

A multiscale model of the human cardiovascular system can account for the Frank-Starling mechanism effect on vascular filling therapy

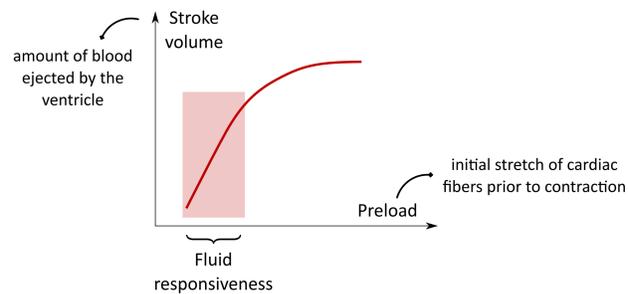
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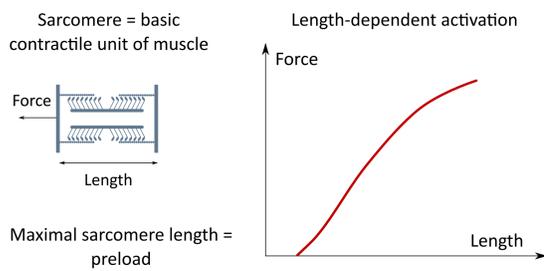
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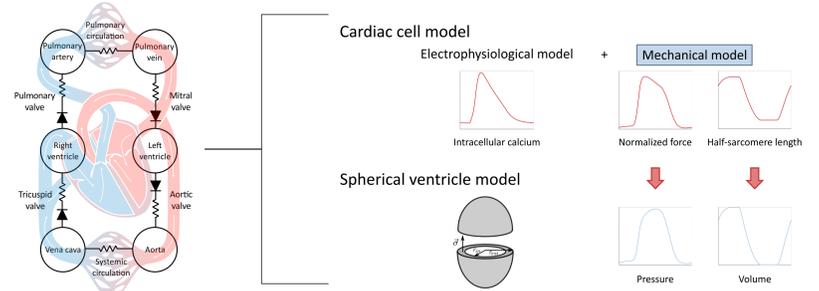
Frank-Starling law of the heart : an increase in ventricular preload leads to an increase in stroke volume (SV)



The Frank-Starling mechanism originates from the subcellular scale:

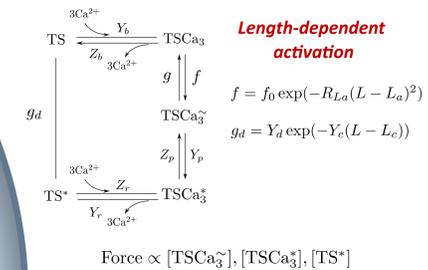


Multiscale model of the human cardiovascular system : 6-chamber lumped-parameter model where ventricular contraction is described at the cellular scale



Mechanical model

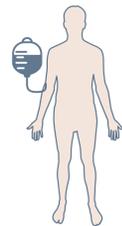
Vascular filling simulations



Increase in circulating blood volume is modeled with an increase in the stressed blood volume (SBV) → Total blood volume responsible for a non-zero pressure inside the cardiovascular system (parameter of the model)

Vascular filling therapy

= intravenous fluid administration in order to increase the stroke volume

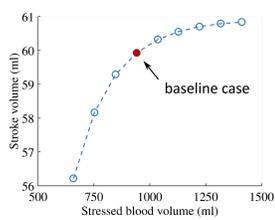


The patient is **fluid-responsive**, the stroke volume increases

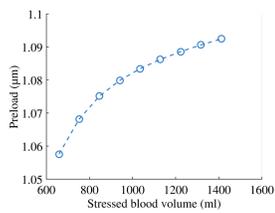
The patient is **not fluid-responsive** (the stroke volume does not substantially increase or eventually decreases)

Which mechanisms/factors are responsible for fluid responsiveness ?

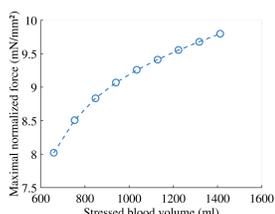
Vascular filling simulations



SV increase with increasing SBV and there is a saturating phenomenon for high SBV values.

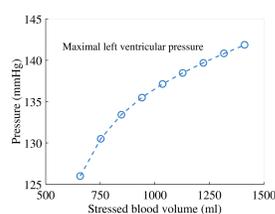


Preload increases with SBV, which leads to an increase in the maximal produced force (length-dependent activation)

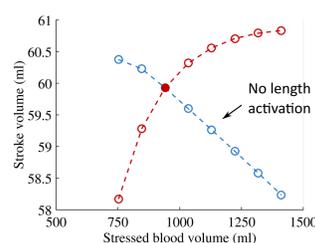


Since the force increases, the developed pressure also increases and, as a consequence, more blood is ejected by the ventricle and SV increases.

length-dependent activation



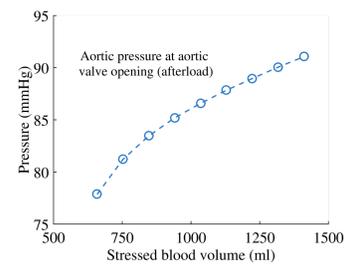
Significance of the Frank-Starling mechanism



If the length-dependent activation property is deactivated from the cell model, the Frank-Starling mechanism is no longer present and the fluid responsiveness is completely lost.

Role of afterload

The afterload can be defined as the resistance to blood ejection by the ventricle. The aortic pressure at the opening of the aortic valve is a component of the afterload and it increases with vascular filling.



Preload and afterload are actually competing:

- for low SBV values, the preload increases enough to counterbalance the increase in afterload and vascular therapy may be considered.
- for high SBV values, fluid responsiveness is lost. This is not the consequence of a saturating Frank-Starling mechanism, but rather the result of a sharper afterload increase

Our model corroborates the significance of the Frank-Starling mechanism for fluid responsiveness. However, other factors such as afterload should also be taken into account when considering vascular therapy. It is worth noticing that the loss of fluid responsiveness for high SBV values is not the consequence of the saturating Frank-Starling mechanism, but rather the result of the sharper afterload increase, which counterbalances the Frank-Starling mechanism.

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