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

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

\[ P_2 = e(t)E_{es}(V-V_d)+(1-e(t))P_0(e^{\lambda(V-V_d)}-1) \]
\[ e(t) = e^{-80\left(\frac{t}{\text{period}}\right)^2} \]

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.

Open-chest surgery
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
As the pulmonary embolism grows, the $R_{\text{pul}}$ increases.

$R_{\text{sys}}$ also increases as a reflex response to raise blood pressure and divert more blood to the heart.
• RVEDV/LVEDV increases resulting from the expansion of the RV due to the increased afterload.

• Without VI ($V_{\text{spt}}=0$) 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

<table>
<thead>
<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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<tr>
<td>1</td>
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<td>40.66</td>
<td>29.10</td>
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<td>3(^1)</td>
<td>24.23</td>
<td>27.16</td>
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<td>53.90</td>
<td>11.00</td>
<td>14.64</td>
<td>14.00</td>
</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