Cell-based description of ventricular contraction in a model of the human cardiovascular system

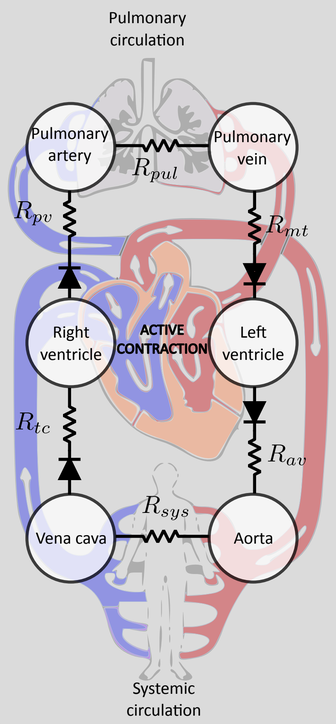
S. Kosta[1], J. Negroni[2], E. Lascano[2], P. C. Dauby[1]

[1]University of Liège, GIGA - Cardiovascular Sciences, Belgium
[2]Department of Comparative Cellular end Molecular Biology, Favaloro University, Buenos Aires, Argentina

Introduction

A multiscale model of the cardiovascular system is presented, where hemodynamics is described by a lumped parameter model, while heart contraction is described at the cellular scale.

Hemodynamic



Passive chamber:

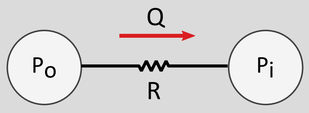
$$P = E.V$$

elastance: E; pressure: P; volume: V

Active chamber:

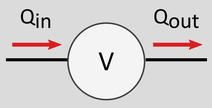
$$P = \cancel{E.V}$$

Flow through the vessels:



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

Volume variation:

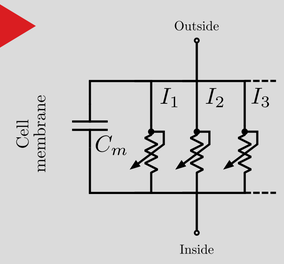


$$\frac{\mathrm{d}V}{\mathrm{d}t} = Q_{in} - Q_{out}$$

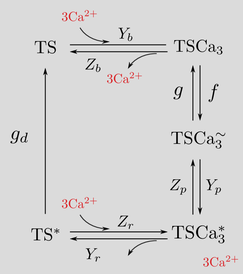
Cardiac valve:

Cellular model

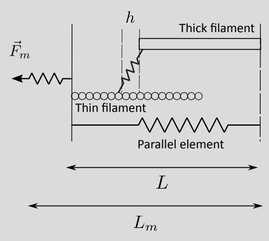
Electrophysiology



Calcium kinetics



Mechanical contraction

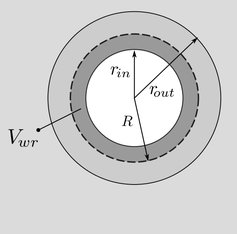


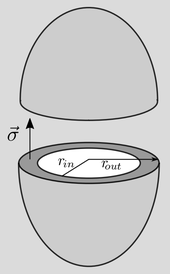
From cell to ventricle

$$L_m = \frac{2\pi R}{N}$$

$$V_{in} = \frac{4}{3}\pi r_{in}^3$$

$$V_{in} + V_{wr} = \frac{4}{3}\pi R^3$$



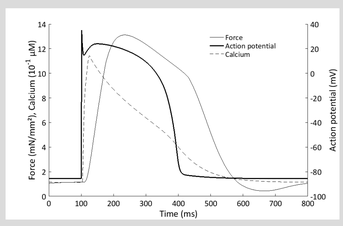


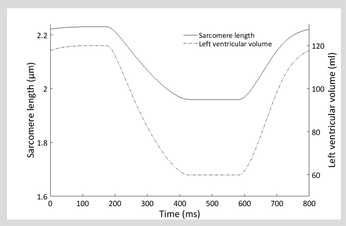
$$\sigma = F_m \frac{L_m}{L_r}$$

$$P = \sigma\left(\frac{r_{out}^3}{r_{in}^3} - 1\right)$$

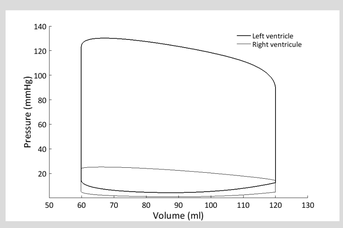
Results

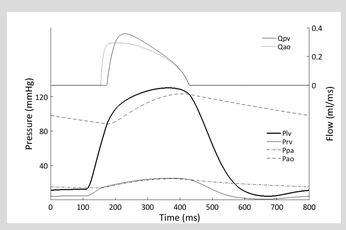
Baseline





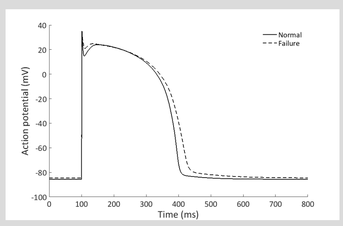
Particular attention was paid to the sarcomere length, which must vary between physiological extremes.

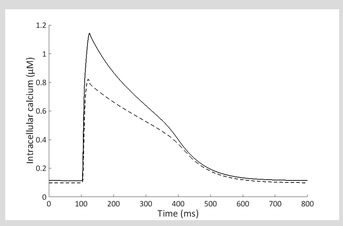




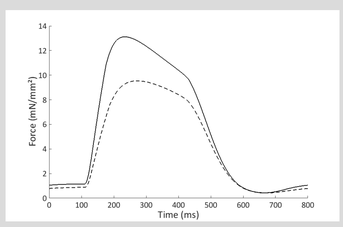
Pressure-volume loops are correctly reproduced, as well as the different flows and pressures time evolution.

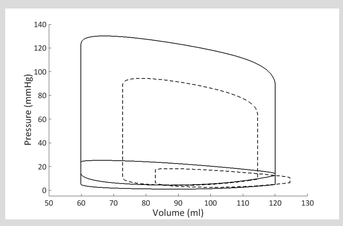
Heart failure





A prolonged action potential, a lower intracellular calcium and a weaker produced force are characteristic symptoms of heart failure.



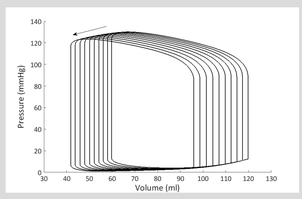


This leads to smaller pressure-volume loops.

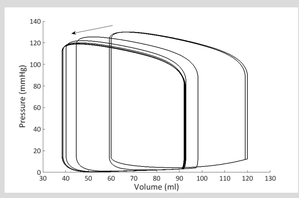
End-systolic elastance: a good index of cardiac contractility ?

A good cardiac contractility index should only vary with inotropy and not with load. End-systolic elastance (Ees) is the gold standard for assessing cardiac contractilty, but with our model we show that this index is load-dependent.

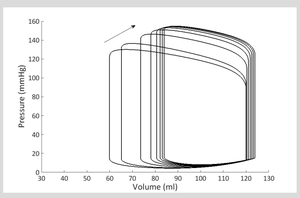
Load variation



Hemorrhage (preload decrease)

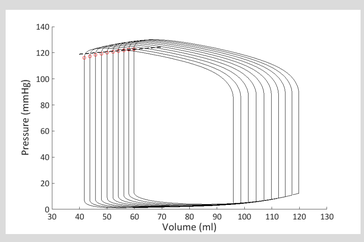


Rmt increase (preload decrease)



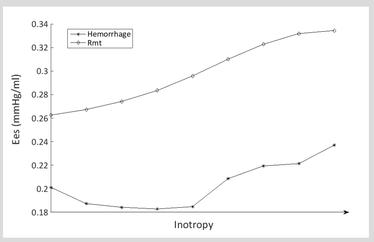
Rsys increase (afterload increase)

Ees calculation



Ees is calculated with a linear regression over the three first end-systolic points of the PV loop

Results



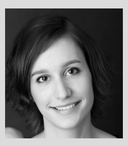
Conclusion

Our multiscale model of the human cardiovascular system is able to reproduce baseline results at both scales (cellular and hemodynamic). It can also reproduce pathological behaviors that originate at the cellular scale, like heart failure. It also indicates that the end-systolic elastance is not load-independent, as often assumed in many CVS models using the varying elastance to describe heart contraction.

Acknowledgements

P. D. acknowledges for FRS-FNRS travel support.

Contact



sarah.kosta@ulg.ac.be