Model-based sensor of hemodynamics in critical care

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• **Problem:** Cardiac disturbances difficult to diagnose and treat
  – Limited
  – Reflex actions
  → experience and intuition (mental models)

• **Solution:** Minimal Model + Patient-Specific Parameter ID
  – Interactions of *simple* models to create *complex* dynamics
  – Primary parameters
  – Identification must use common ICU measurements
  – E.g. increased resistance in pulmonary artery → pulmonary embolism, atherosclerotic heart disease

• **However:** Identification for diagnosis requires fast parameter ID
  – Must occur in “clinical real-time”
  – Limits model and method complexity (e.g. parameter numbers, non-linearities, …)
D.E.’s and PV diagram

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

\[ R_2 = \epsilon(t) E_{es}(V - V_d) + (1 - \epsilon(t)) \frac{V^2}{2} (e^{2V - V_0} - 1) \]

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

V = Volume at zero pressure
Vd = Unstressed chamber volume

\[ P_{os}(V) = P_0 \exp(\lambda(V-V_0)) - 1 \]

Ventricle Pressure
Ventricle Volume
Reflex Actions

- Vaso-constriction - contract veins
- Venous constriction – increase venous dead space
- Increased HR
- Increased ventricular contractility

Varying HR as a linear function of $\Delta P_{ao}$

→ Simple interactions to create overall complex dynamic behaviour in the full system model
Disease States

- **Pericardial Tamponade:**
  - Build up of fluid in pericardium
  - Increase: dead space volume V0,pcd

- **Pulmonary Embolism:**
  - Increase: Rpul

- **Cardiogenic shock:**
  - Not enough oxygen to myocardium (e.g. from blocked coronary artery)
  - Decrease: Ees,lvf, Increase: P0,lvf → A more complex set of changes/interactions

- **Septic shock:**
  - Blood poisoning
  - Decrease: Rsys = systemic resistance

- **Hypovolemic shock:**
  - Severe decrease in total blood volume = sum of individual volumes

**Current Status:**
- Clinical results for Pulmonary Embolism
- Clinical results for Septic Shock
- Clinical results for PEEP interventions
- Simulated results for others
## A Healthy Human Baseline

<table>
<thead>
<tr>
<th>Output</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume in left ventricle</td>
<td>111.7/45.7 ml</td>
</tr>
<tr>
<td>Volume in right ventricle</td>
<td>112.2/46.1 ml</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>5.3 L/min</td>
</tr>
<tr>
<td>Max Plv</td>
<td>119.2 mmHg</td>
</tr>
<tr>
<td>Max Prv</td>
<td>26.2 mmHg</td>
</tr>
<tr>
<td>Pressure in aorta</td>
<td>116.6/79.1 mmHg</td>
</tr>
<tr>
<td>Pressure in pulmonary artery</td>
<td>25.7/7.8 mmHg</td>
</tr>
<tr>
<td>Avg pressure in pulmonary vein</td>
<td>2.0 mmHg</td>
</tr>
<tr>
<td>Avg pressure in vena cava</td>
<td>2.0 mmHg</td>
</tr>
</tbody>
</table>
Simulation of Disease States

- **Pericardial Tamponade**
  - $P_{pu} = 7.9 \, \text{mmHg}$
  - $CO = 4.1 \, \text{L/min}$
  - $MAP = 88.0 \, \text{mmHg}$

- **Pulmonary Embolism:** $R_{pul}$ increases as embolism induced

- **All other disease states similarly capture physiological trends and magnitudes**
Integral Method - Concept

- \( \dot{x} = ax + b \sin(t) + c, \quad x(0) = 1 \)
- \( a = -0.5, \quad b = -0.2, \quad c = 0.8 \)

(simple example with analytical solution)

Discretised solution analogous to measured data

- Work backwards and find a, b, c
- Current method – solve D. E. numerically or analytically

\[
x(t) = \frac{1}{(a^2 + 1)a} (e^{at}(a + c + ab + ca^2 + a^3) - (ab \cos t + ba^2 \sin t + ca^2 + c))
\]

- Find best least squares fit of x(t) to the data
- Non-linear, non-convex optimization, computationally intense

- integral method
  – reformulate in terms of integrals
  – linear, convex optimization, minimal computation
Integral Method - Concept

- Integrate $\dot{x} = ax + b \sin(t) + c$, both sides from $t_0$ to $t$ ($t_0 = 4\pi$)

\[
\int_{t_0}^{t} \dot{x} \, dt = \int_{t_0}^{t} (ax + b \sin(t) + c) \, dt
\]

\[
\Rightarrow x(t) - x(t_0) = a \int_{t_0}^{t} x \, dt + b \int_{t_0}^{t} \sin(t) \, dt + c \int_{t_0}^{t} 1 \, dt
\]

\[
\Rightarrow x(t) = x(t_0) + a \int_{t_0}^{t} x \, dt + b(\cos(t_0) - \cos(t)) + c(t - t_0)
\]

- Choose 10 values of $t$, between $t_0 = 4\pi$ and $6\pi$ form 10 equations in 3 unknowns $a, b, c$

\[
a \int_{t_0}^{t_i} x \, dt + b(1 - \cos(t_i)) + c(t_i - t_0) = x(t_i) - x(t_0), \quad i = 1, \ldots, 10
\]
Integral Method - Concept

\[
\begin{bmatrix}
\int_0^1 x \, dt \\
\vdots \\
\int_0^{10} x \, dt
\end{bmatrix}
\begin{bmatrix}
\cos(t_0) - \cos(t_1) \\
\vdots \\
\cos(t_0) - \cos(t_{10})
\end{bmatrix}
\begin{bmatrix}
t_1 - t_0 \\
\vdots \\
t_{10} - t_0
\end{bmatrix}
\begin{bmatrix}
a \\
\vdots \\
c
\end{bmatrix}
= 
\begin{bmatrix}
x(t_1) - x(t_0) \\
\vdots \\
x(t_{10}) - x(t_0)
\end{bmatrix}
\]

- Linear least squares (unique solution)

<table>
<thead>
<tr>
<th>Method</th>
<th>Starting point</th>
<th>CPU time (seconds)</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integral</td>
<td>-</td>
<td>0.003</td>
<td>[-0.5002, -0.2000, 0.8003]</td>
</tr>
<tr>
<td>Non-linear</td>
<td>[-1, 1, 1]</td>
<td>4.6</td>
<td>[-0.52, -0.20, 0.83]</td>
</tr>
<tr>
<td>Non-linear</td>
<td>[1, 1, 1]</td>
<td>20.8</td>
<td>[0.75, 0.32, -0.91]</td>
</tr>
</tbody>
</table>

- Integral method is at least 1000-10,000 times faster depending on starting point
- Thus very suitable for clinical application
Clinical trials - Belgium

- **Pulmonary embolism** induced in pigs (collaborators in Liege, Belgium)
  - blood clots injected every two hours (6 pigs, 32.75kg ± 1.83kg)

Open chest

Ventilated and sedated

12 Electrode Conductance Catheter
  (Vlv,Vrv,Plv,Prv)

Also measure Pao,Ppa
Coronary arteries (structure similar to humans)

Ischemia
Clinical setting
Clinical Results - Pulmonary Embolism

- Use only: Pao, Ppa, min/max(Vlv, Vrv) to ID all parameters
- Far fewer measurements than in simulation
Animal Model Results – PV loops

Left Ventricle (120 mins)

Right Ventricle (120 mins)

Left Ventricle (180 mins)

Right Ventricle (120 mins)
Animal Model Results Over Time

PV loops (Pig 2)

Pulmonary resistance (Pig 2)

Reflex actions (Pig 2)

Septum Volume (Pig 2)

Right ventricle expansion index (Pig 2)

Rpul – All pigs
**Model-based coupling**

Coupling preserved in first 30 minutes

**Pig 2**

**Pig 4**

Decoupling (same Ees_rvf, Rpul ↑)

- Invasive measure:
  
  \[
  \text{start} = 2.78 \pm 0.16, \quad \text{end} = 0.72 \pm 0.24
  \]

- Model-based measure:
  
  \[
  \text{start} = 2.01 \pm 0.47, \quad \text{end} = 0.70 \pm 0.20
  \]
• Coronary flow ↑ to preserve coupling
• RV requires more oxygen to maintain CO (less efficient)
New results on Septic Shock

Coupling = \frac{Contractility}{Afterload}

Model-based coupling

- Seven pigs (Belgium) - Endotoxin infusion over first 30 minutes
- Therapy ➔ large-pore membrane Hemofiltration from 60-240 minutes
- Model accurately matches all hemodynamic response < 8% error
- Preserved coupling validated with invasive rapid vena cava occlusion maneuver
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
  - **Simulation**: ID errors from 0-10%, with 10% noise
  - **Animal models**: Pressures (Total Error) = 2.22±2.17 mmHg (< 5%)
    Volumes (Total Error) = 2.37±2.01 ml (< 5%)
  - **PEEP Therapy prediction**: within 10% error

- **Identifiable using a minimal number of common measurements**
  - Rapid ID method, easily implemented in Matlab
  - Rapid ID = Rapid diagnostic feedback

- **Future Work** = septic shock (currently), ischemia, human trials and other disease states (2007-)
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Questions ???