Vascular filling and the Frank-Starling mechanism

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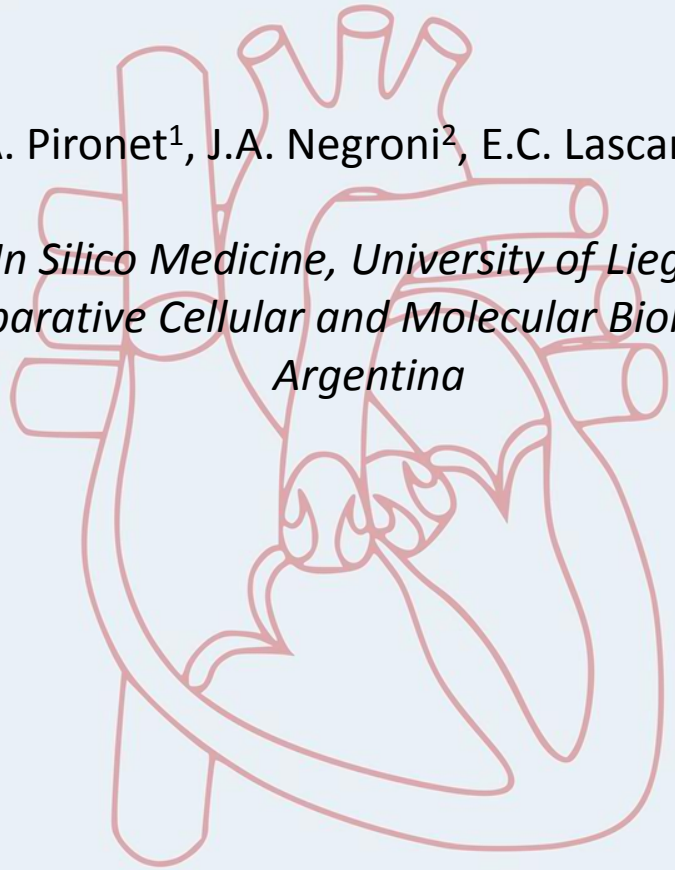
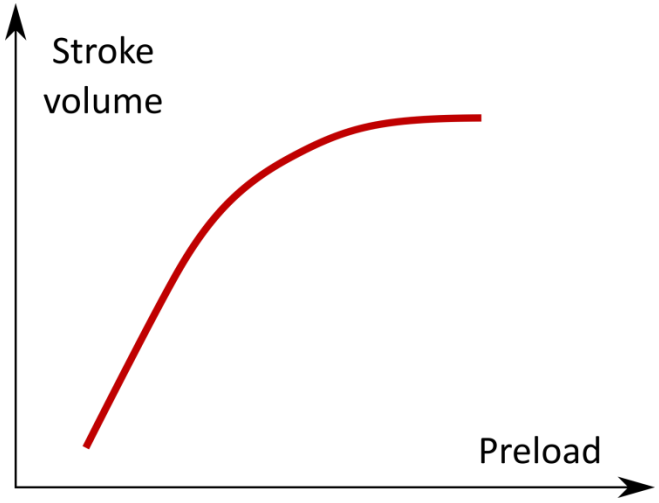


Vascular filling

- Vascular filling = intravenous administration of fluid to a patient in order to increase the stroke volume
- Clinical treatment proposed because of the Frank-Starling mechanism



- An increase in preload (= stretching of the heart muscle fibers before contraction) leads to an increase in stroke volume (= volume of blood ejected by the ventricle)

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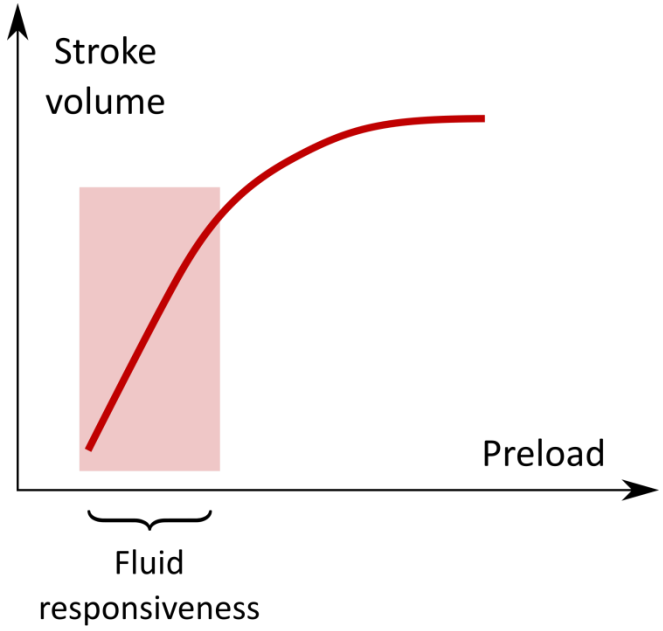
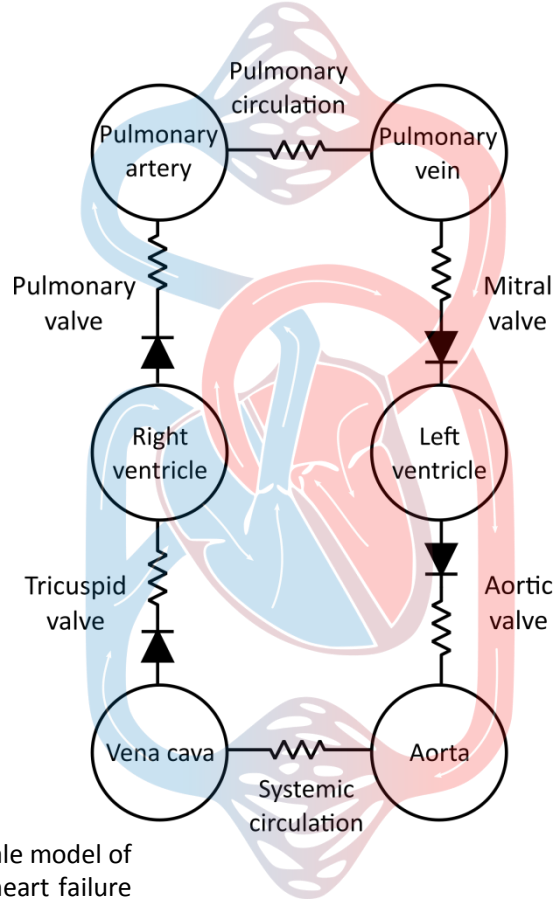


- An increase in preload (= stretching of the heart muscle fibers before contraction) leads to an increase in stroke volume (= volume of blood ejected by the ventricle)
- A patient will be « fluid-responsive » if the increase in circulating blood volume substantially increases stroke volume.

Human cardiovascular system model

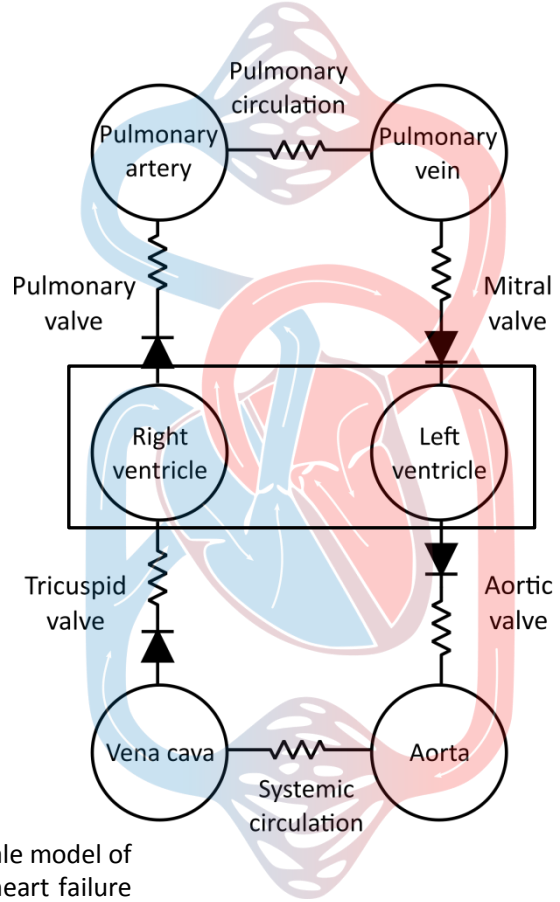
Human CVS is assimilated to a six-chamber model



S. Kosta, J. Negroni, E. Lascano, P.C. Dauby, Multiscale model of the human cardiovascular system: Description of heart failure and comparison of contractility indices, Mathematical Biosciences, in press.

Human cardiovascular system model

Ventricular contraction is described at the cellular scale



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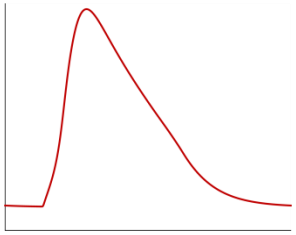
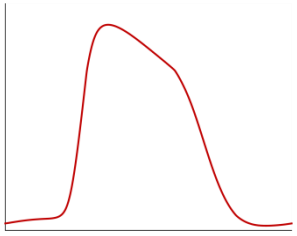
Human cardiovascular system model

Cardiac cell model

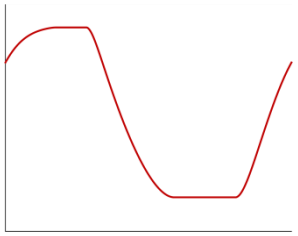
Electrophysiological model + Mechanical model



Intracellular calcium

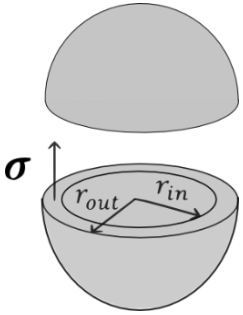


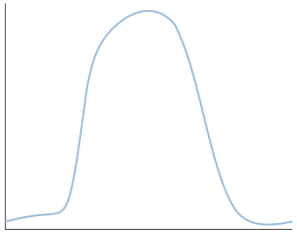
Normalized force



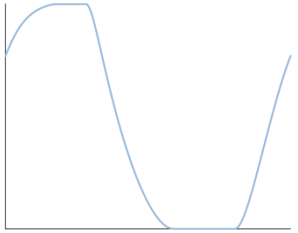
Half-sarcomere length

Spherical ventricle model





Ventricular pressure



Ventricular blood volume

Shim, Eun Bo, et al. "The cross-bridge dynamics during ventricular contraction predicted by coupling the cardiac cell model with a circulation model." *The Journal of Physiological Sciences* 57.5 (2007): 275-285.

Stressed blood volume

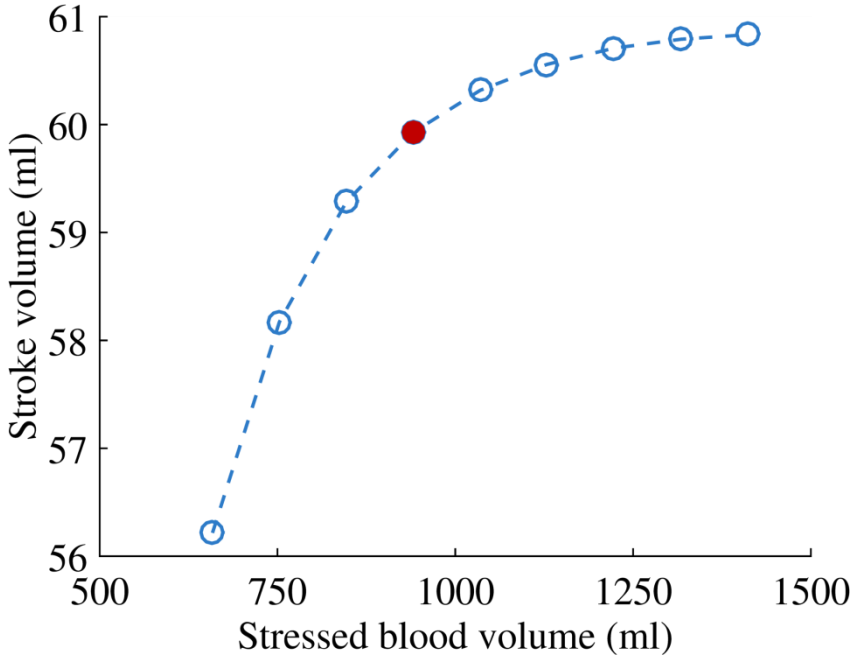
- The total stressed blood volume (SBV) is defined as the total blood volume responsible for a non-zero pressure inside the cardiovacular system
- In our 6-chamber model:

$$SBV = V_{lv} + V_{rv} + V_{ao} + V_{vc} + V_{pv} + V_{pa}$$

- Vascular filling experiments (fluid injections) are modeled with an increase in SBV

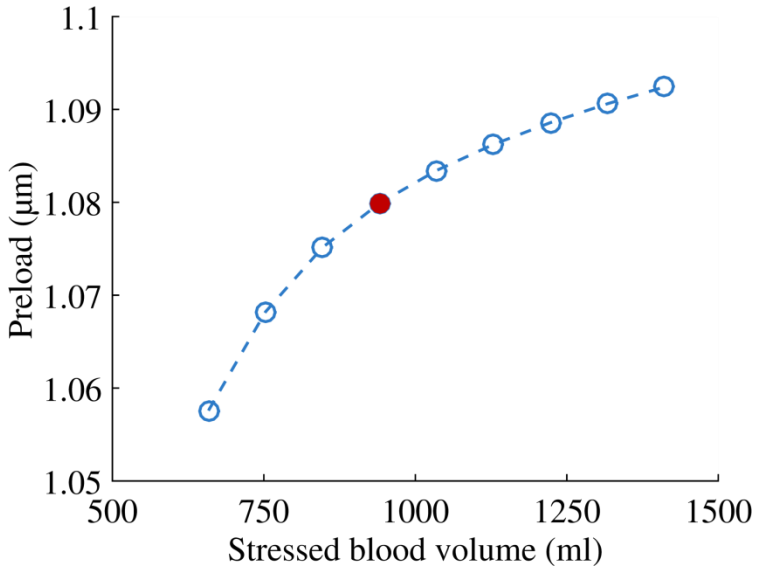
Vascular filling simulations

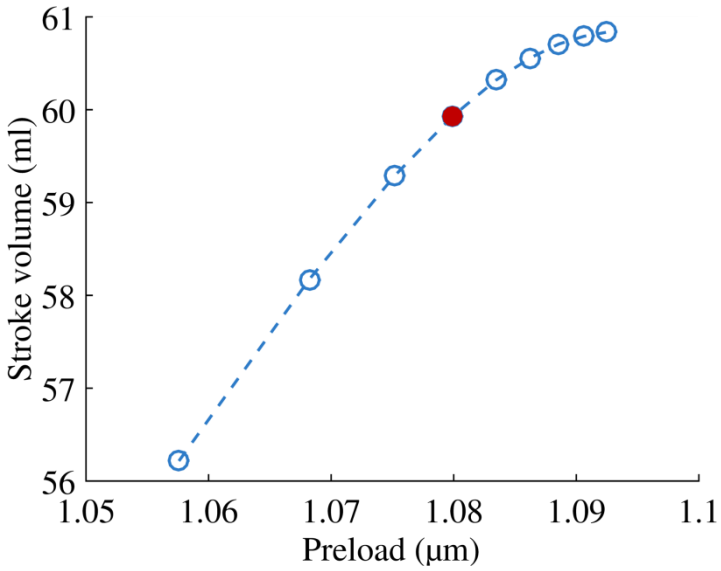
- Stroke volume is calculated for different values of SBV once the system has reached its steady state



Link with the Frank-Starling mechanism

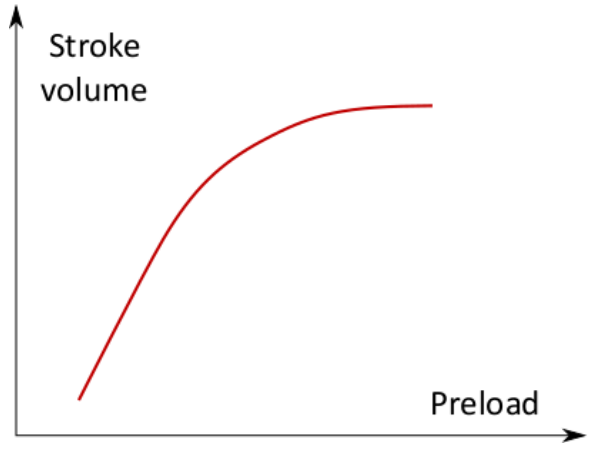
- The increase in SBV lead to an increase in preload

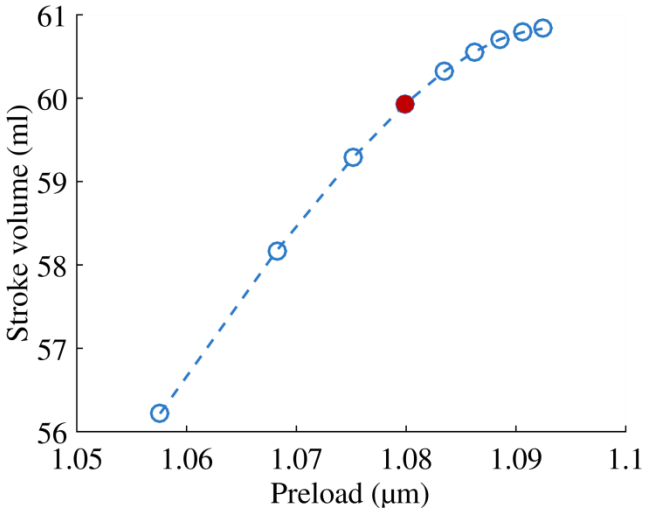




Link with the Frank-Starling mechanism

- The vascular filling curves can not be directly compared to the Frank-Starling curves





Transitory effect of an increase in preload
⇒ All other variables remain unchanged

≠

Stabilized behavior following an increase in SBV
⇒ Other variables are altered

Instantaneous preload increase

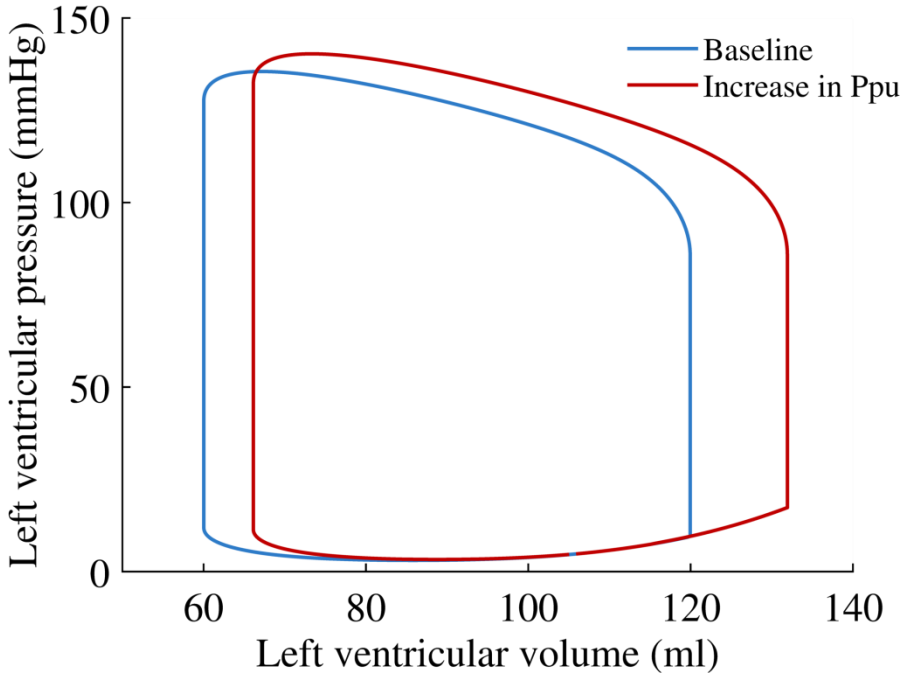
Simulation of an instantaneous increase of the pulmonary pressure during left ventricular filling

$\Rightarrow$ increase in the blood flow entering the ventricle

$\Rightarrow$ increase in preload

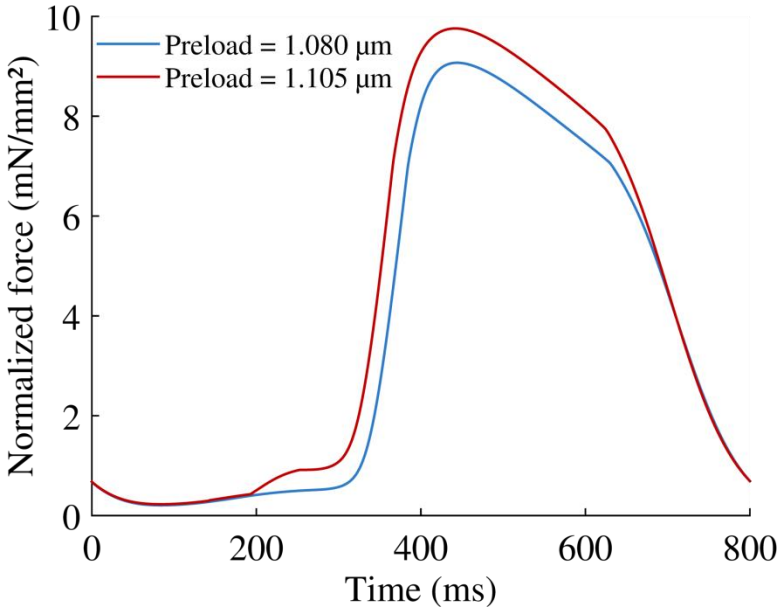
Instantaneous preload increase

The resulting pressure-volume loop shows that the stroke volume and the maximal developed pressure increase



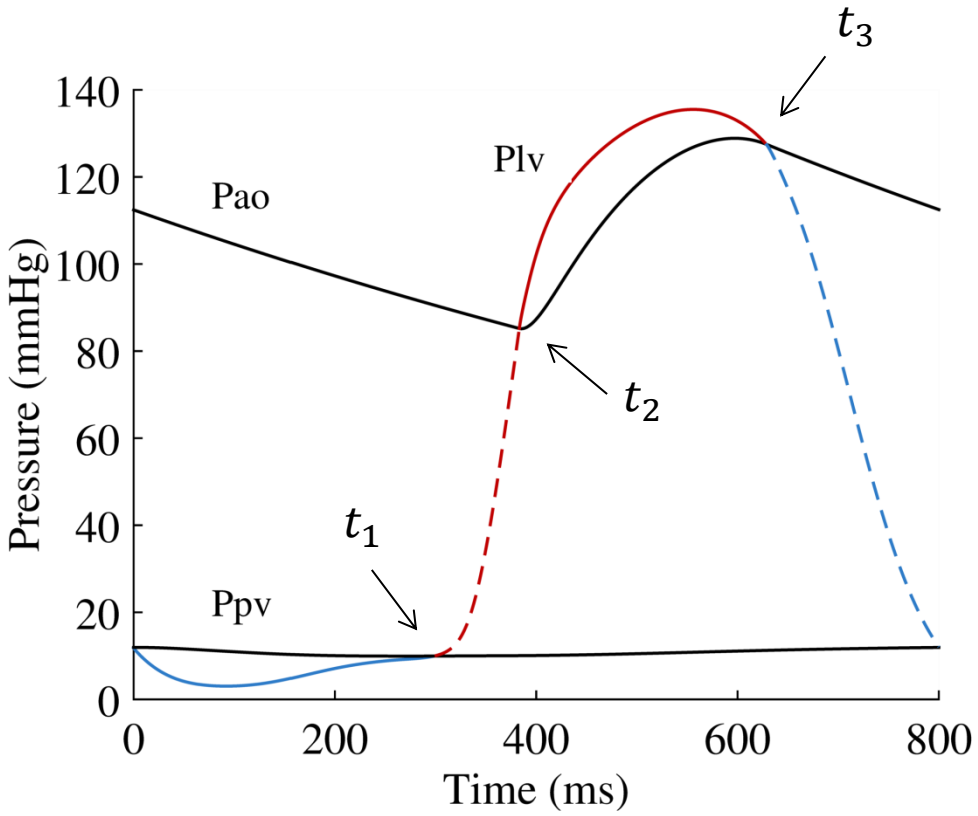
Length effect

- Increase in half-sarcomere length ⇒ increase in the developed cardiac cellular force (length-dependent activation)
- Increase in force ⇒ increase in ventricular pressure ⇒ increase in stroke volume



But the timescale of the cardiac beat is also affected !

Timing effect



- Ventricular filling (stops at the mitral valve closing)
- Isovolumic contraction (stops at the aortic valve opening)
- Blood ejection (stops at the aortic valve closing)
- Isovolumic relaxation (stops at the mitral valve opening)

Timing effect

	Baseline	Preload increase
t_1 (mitral valve closing)	142,4 ms	110,4 ms
t_2 (aortic valve opening)	226,4 ms	222,4 ms
t_3 (aortic valve closing)	471,2 ms	483,2 ms
Isovolumic contraction $(t_2 - t_1)$	84 ms	112 ms
Blood ejection $(t_3 - t_2)$	244,8 ms	260,8 ms

$\Rightarrow$ The isovolumic contraction starts earlier
$\Rightarrow$ The isovolumic contraction and the blood ejection phases last longer
$\Rightarrow$ The timing of valves opening and closing also affects the stroke volume

Length & timing effect

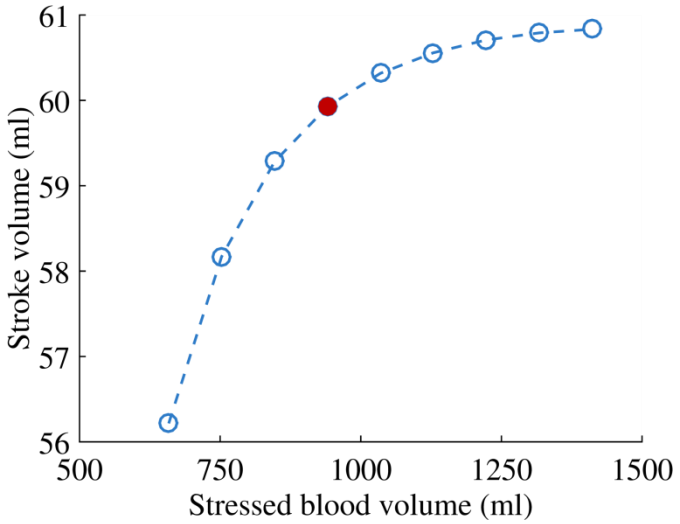
- Instantaneous increase in preload

  $\Rightarrow$ increase in the developed cardiac cellular force (length-dependent activation) and in ventricular pressure

  $\Rightarrow$ longer isovolumic contraction and blood ejection phases

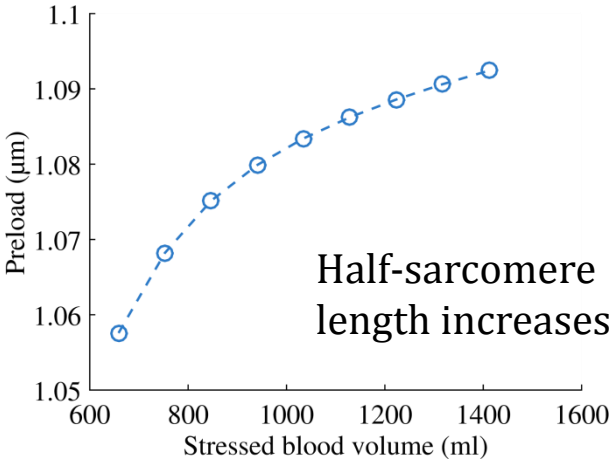
  $\Rightarrow$ increase in stroke volume

- Do the length and timing effect play a role in the vascular filling results ?

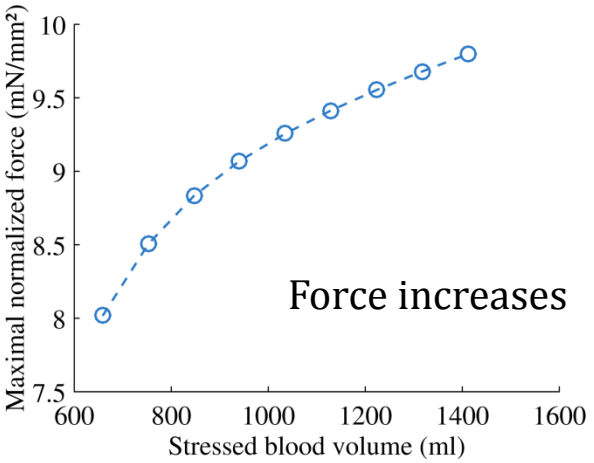


Length effect and vascular filling

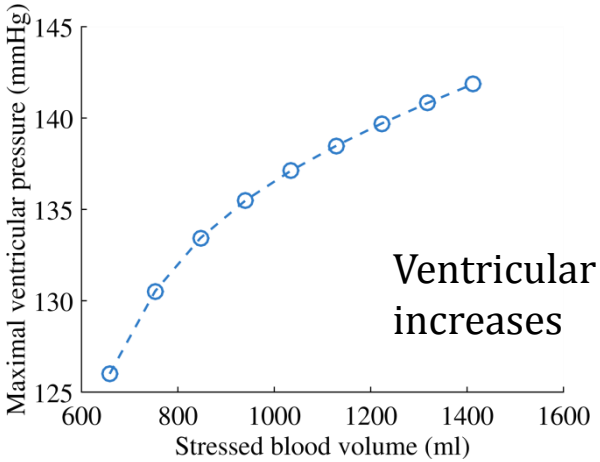
As SBV increases,



Half-sarcomere length increases



Force increases



Ventricular pressure increases

Timing effect and vascular filling

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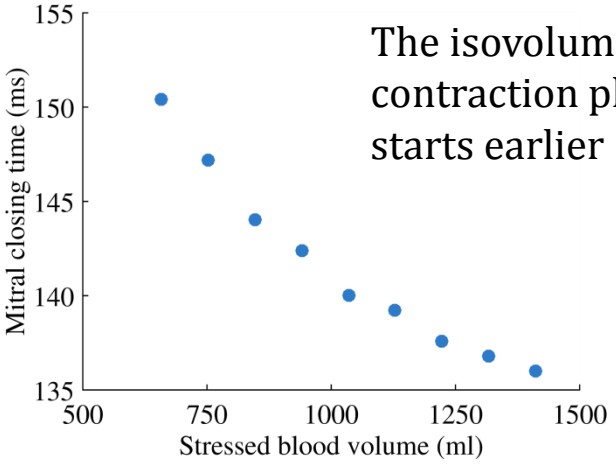
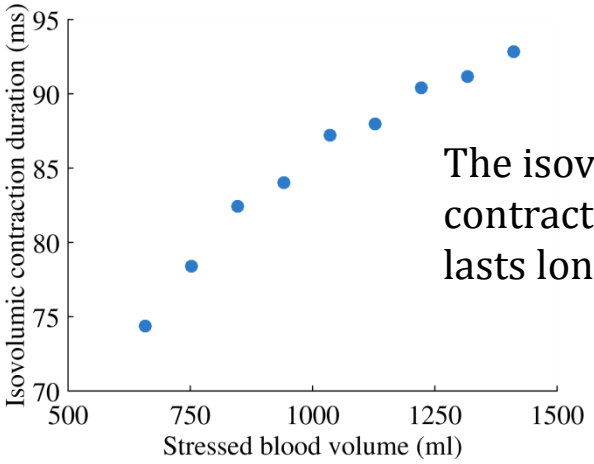
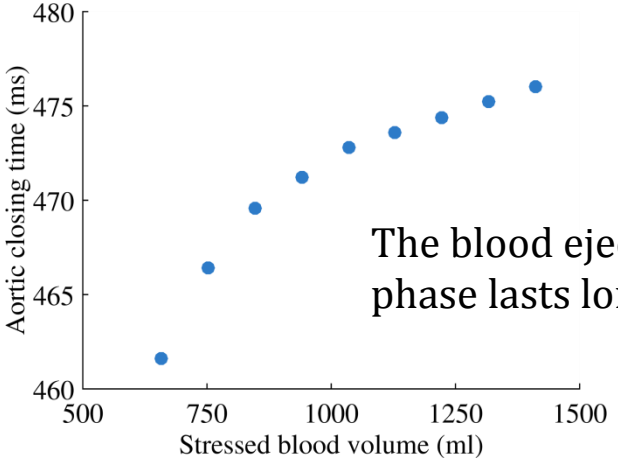


The isovolumic contraction phase starts earlier



The isovolumic contraction phase lasts longer

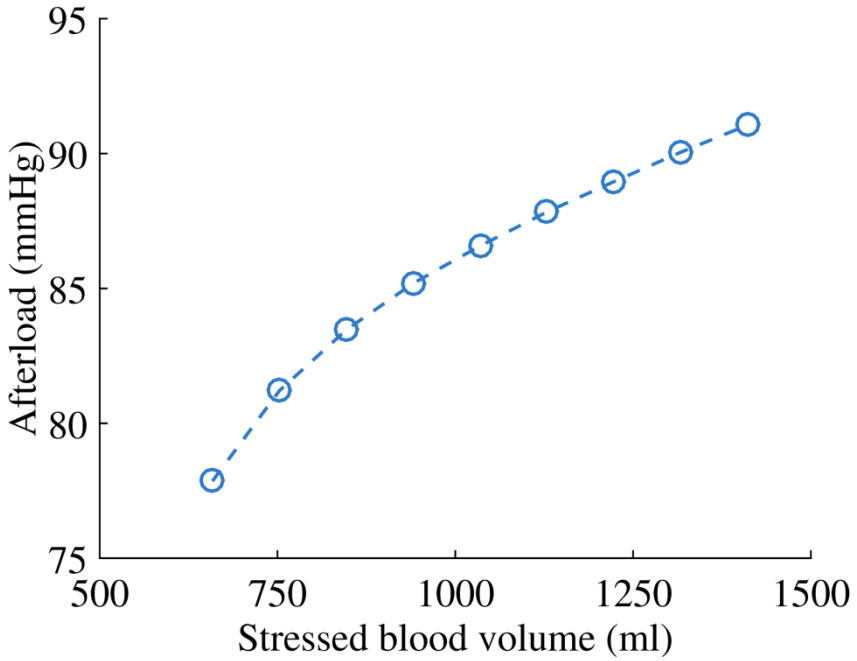


The blood ejection phase lasts longer

⇒ There is a link between the Frank-Starling mechanism and the vascular filling effect on stroke volume

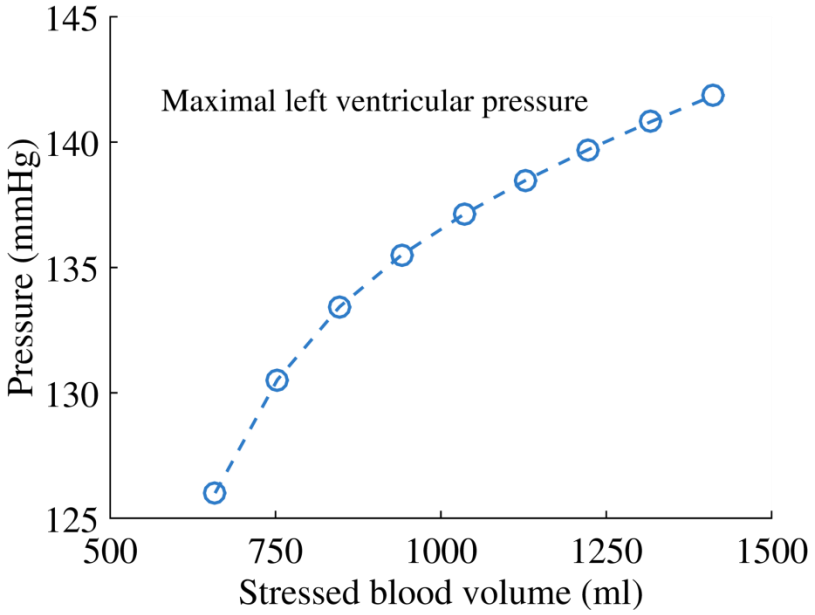
Afterload effect

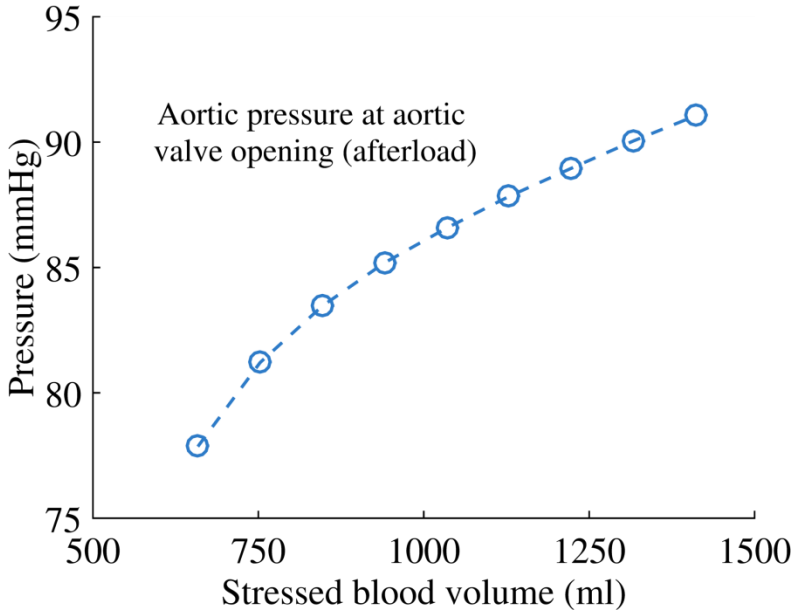
- Variables other than preload are affected by the SBV increase
- The afterload (= aortic pressure at the opening of the aortic valve) also increases with SBV



Afterload effect

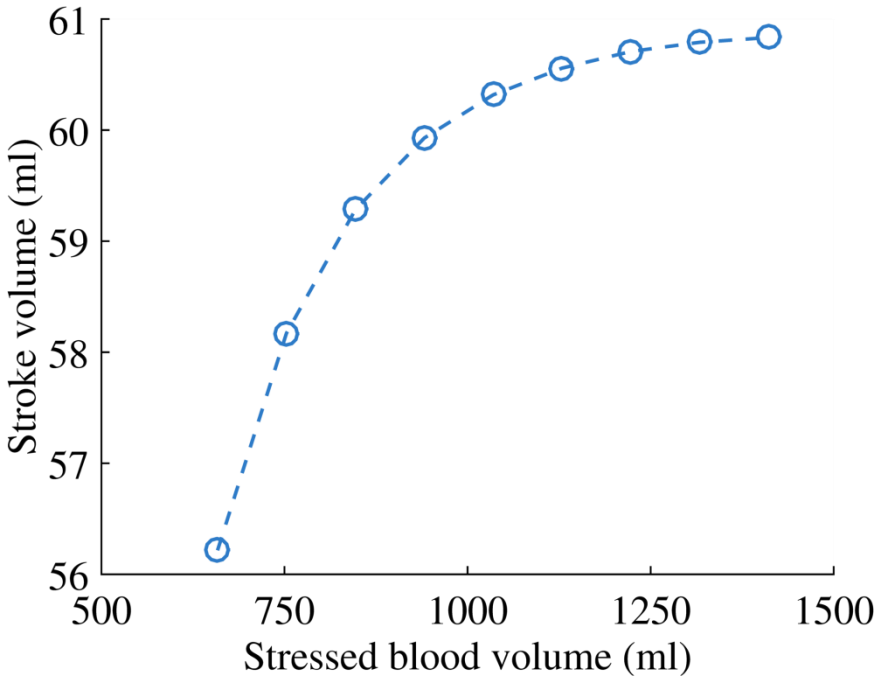
- The stroke volume depends on the blood flow through the aortic valve, which is dictated by the difference between ventricular and aortic pressure





Afterload effect

- The saturating portion of the vascular filling curve occurs because the preload increase is not large enough to counterbalance the afterload increase



Conclusion

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- Those two effects are also found in the vascular filling experiments

  ⇒ The Frank-Starling mechanism plays a role in the stroke volume increase following an increase in SBV

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- Vascular filling simulations : SBV ↗ ⇒ preload ↗ ⇒ stroke volume ↗
- A length and a timing effect are involved in the instantaneous Frank-Starling mechanism
- Those two effects are also found in the vascular filling experiments

  ⇒ The Frank-Starling mechanism plays a role in the stroke volume increase following an increase in SBV
- Vascular filling also increases afterload and as a consequence fluid responsiveness may be compromised for high preloads (or high SBV values)

  ⇒ The Frank-Starling effect is not the only determinant of fluid responsiveness