Study of ventricular interaction during pulmonary embolism using clinical identification in a minimum cardiovascular system model

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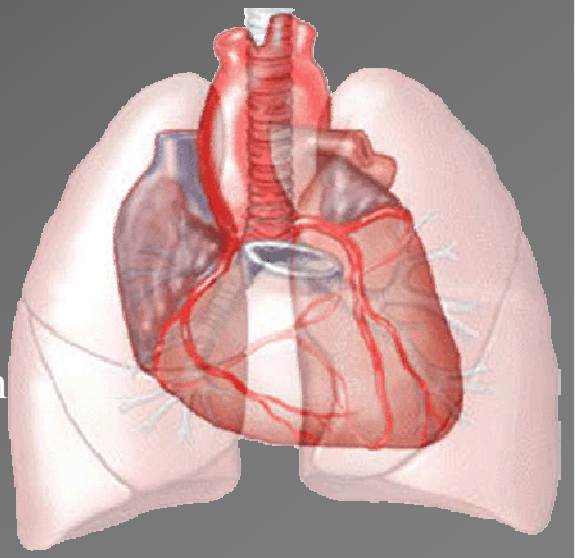
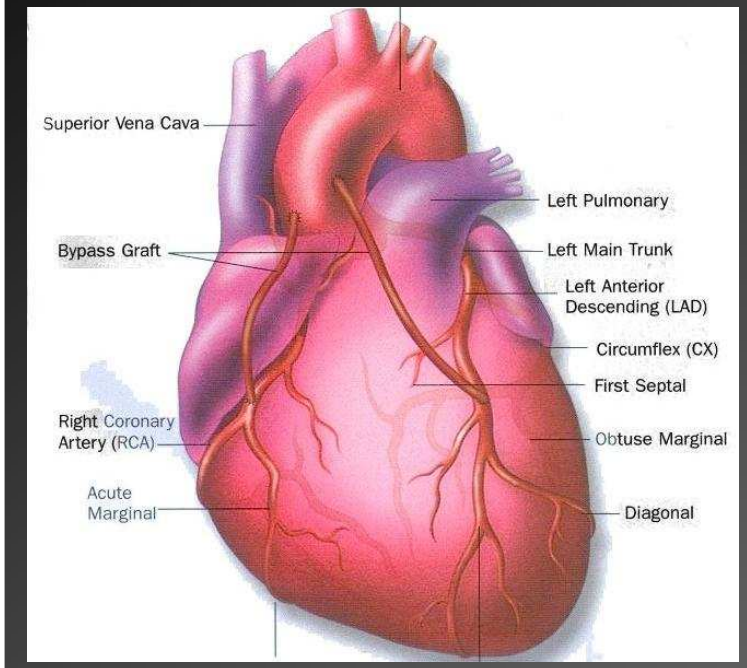
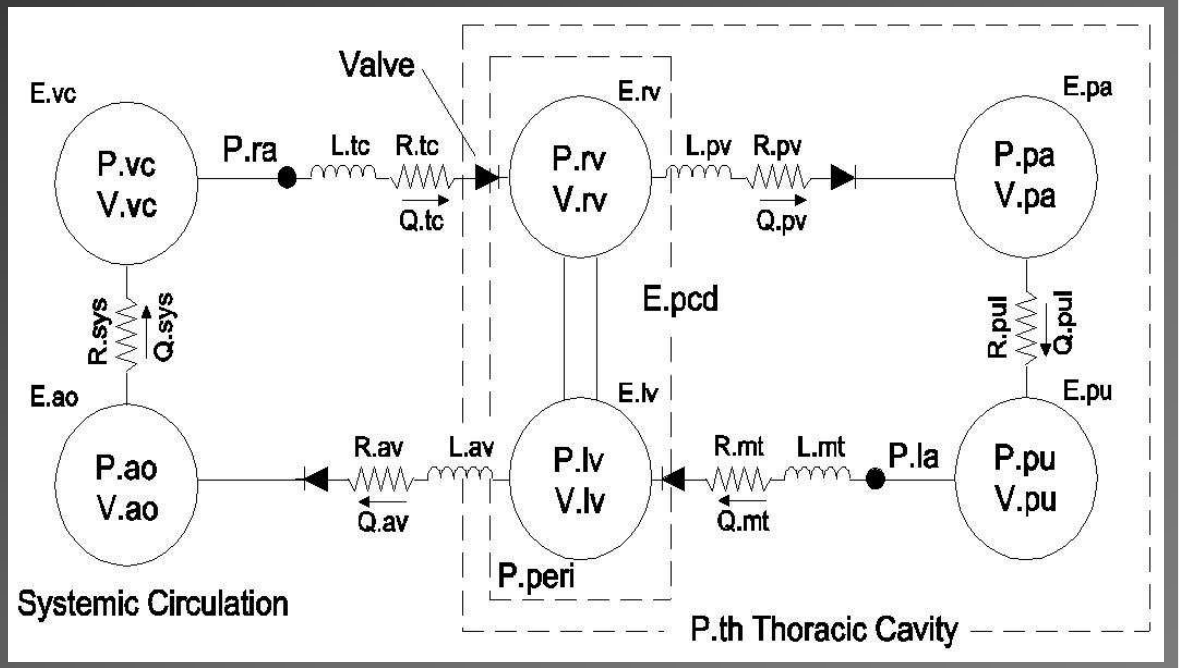


Introduction

- **General problem**: Cardiovascular disturbances are difficult to diagnose and treat
  - Large range of possible dysfunctions
  - Reflex actions can mask the symptoms
    - → Conflicting clinical data
    - → Medical professionals often rely on experience and intuition to optimize the hemodynamics in the critically ill
- **Solution**: physiological, identifiable and validated computer model
  - Minimal Model + Patient-Specific Parameter ID process
  - Identification must use common ICU measurements
- **Application**: evolution of induced pulmonary embolism in porcine data

Heart model





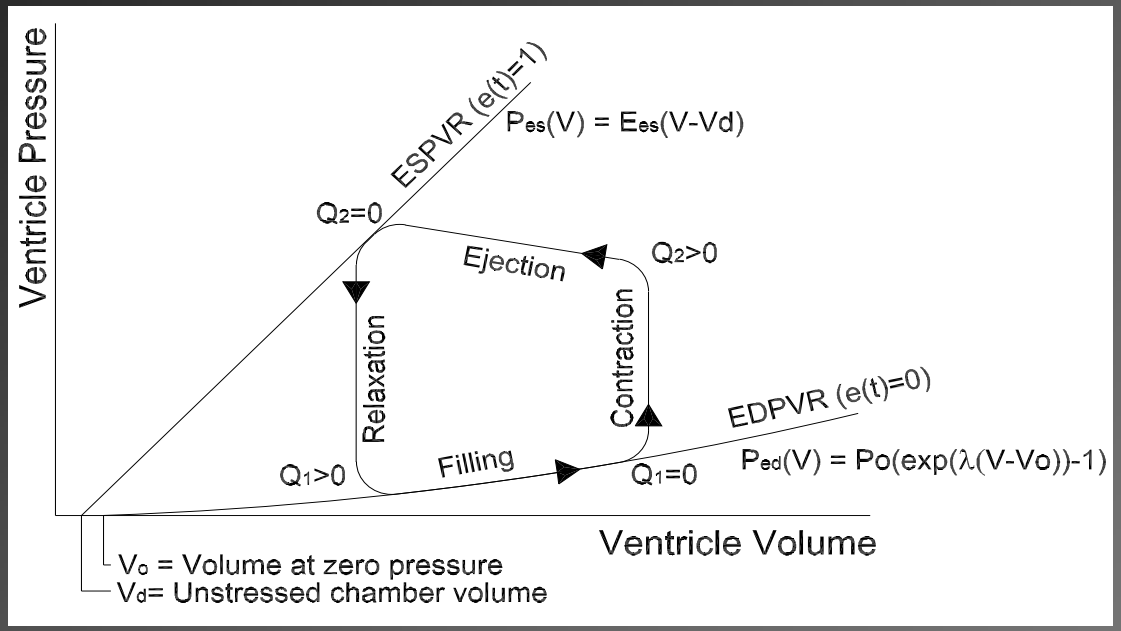
Minimal cardiovascular model:

- Physiologically validated
- Capable of capturing patients dynamics commonly seen in the Intensive Care Unit (ICU)
- Using a small number of physiological variables

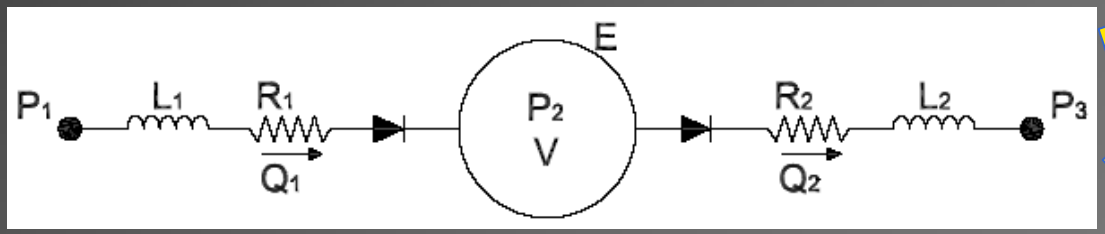
→ **Suitable for rapid diagnostic feedback**

Mathematical model

P-V diagram



One chamber model



$$\dot{V} = Q_1 - Q_2$$

$$\dot{Q}_1 = \frac{P_1 - P_2 - Q_1 R_1}{L_1}$$

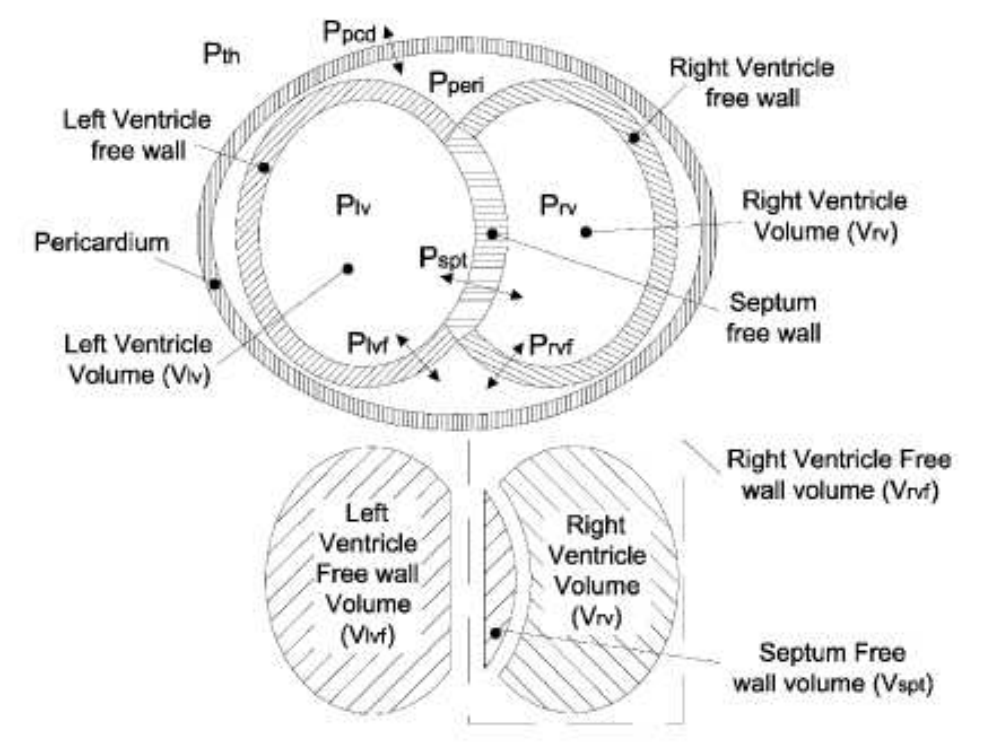
$$\dot{Q}_2 = \frac{P_2 - P_3 - Q_2 R_2}{L_2}$$

$$P_2 = e(t)E_{es}(V - V_d) + (1 - e(t))P_0(e^{\lambda(V - V_0)} - 1),$$

$$e(t) = e^{-80\left(t - \frac{period}{2}\right)^2}$$

B. W Smith et al., *Medical Engineering & Physics*, 26(2), 131-139, 2004

Ventricular interaction (VI)



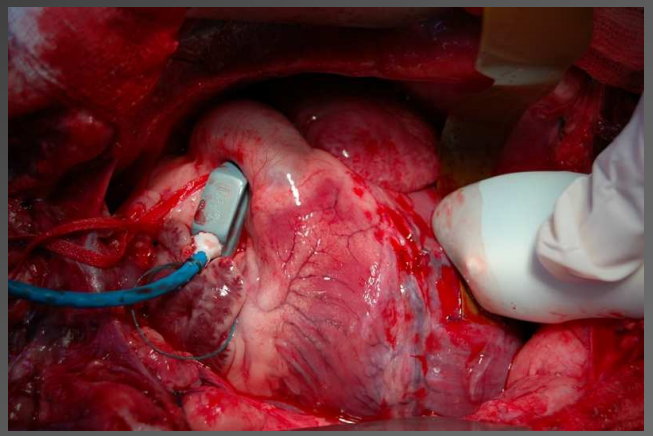
- Direct ventricular interaction (VI) has a significant impact on cardiovascular dynamics.
- It is caused by both the septum and the pericardium.
- V_{lvf}, V_{rvf} and V_{spt}, are not physical volumes, but are defined to capture the deflection of the cardiac free walls relative to the ventricle volumes.

$$e(t)E_{es,spt}(V_{spt}-V_{d,spt})+(1-e(t))P_{0,spt}(e^{\lambda_{spt}(V_{spt}-V_{0,spt})}-1)$$
$$=e(t)E_{es,lvf}(V_{lv}-V_{spt})+(1-e(t))P_{0,lvf}(e^{\lambda_{lvf}(V_{lv}-V_{0,spt})}-1)$$
$$-e(t)E_{es,rvf}(V_{rv}+V_{spt})-(1-e(t))P_{0,rvf}(e^{\lambda_{rvf}(V_{rv}+V_{0,spt})}-1)$$

Time-varying septal P-V relationship

Experimental trials: pulmonary embolism

Open-chest surgery



- Pulmonary embolization induced in pigs with autologous blood clots.
- Clots injected every two hours with decreasing concentrations.
- Aortic pressure and pulmonary artery pressure measured using micromanometer-tipped catheters (Sentron pressure-measuring catheter; Cordis, Miami, FL)
- Pressures and volume of both ventricles measured with 7F, 12 electrodes (8-mm interelectrode distance) conductance micromanometer tipped catheters (CD Leycom, Zoetermeer, The Netherlands)
- Hemodynamics variables are recorded every 30 min.
- Data from 6 pigs used in this study.

Integral based parameter identification

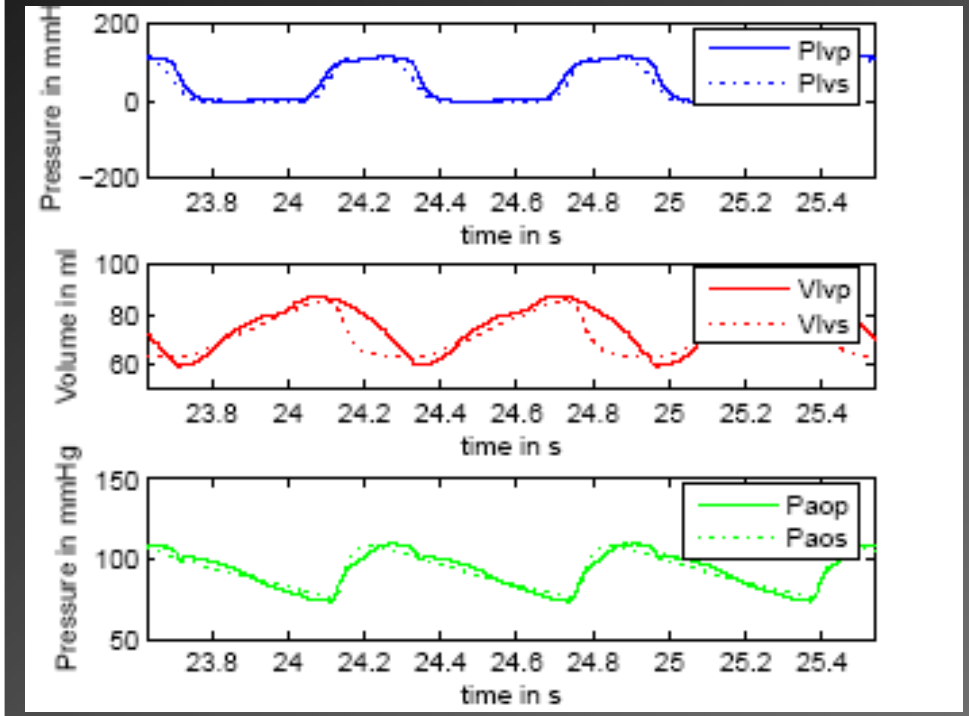
- Transforms typically non-linear and non convex ID problem into linear and convex problem
- Limited data and minimal computation

  ⟶ **Very suitable for clinical applications**
- Available experimental data: P_{ao}, P_{pa}, P_{lv}, P_{rv}, V_{lv}, V_{rv}
- System of linear equations for the full CVS model
- Parameters identified for each period of experimental data (30 min.)

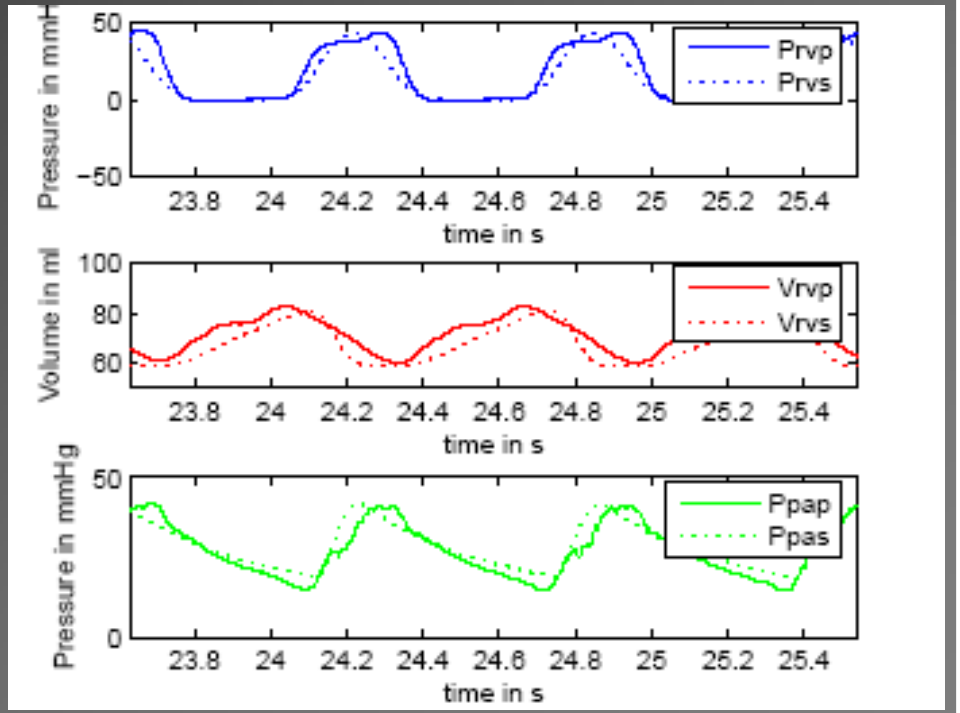
C.E. Hann et al., *Computer Methods and Programs in Biomedicine*, 81(2): 181-192 (2006)

Results - Pulmonary Embolism

Left Ventricle (30 min)



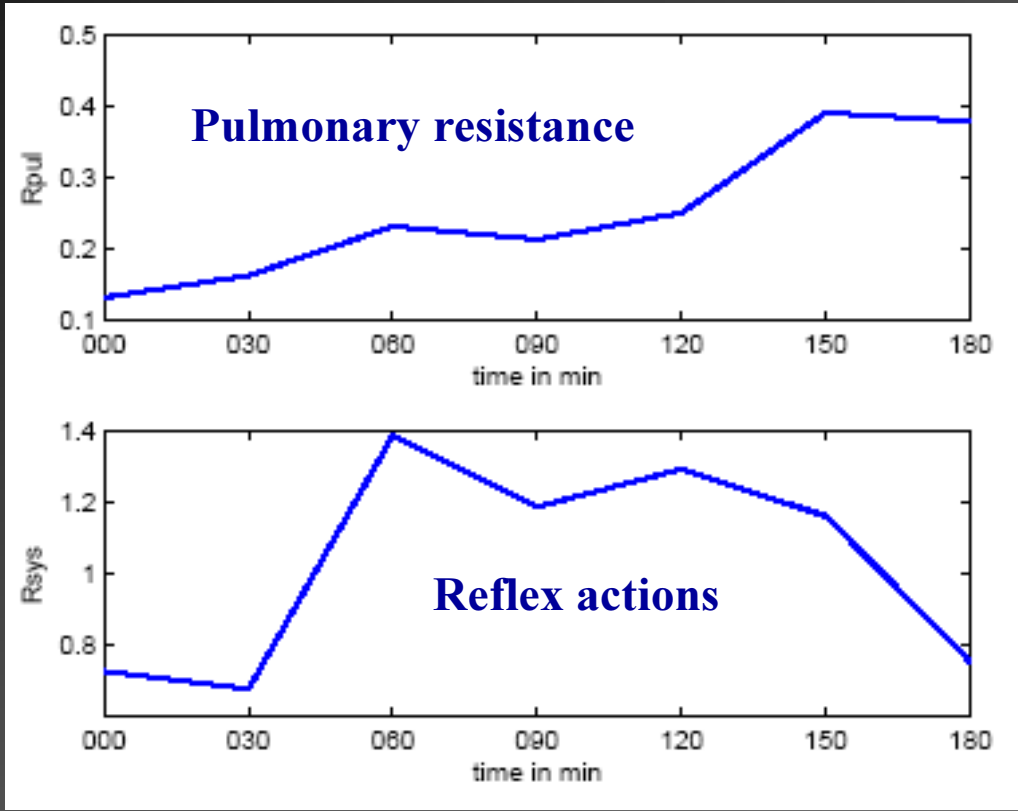
Right Ventricle (30 min)



Errors ~5%

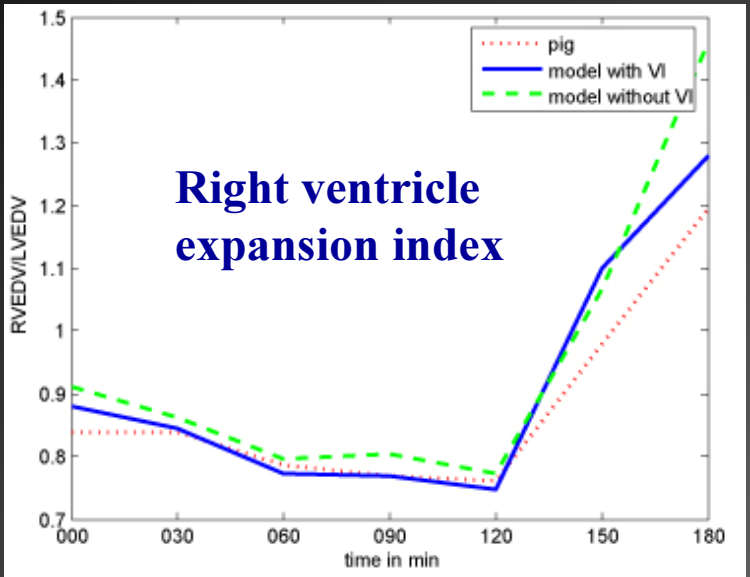
- Dashed lines: model output – solid lines: experimental data
- Use only: Pao, Ppa, min/max(Vlv, Vrv) to ID all parameters

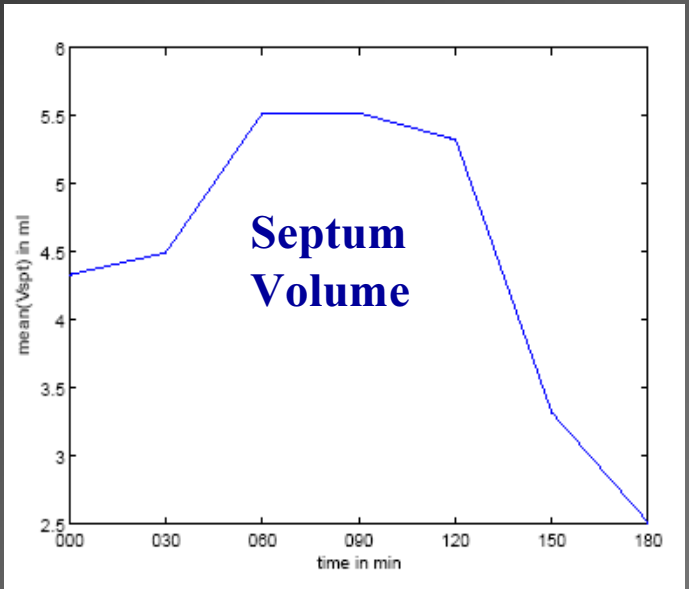
Results over time (pig 2)



- As the pulmonary embolism grows, the R_{pul} increases
- R_{sys} also increases as a reflex response to raise blood pressure and divert more blood to the heart

VI (pig 2)





- RVEDV/LVEDV increases resulting from the expansion of the RV due to the increased afterload.

- Without VI (V_{spt}=0) the model overpredicts the RV expansion.

- Main problem about VI: difficult to measure experimentally and very little data are available in the literature.

  ⟶ Wheter or not the dynamic of VI is important for diagnosis in the ICU remains to be shown in future human clinical trials.

- VI changes are captured: decreasing septal volume resulting from the compression of the LV by the overfilled RV.

Hemodynamic parameters: summary

Pig	% increase R_{pul}	% increase R_{sys}	% increase E_{eslvf}	% increase E_{esrvf}	% increase V_{spt}
1	261.44	40.66	29.10	154.60	9.13
2	89.98	49.34	74.78	20.56	40.15
3[1]	24.23	27.16	0.81	9.74	8.37
4	166.85	39.21	19.06	56.44	19.84
5	103.63	21.16	71.51	80.07	27.64
6	99.52	53.90	11.00	14.64	14.00
	↗	↗ (reflex)	↗	↗	↗

[1] Limited data for this pig and insufficient time for the parameters to change significally

Conclusions

- **Minimal cardiac model** → simulate time varying disease states
  - Accurately captures physiological trends and magnitudes
  - Accurately captures a wide range of dynamics
  - Very Fast simulation methods available
- **Integral-based parameter ID** → patient specific models
  - Error on max/min pressures/volumes < 5%
  - Identification needs a minimal number of common measurements
  - Rapid ID = Rapid diagnostic feedback
- **Pulmonary embolism**:
  - Hemodynamics successfully captured over time
  - Physiological responses to pulmonary embolism also captured
- **Future Work = septic shock currently in progress**