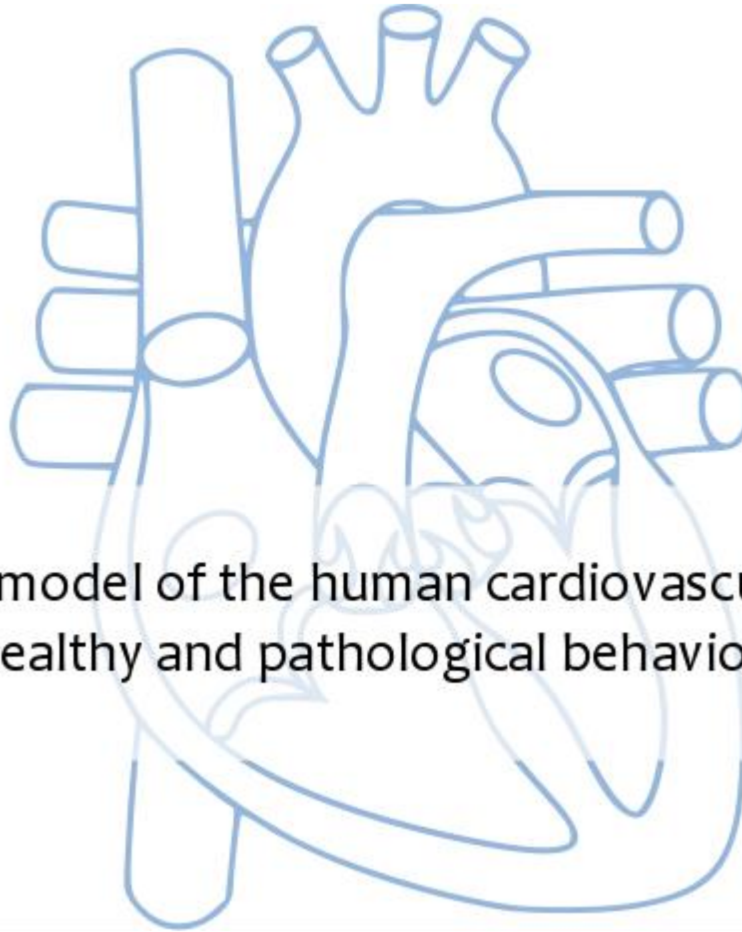
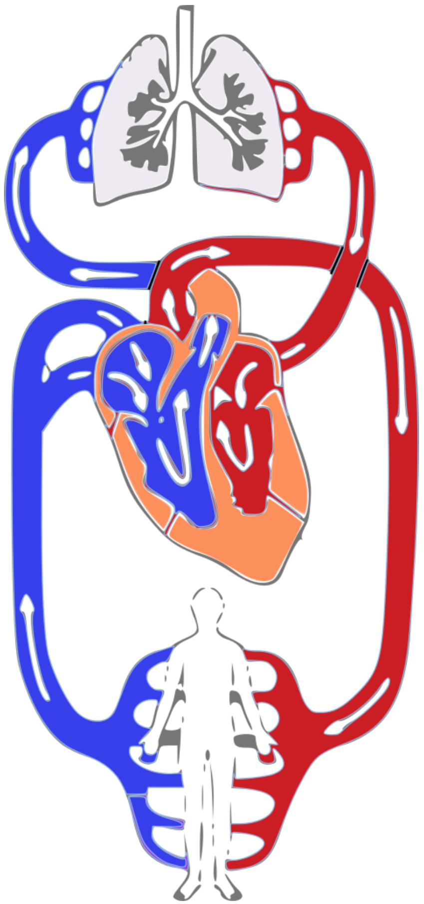
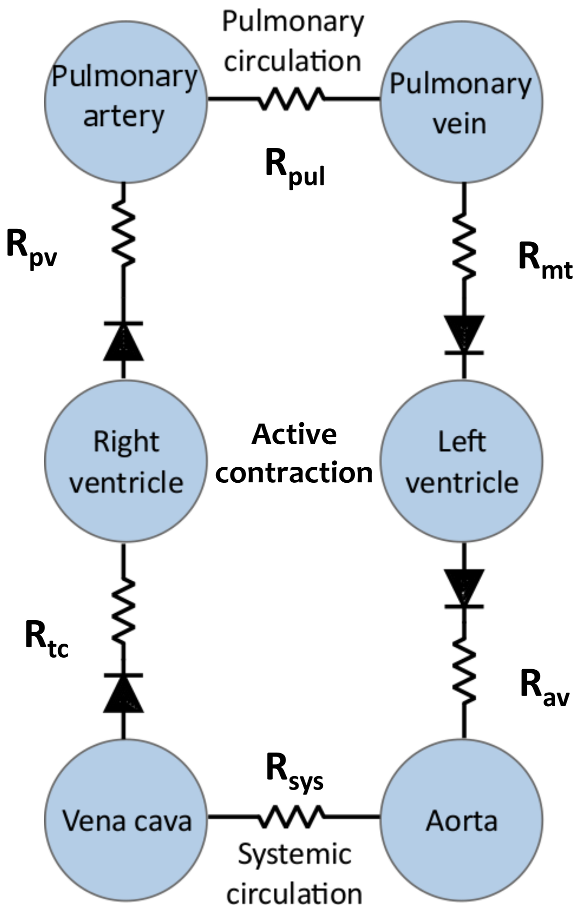


Multiscale model of the human cardiovascular system: healthy and pathological behaviors

Sarah Kosta

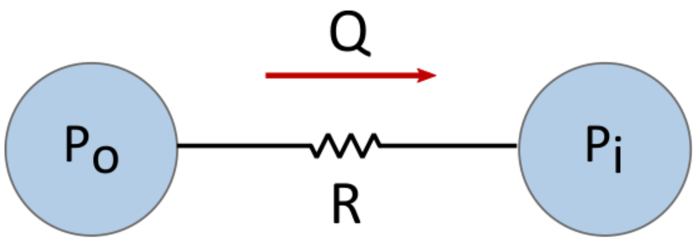
Cardiovascular system model (CVS)





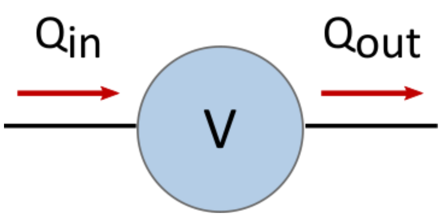
Hemodynamics

- Flow through the vessels



$$Q = \frac{P_o - P_i}{R}$$

- Volume variation



$$\frac{dV}{dt} = Q_{in} - Q_{out}$$

- Cardiac valves (mitral, tricuspid, aortic and pulmonary)

 = unidirectionnality of the blood flow

Hemodynamics

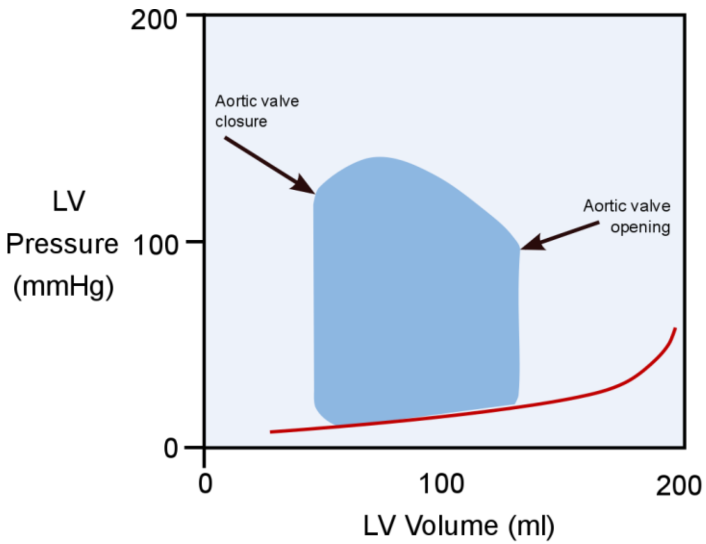
- Pressure-volume relationship :
  - Passive chamber : $P = E\,.V$ → elastance of the chamber
  - Active chamber (both ventricles) : ~~$P = E\,.V$~~

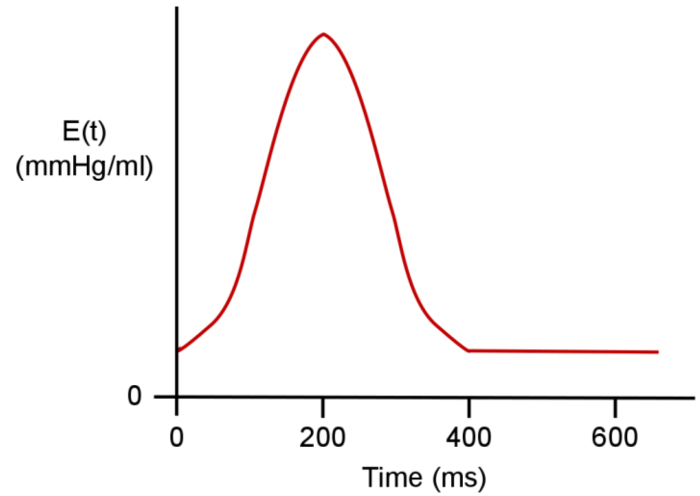
→ Varying-elastance model

$$P = E(t)\,.V$$

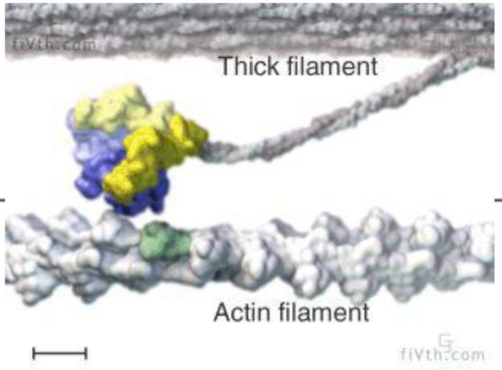
↓

Input function

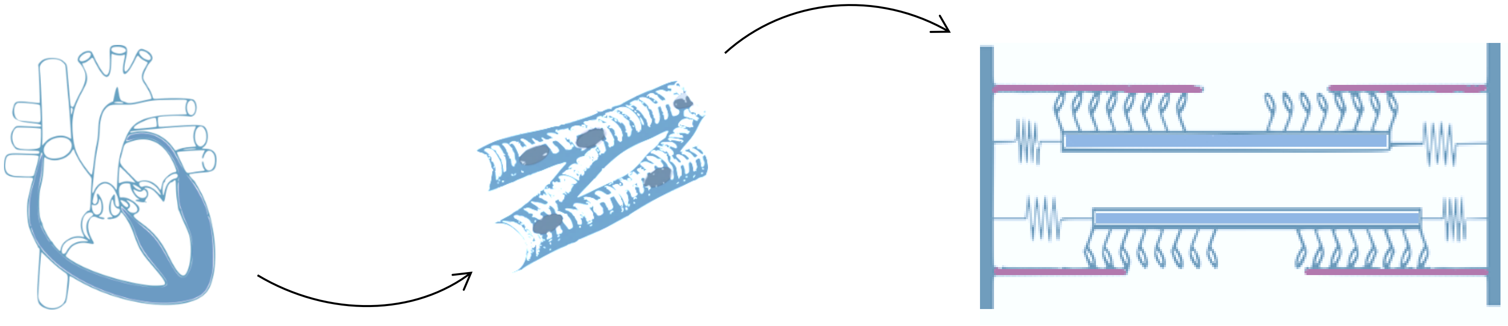




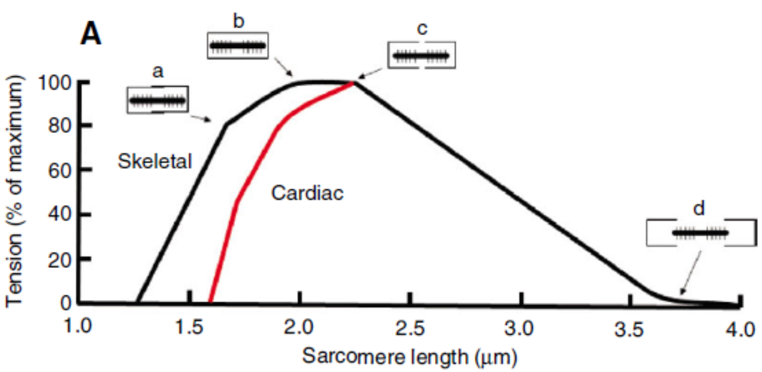
Cardiac contraction



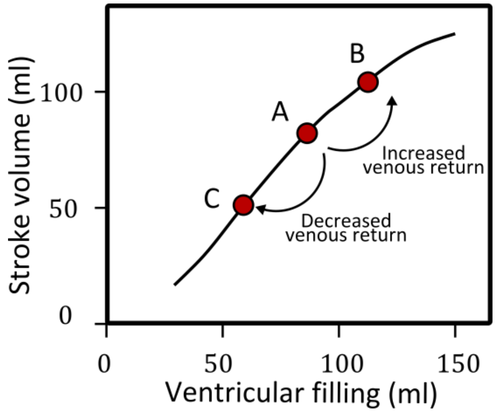
- From macroscopic to microscopic scale



- From microscopic to macroscopic properties: Franck-Starling law



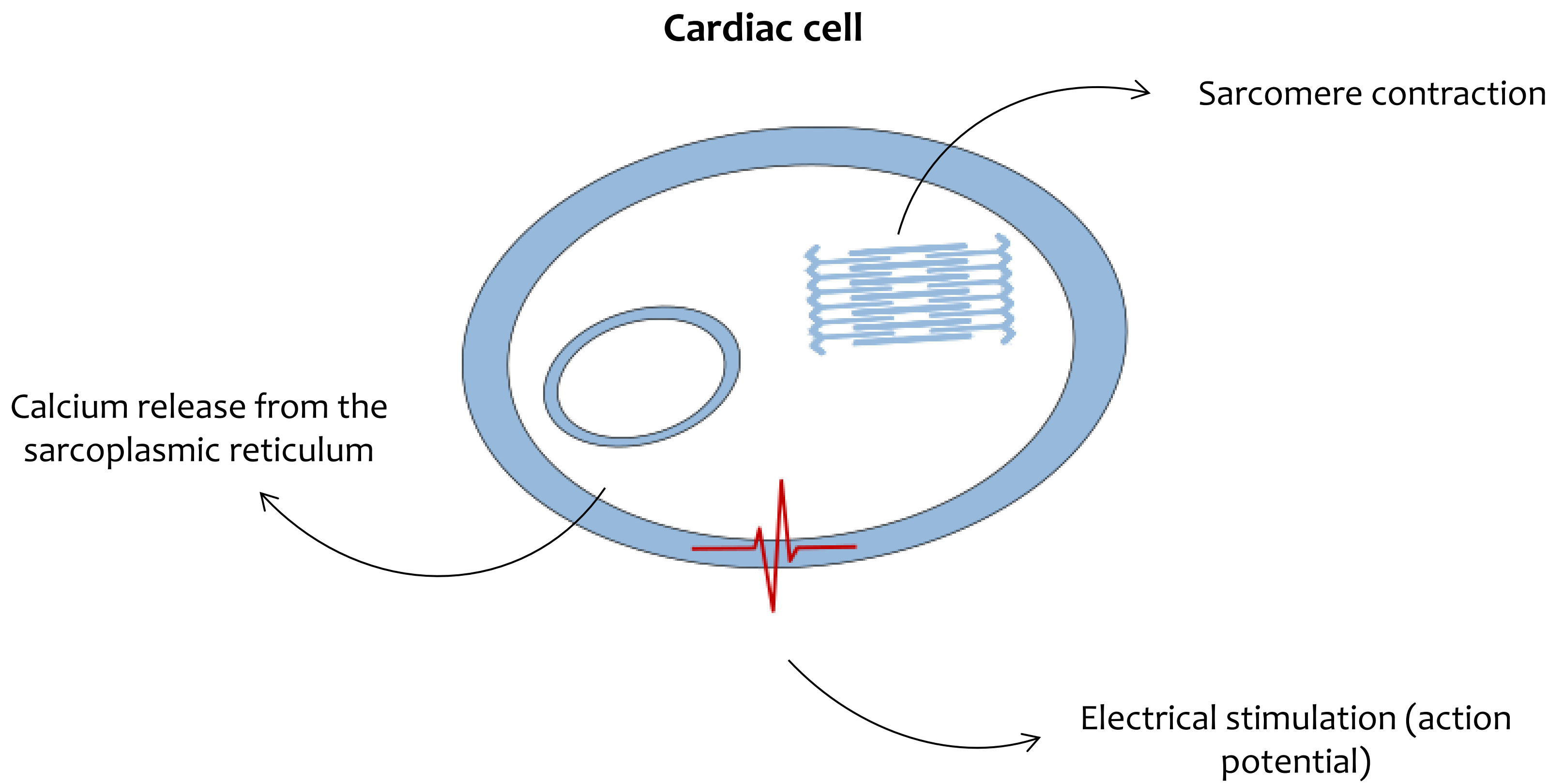
Shiels, H. a & White, E. The Frank-Starling mechanism in vertebrate cardiac myocytes. *J. Exp. Biol.* **211,** 2005–2013 (2008).



Adapted from Klabunde, R. (2011). Cardiovascular physiology concepts. Lippincott Williams & Wilkins.

Modeling cardiac contraction

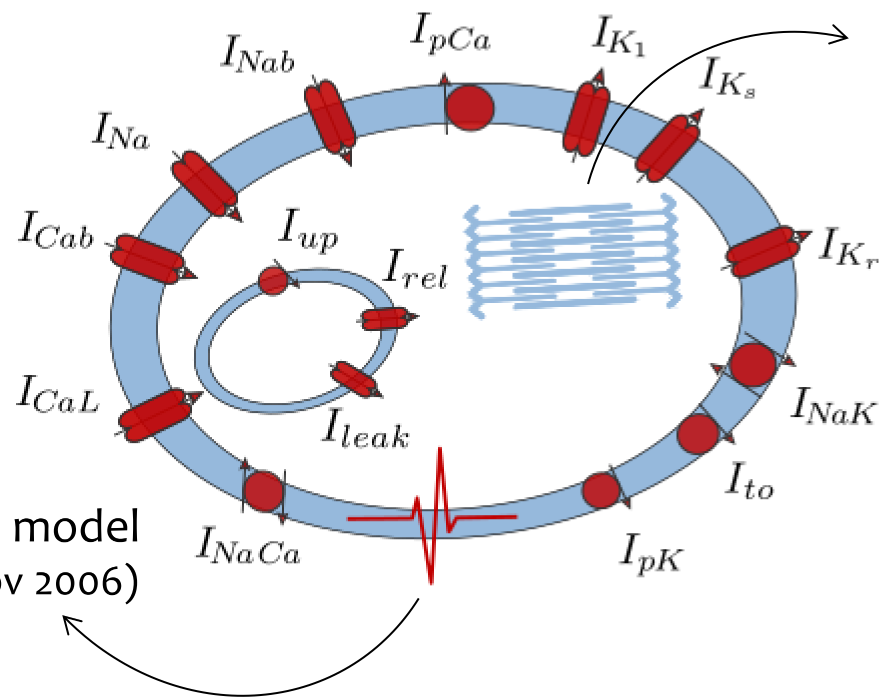
~~Varying elastance model~~ → cell-based model



Modeling cardiac contraction

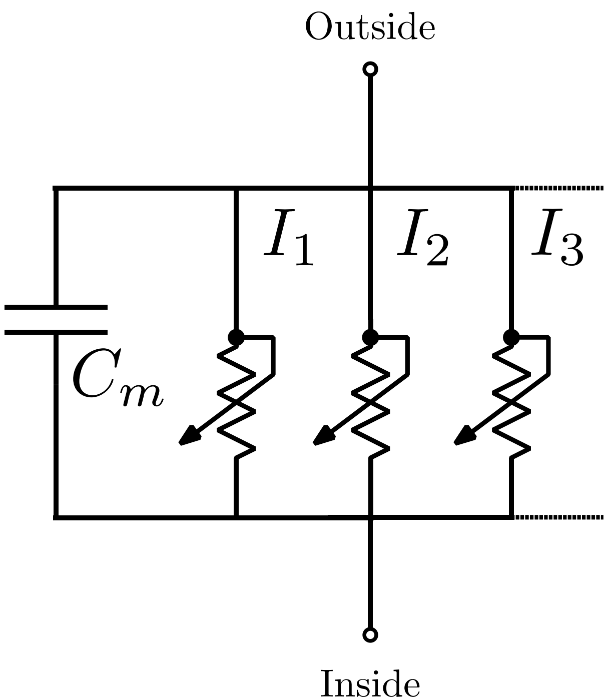
~~Varying elastance model~~ → cell-based model

Mechanical model
(Negroni & Lascano 2008)



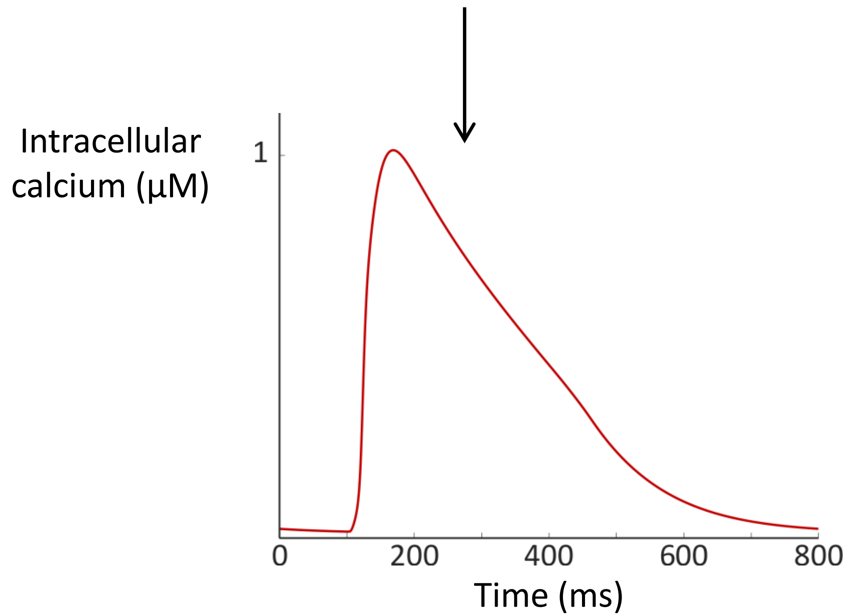
Electrophysiological model
(ten Tusscher & Panfilov 2006)

Electrophysiology

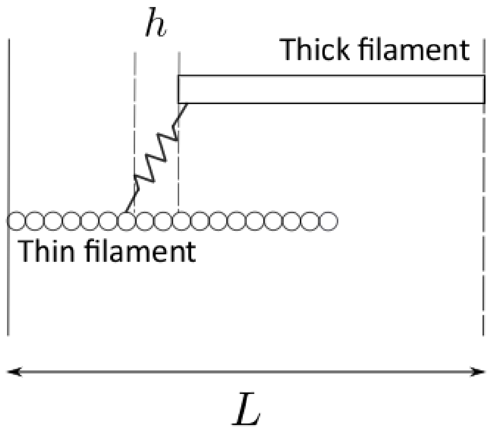


$$C_m \frac{dV}{dt} + \sum_i I_i + I_{stim} = 0$$

$$\frac{d[Ion]_i}{dt} = \frac{I_{in} - I_{out}}{z_{ion}\, V_c\, F}$$



Sarcomere contraction

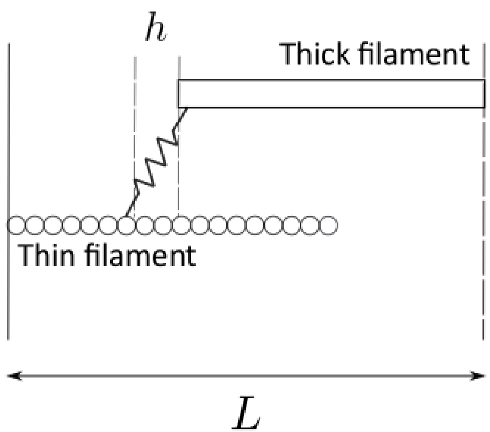


elastic length

$$L = X + h$$

inextensible length

Sarcomere contraction

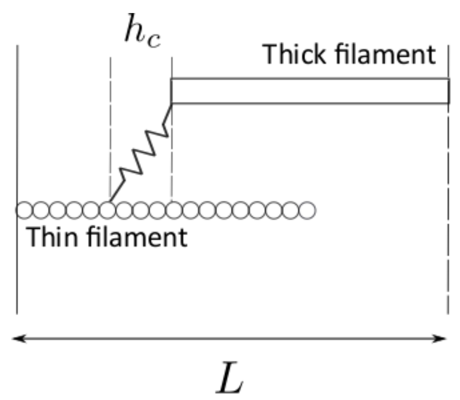


$$L = X + h$$

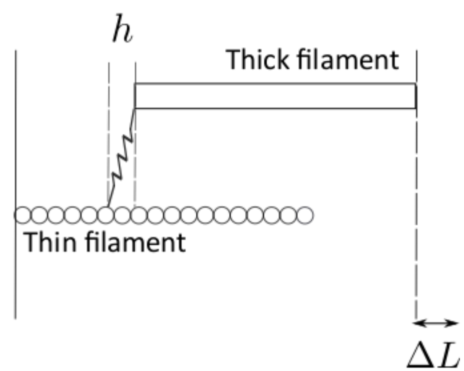
elastic length

inextensible length

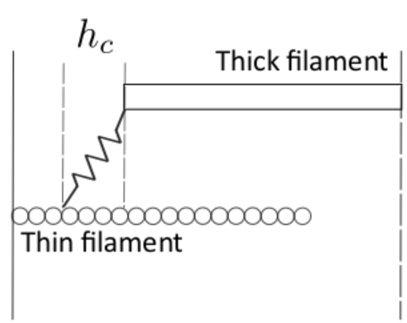
$$F_m \propto h$$



h_c = steady elongation



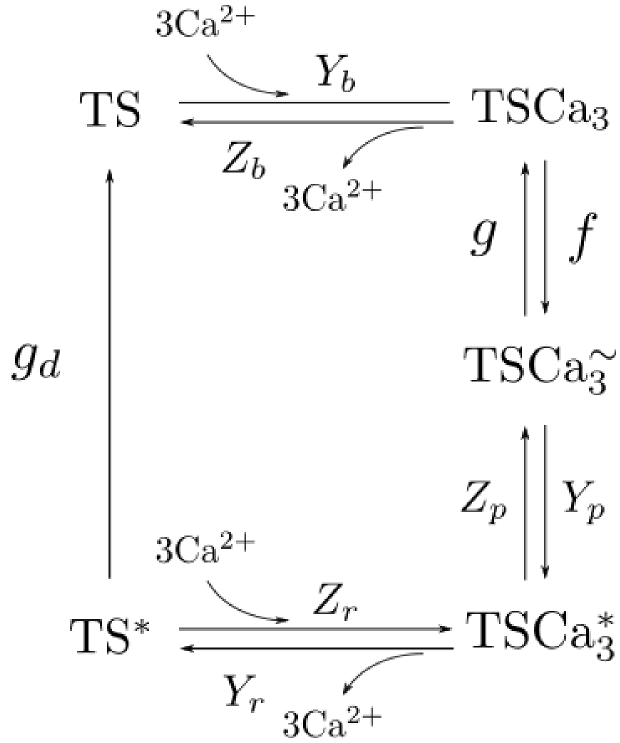
$$\Delta h = \Delta L$$



$$\frac{dX}{dt} = B.(h - h_c)$$

sliding velocity

Excitation-contraction coupling



$$[TS] = [TS]_{tot} - [TSCa_3] - [TSCa_3^{\sim}] - [TSCa_3{}^*] - [TS^*]$$

$$\frac{d[TSCa_3]}{dt} = g\,[TSCa_3^{\sim}] - f[TSCa_3] + Y_b\,[Ca_i]^3\,[TS] - Z_b[TSCa_3]$$

$$\frac{d[TSCa_3^{\sim}]}{dt} = f[TSCa_3] - g\,[TSCa_3^{\sim}] - Y_p\,[TSCa_3^{\sim}] + Z_p[TSCa_3{}^*]$$

$$\frac{d[TSCa_3^*]}{dt} = Z_r\,[Ca_i]^3[TS^*] - Y_r[TSCa_3{}^*] + Y_p\,[TSCa_3^{\sim}] - Z_p[TSCa_3{}^*]$$

$$\frac{d[TS^*]}{dt} = Y_r\,[TSCa_3{}^*] - Z_r\,[Ca_i]^3[TS^*] - g_d[TS^*]$$

$$f = f_0 \exp(-R_{La}\,(L - L_a))$$

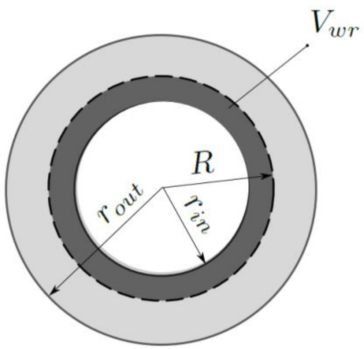
$$g = Z_a + Y_v(1 - \exp(-\gamma\,(h - h_{wr})^2)$$

$$g_d = Y_d \exp(-Y_c(L - L_c))$$

$$F_m \propto [TSCa_3^{\sim}]\,,\,[TSCa_3{}^*], [TS^*]$$

From cell to organ

Both ventricles are assimilated to simple spheres and the pressure and volume can be related to the force and half-sarcomere length:

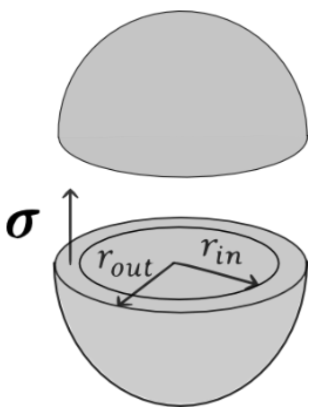


N half-sarcomeres are aligned along a circle of radius R: $L_m = \frac{2\pi R}{N}$

Blood volume inside the ventricular cavity is given by: $V_{int} = \frac{4}{3}\pi\, r_{int}^3$

R and V_{int} are related by: $V_{int} + V_{wr} = \frac{4}{3}\pi R^3$

$\Rightarrow$ L_m and V_{int} are linked



The wall stress σ is considered constant and is related to the pressure inside the ventricular cavity: $P = \sigma\,(\frac{r_{out}^2}{r_{in}^2} - 1)$

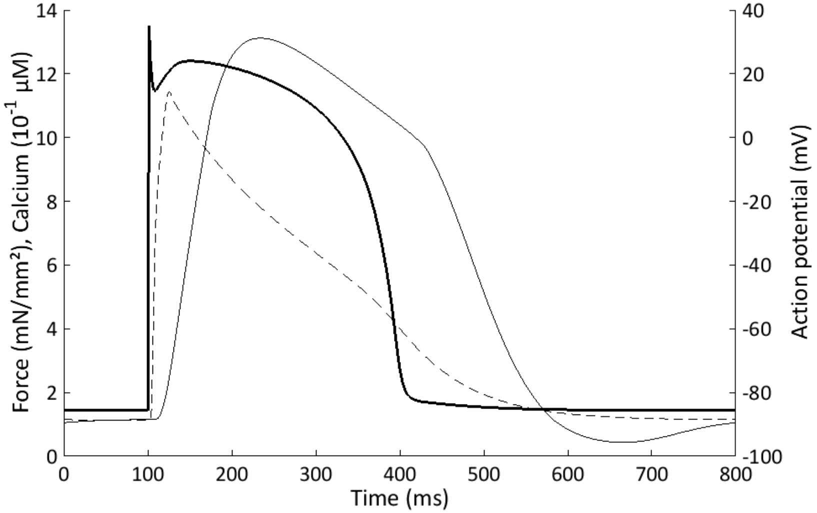
The wall stress is also related to the normalized force F_m given by the sarcomere model: $\sigma = F_m \frac{L_m}{L_r}$

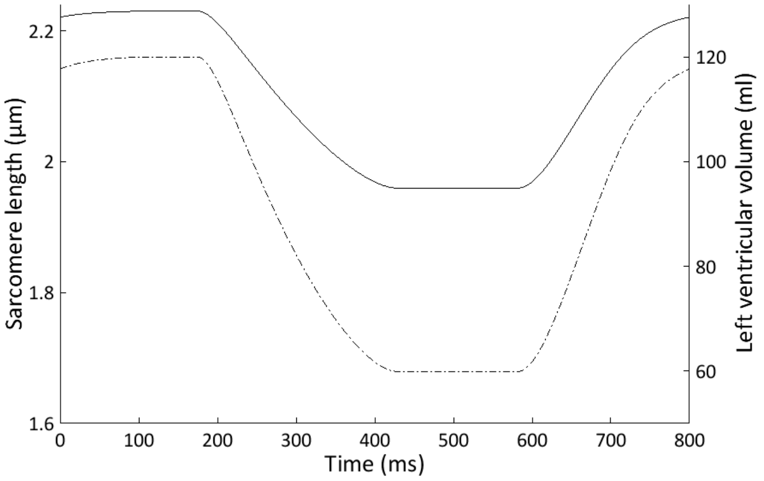
$\Rightarrow$ P and F_m are linked

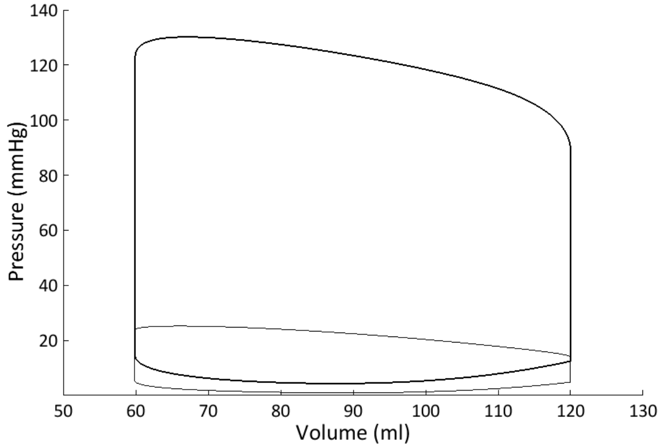
Shim, E. B., Amano, A., Takahata, T., Shimayoshi, T. & Noma, A. The cross-bridge dynamics during ventricular contraction predicted by coupling the cardiac cell model with a circulation model. *J Physiol Sci* **57,** 275–285 (2007).

Cardiovascular system model (CVS)

Results : Baseline

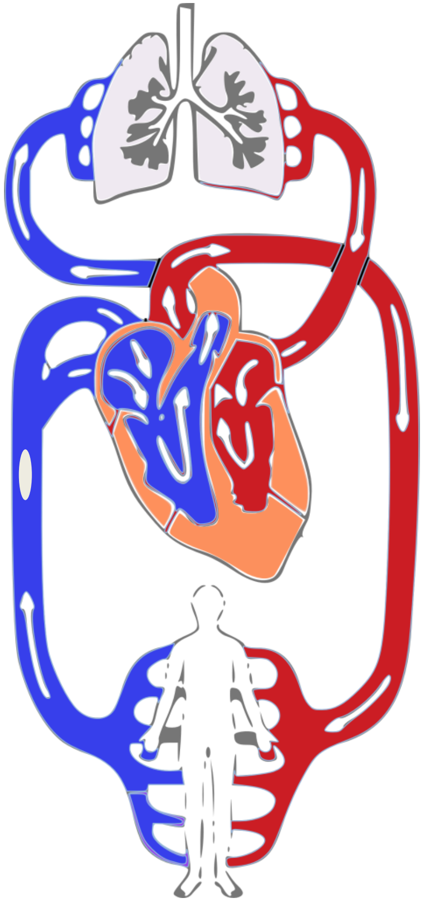


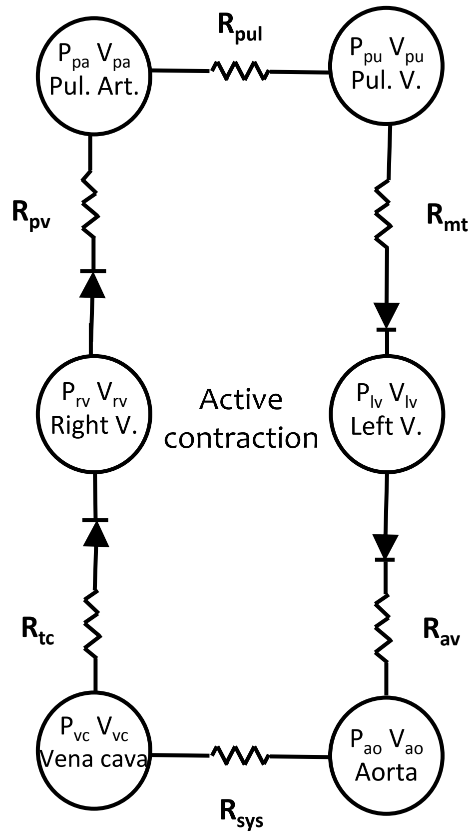


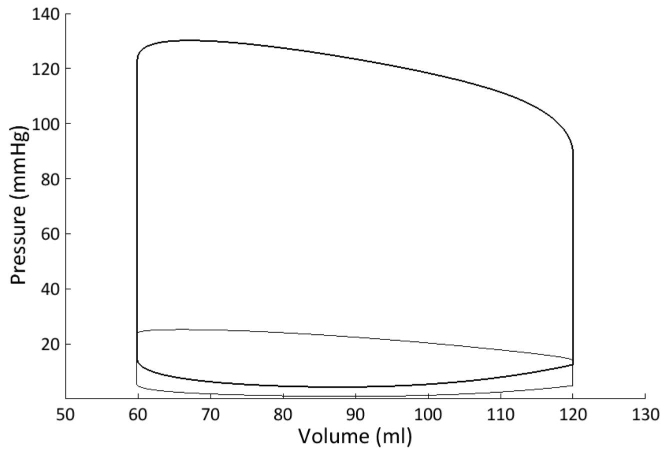


Cardiovascular system model (CVS)

Results : Fogarty balloon

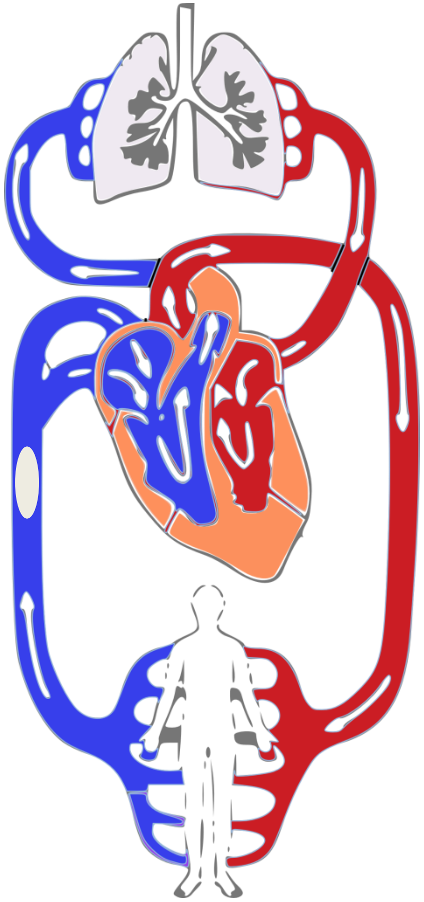


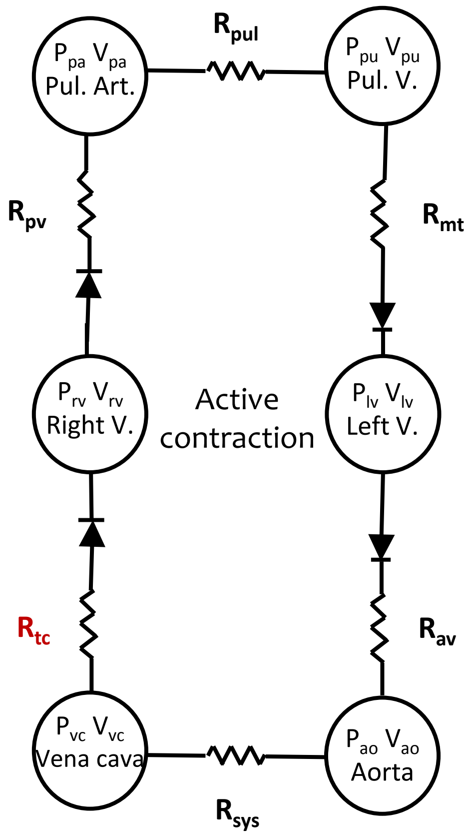


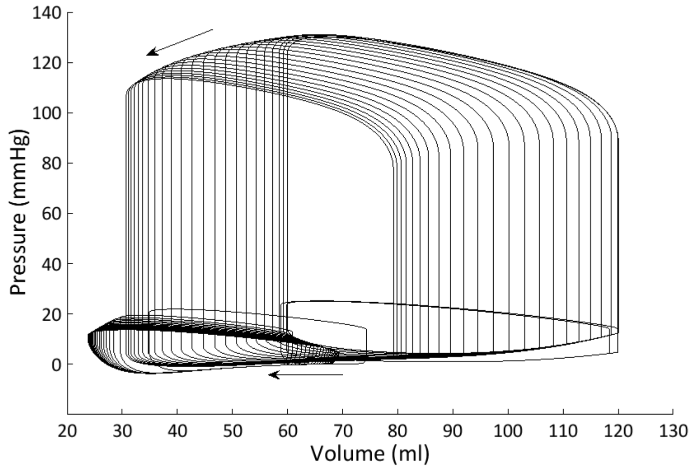


Cardiovascular system model (CVS)

Results : Fogarty balloon

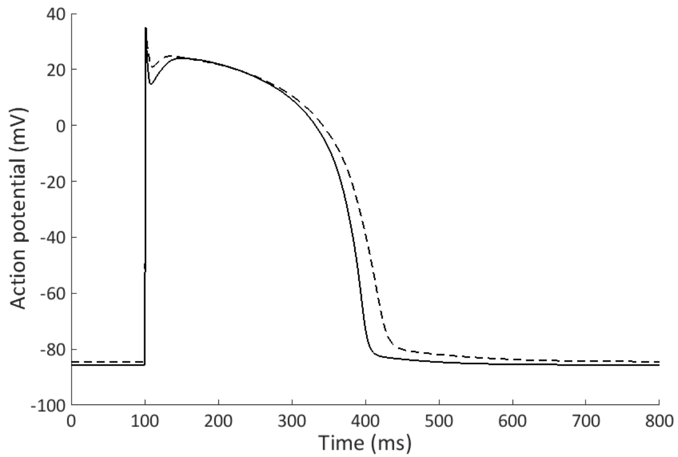


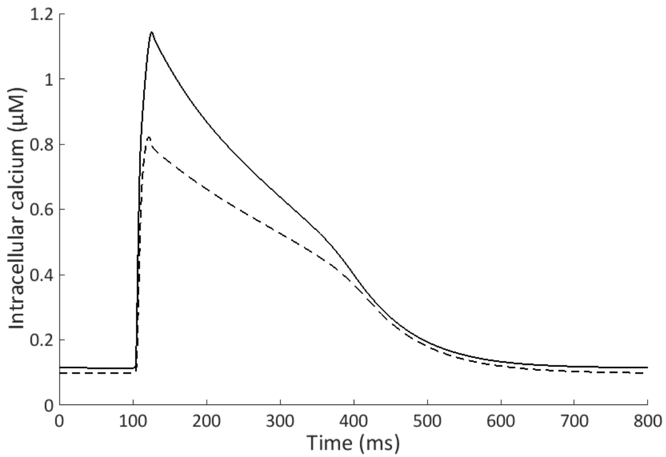


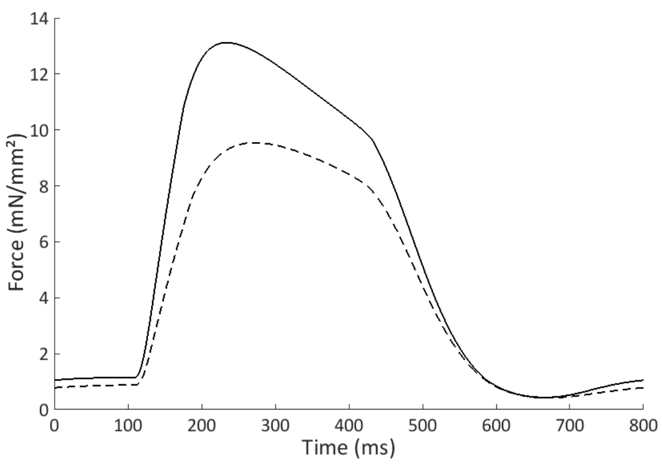


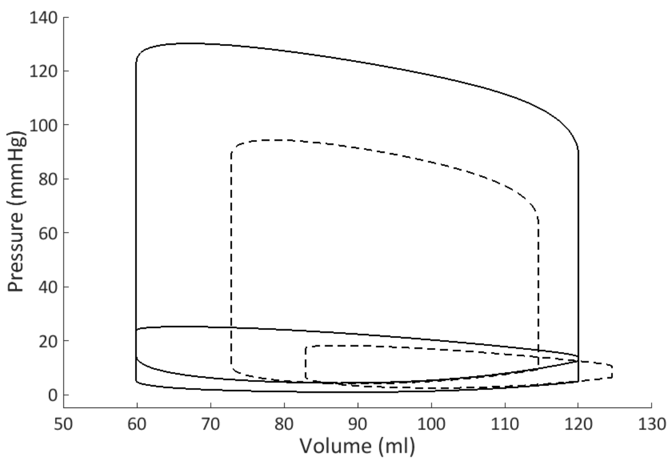
Cardiovascular system model (CVS)

Results : Ventricular failure







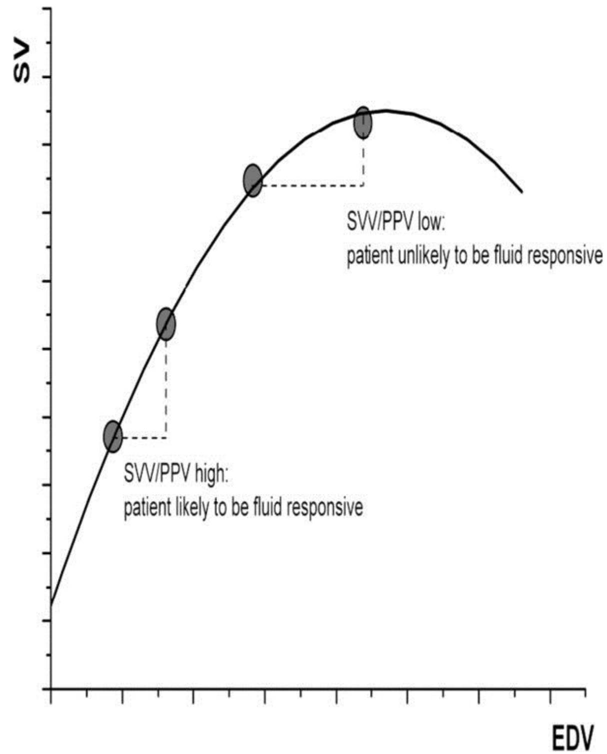


Cardiovascular system model (CVS)

Future perspectives:

- Fluid therapy: « Will a patient be fluid responsive ? »

  -> Need for indicators of fluid responsiveness



Cardiovascular system model (CVS)

Future perspectives:

- Fluid therapy: « Will a patient be fluid responsive ? »

  -> Need for indicators of fluid responsiveness

- Contractility index: « What is the contractile state of a patient's heart ? »

  -> Need for a contractility index that is not load dependent (and preferably available with non-invasive measures)

  -> comparison of different proposed indices