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
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

\[ \dot{V} = Q_1 - Q_2 \]
\[ \dot{Q}_1 = \frac{P_1 - P_2 - Q_1 R_1}{L_1} \]
\[ \dot{Q}_2 = \frac{P_2 - P_3 - Q_2 R_2}{L_2} \]

\[ P_2 = e(t)e_{es}(V - V_d) + (1 - e(t))P_0(e^{\frac{2}{\text{period}}(V - V_0)} - 1), \]

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

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

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

Time-varying septal P-V relationship
Experimental trials: pulmonary embolism

- **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.)

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Results - Pulmonary Embolism

Left Ventricle (30 min)

Right Ventricle (30 min)

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

Errors ~5%
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.

  -> Whether 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

<table>
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<tr>
<th>Pig</th>
<th>% increase $R_{pul}$</th>
<th>% increase $R_{sys}$</th>
<th>% increase $E_{eslvf}$</th>
<th>% increase $E_{esrvf}$</th>
<th>% increase $V_{spt}$</th>
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<td>1</td>
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<td>53.90</td>
<td>11.00</td>
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</tr>
</tbody>
</table>

\(^1\) Limited data for this pig and insufficient time for the parameters to change significantly
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**