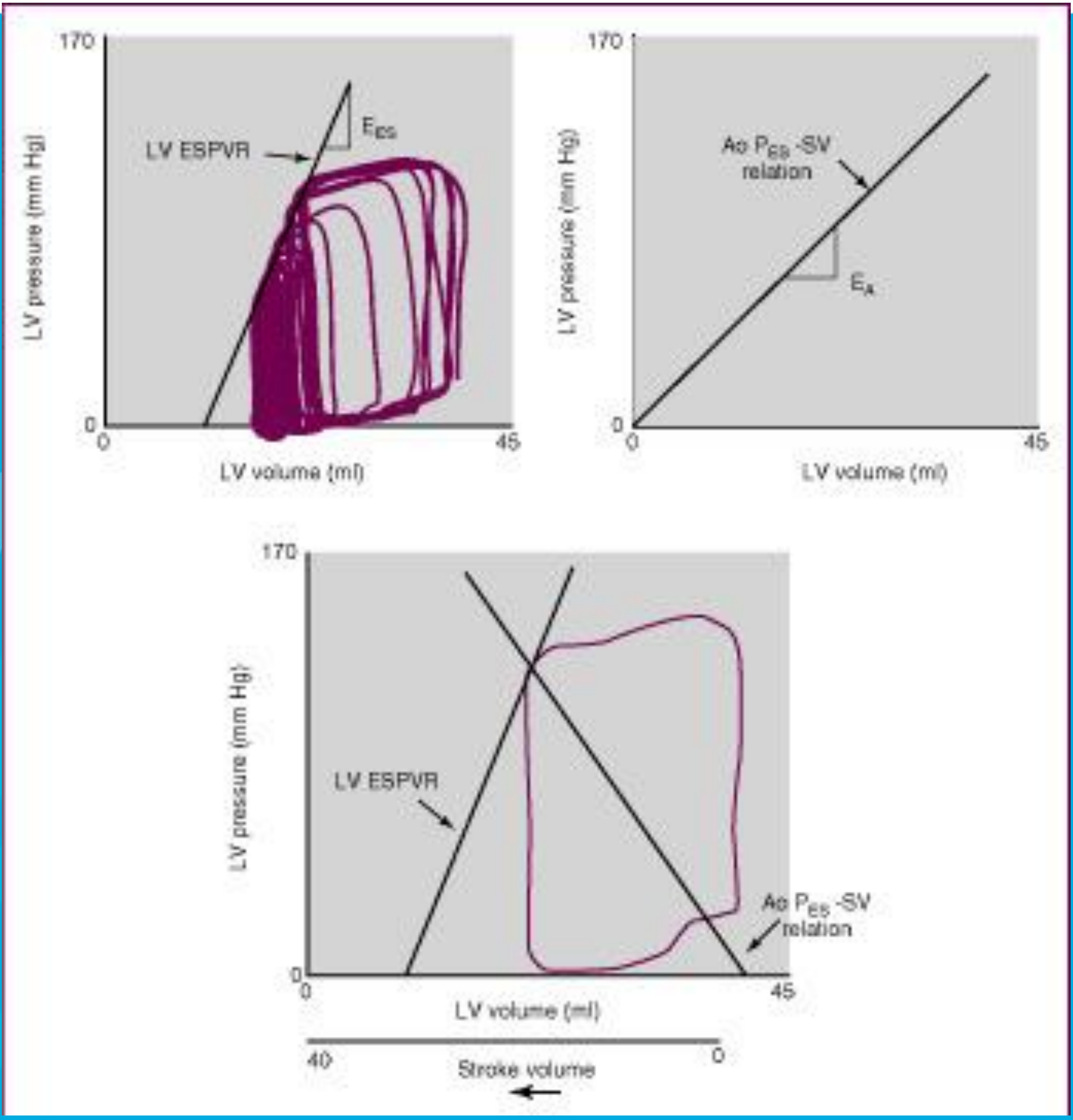


- **Radial strain rate**

➢ Secondarily dependent on LVMV

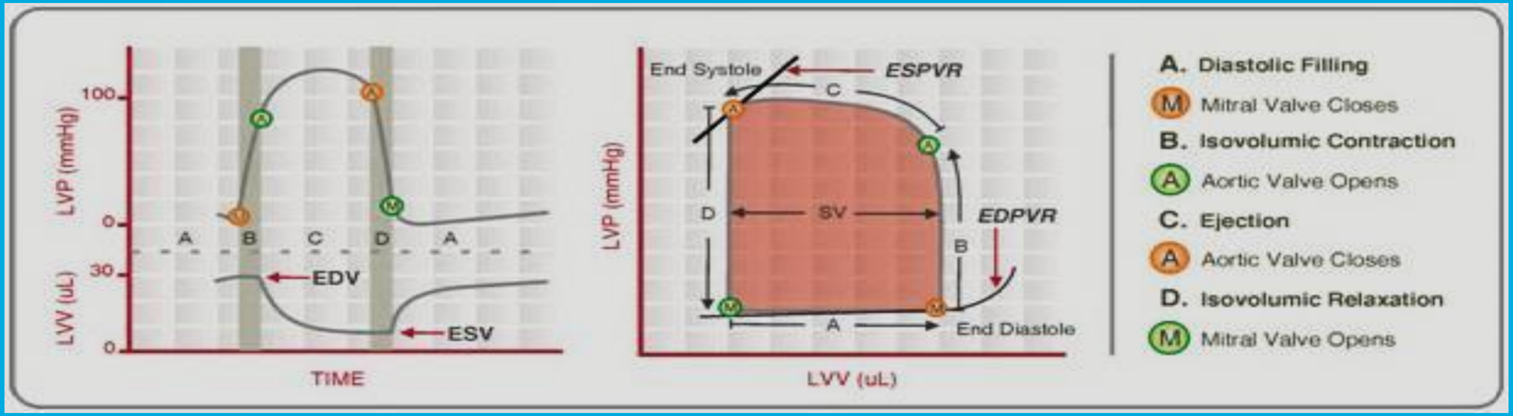
-> increased LV mass – decreased radial LV function

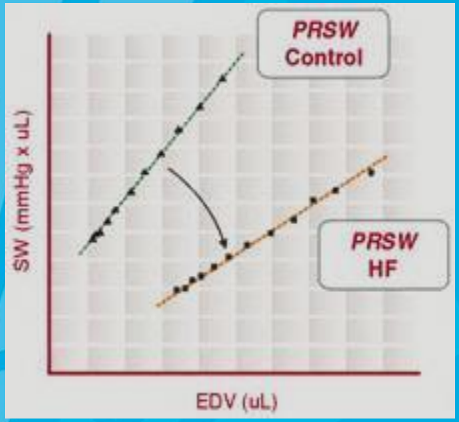
=> Strain rate as reliable and valuable surrogate of true ventricular contractility

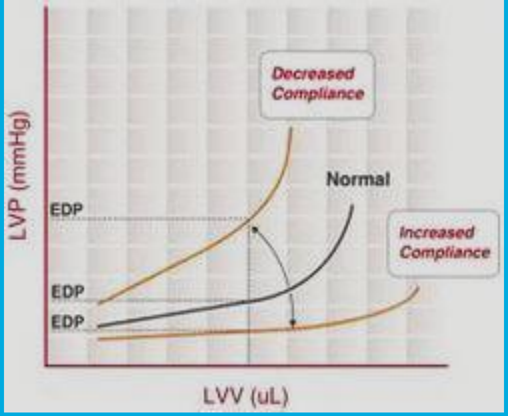


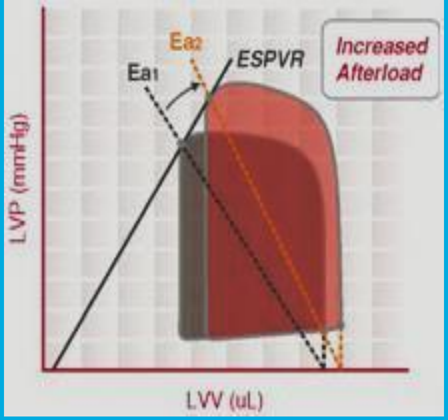
170
LV ESPVR
E_ES
LV pressure (mm Hg)
0
0
45
LV volume (ml)
170
Ao P_ES -SV relation
E_A
LV pressure (mm Hg)
0
0
45
LV volume (ml)
170
LV ESPVR
LV pressure (mm Hg)
Ao P_ES -SV relation
0
0
45
LV volume (ml)
40
0
Stroke volume

Ventricular performance









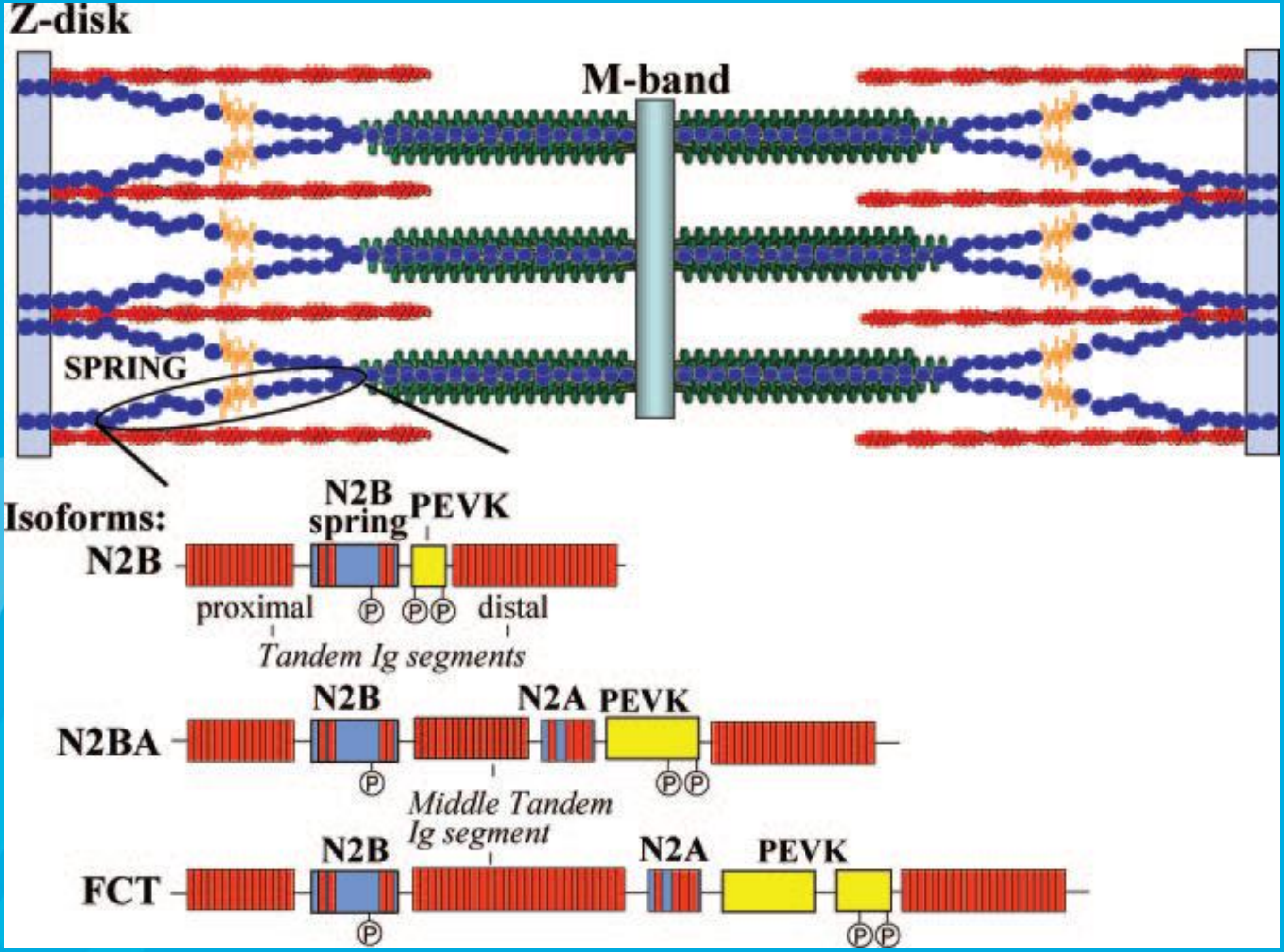
PRSW <-> EDP/EDV <-> Ea = ESP/SV

linear index of myocardial contractility

measure for preload

measure for afterload

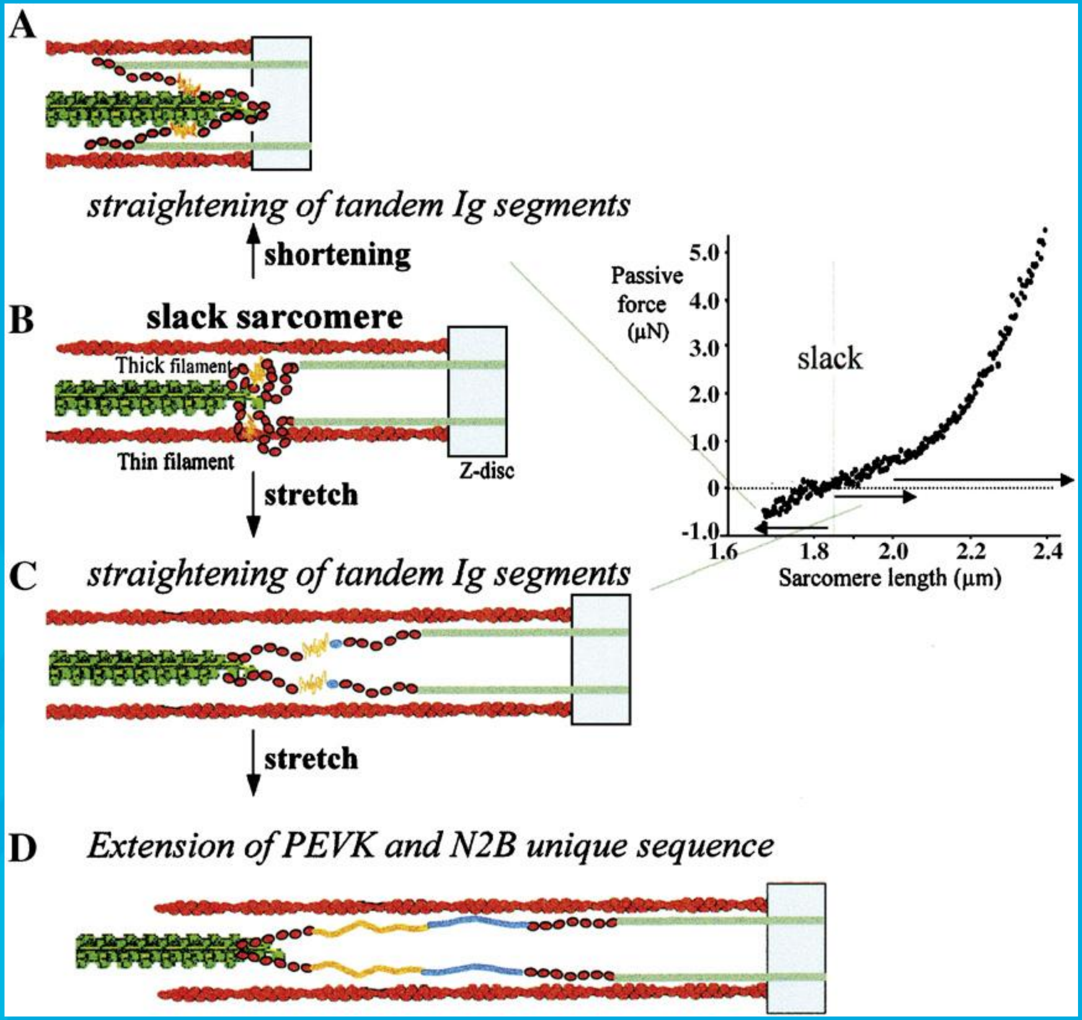
Titin molecule



Circled P’s indicate phosphorylatible sites.

Circulation 2010;121;2137-2145

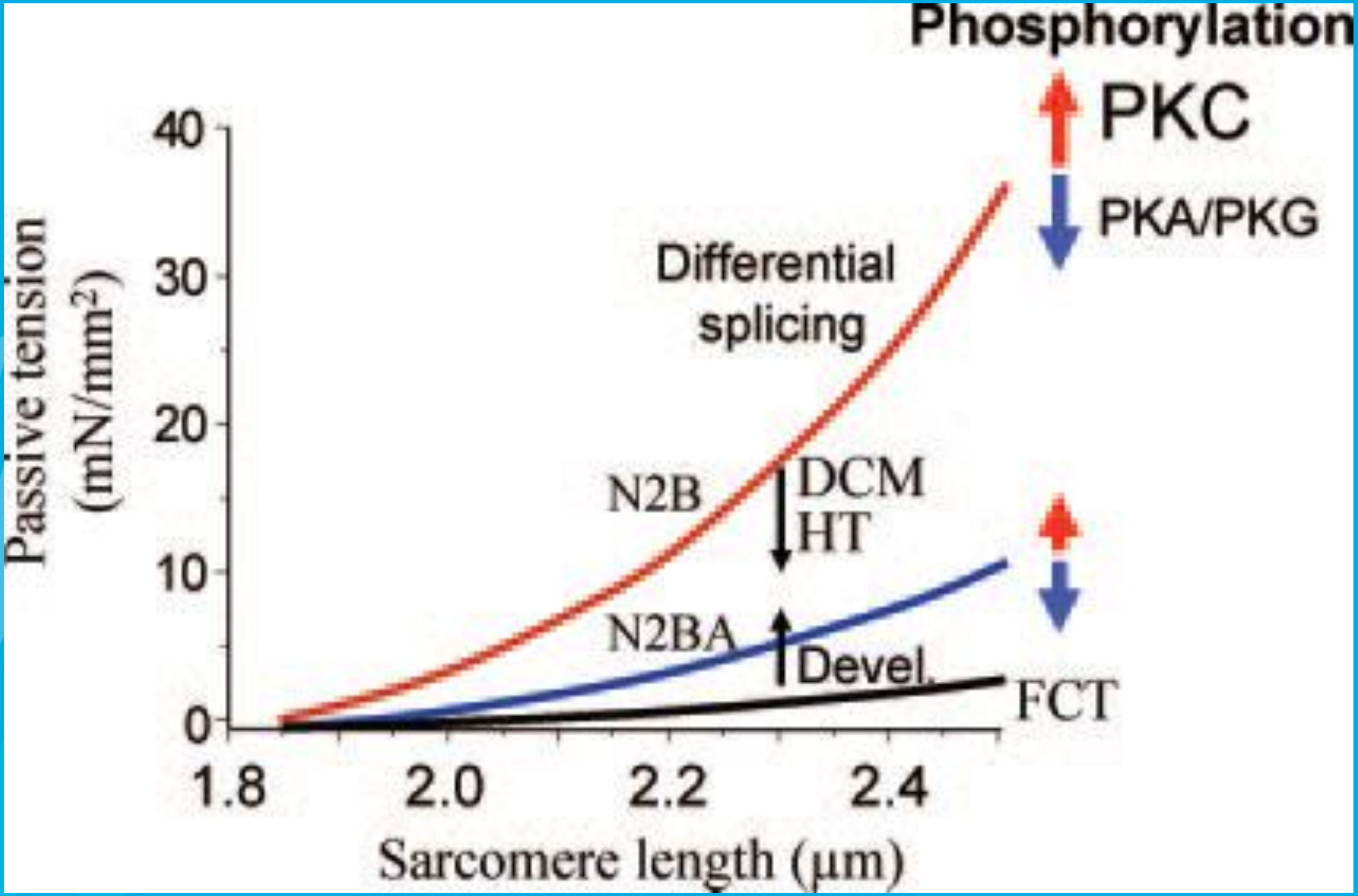
Stretching Titin



Stretching of the sarcomere from slack length (panel B) results in sequential extension of tandem Ig (panel C) and then PEVK and N2B elements (panel C), each of which is responsible for a segment of the sarcomere length (SL)–passive force relation (right). Shortening below slack length (panel A) results in reverse extension of titin with development of a restoring force

Clinica Chimica Acta 375 (2007) 1–9

Tuning Titin

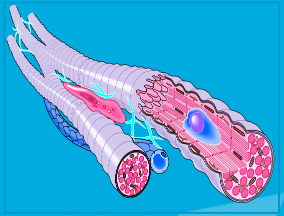


Circulation 2010;121;2137-2145

Summary

Perfusion
Activation

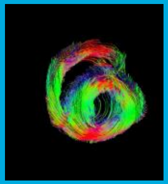
active force development within the fibres 1



cavity pressure development 2

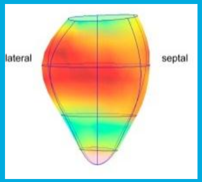
FIBRE ORIENTATION
Fibre rearrangements
for optimal pressure built-up
(shape change during IVC)

15% FIBRE SHORTENING
TO 60% EJECTION FRACTION



GEOMETRY
shape, wall thickness

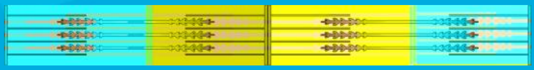
Volumes (preload)



TISSUE CHARACTERISTICS
e.g. ELASTICITY
(collagen matrix, titin)

Systemic
resistance
AFTERLOAD

SEGMENT INTERACTION



Regional mechanical boundary conditions

3
Ejection by wall deformation

Global mechanical boundary conditions