Using Modeling to Characterize Patients with Pulmonary Hypertension

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Pulmonary hypertension

- **Pulmonary hypertension** (PH) is high blood pressure ($\geq 25$ mmHg) in the pulmonary arteries
- Impact on the *structure* of the network
  - Blood vessels harden
  - Pulmonary vascular resistance increases
- PH is a chronic and progressive disease with no cure
Data

• Pressure measurements from right heart catheterization and a pressure cuff
  – **Time-varying data** from right atrium, right ventricle, pulmonary arteries, and pulmonary artery wedge
  – **Static data** (max and min) from systemic arteries and pulmonary veins

• Blood flow measurements for cardiac output (CO) from Swan-Ganz catheter

*Figure: Right heart catheterization pressure waveforms*
Cardiovascular Model

Compartment model analogous to an electric circuit

- Pressure $p$ (mmHg) – Voltage
- Flow $q$ (mL/s) – Current
- Volume $V$ (mL) – Charge
- Resistance $R$ (mmHg·s/mL) – Resistance
- Compliance $C$ (mL/mmHg) – Capacitance

25 parameters and 8 states
Model Equations

Conservation of volume
\[ \frac{dV_{s,i}}{dt} = q_{in} - q_{out} \]

Ohm's law
\[ q_i = \frac{p_{in} - p_{out}}{R_i} \]
\[ q_{valve} = \begin{cases} 
q_i & \text{if } p_{in} > p_{out} \\
0 & \text{otherwise}
\end{cases} \]

Pressure-volume relation
\[ V_i - V_{un,i} = C_i(p_{int} - p_{ext}) \]

Pressure in the heart
\[ p_h = E_h(t)(V_h - V_{un,h}) \]

with time-varying elastance function \( E_h(t) \)

\[ \square \text{ dynamic RHC data} \quad \star \text{ static data} \]
Parameter Subset Selection

- Sensitivity matrix and ranking
  \[ S = \begin{pmatrix} S_{11} & \ldots & S_{1n} \\ \vdots & \ddots & \vdots \\ S_{n1} & \ldots & S_{nn} \end{pmatrix} \text{ for } i, j = 1 \ldots n \]
  where \( S_{i,j} = \frac{\partial y(t_i, \theta)}{\partial \theta_j} \)

- Correlation analysis
  \[ \widetilde{c}_{ij} = \frac{C_{ij}}{\sqrt{C_{ii}C_{jj}}} < \gamma \quad C = (S^T S)^{-1} \]

Figure: Parameters ranked most to least sensitive
Parameter Inference

- Optimization - use the Levenberg Marquardt method to minimize the least squares cost, $J_i$.

$$J_i = r_i^t r_i,$$

$r_i = r_1, r_2$

- Residual Functions - capture the relative differences between data and model.

$r_1 = r_s$ [static values only]

$r_2 = [r_s, r_{ra}, r_{rv}, r_{pa}]$ [static and dynamic values]

$$r_s = \frac{1}{\sqrt{N_s}} \frac{y - y^d}{y^d}$$
Treatment

- Simulate 3 types of PH treatments to improve hemodynamic predictions
  1. Vasodilation drugs
  2. Surgical intervention (BPA)
  3. Combination of both types
- Simulate various treatment intensities by adjusting parameters related to PH
  - reducing resistance
  - increasing compliance
- Mean pulmonary arterial pressure is computed and compared to normotensive predictions

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Parameter</th>
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<tbody>
<tr>
<td></td>
<td>( R_p )</td>
</tr>
<tr>
<td>Vasodilator</td>
<td>( \downarrow )</td>
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<tr>
<td>BPA</td>
<td>( \downarrow )</td>
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<tr>
<td>BPA with vasodilator</td>
<td>( \downarrow )</td>
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Results

- Subset selection analysis
  - Right side heart parameters most influential for $r_1$
  - $T_{crv}$, $T_{rrv}$ and $\tau_{cra}$ are the most influential for $r_2$
  - $[R_{ava}, R_{mva}, R_{pva}, R_{pv}, R_{sv}]$ are consistently noninfluential

- Model predictions
  - $r_1$ improves CO and static max/min prediction
  - $r_2$ improves RA, RV (drastically) and PA (marginally) fit to waveforms

- Treatment
  - Normotensive PA pressure ranges (below 20 mmHg) were achieved for T5 and T8: “cured” after treatment of Patients 3 and 4
Discussion

- Using surgery, CTEPH is the only PH disease that can be “cured”
- Predicting effects of PH treatments on both the pulmonary and systemic arterial side
- Overall, model outcomes are consistent with physiological understanding of the disease
  - PH induces increased PVR, decreased PAC
  - Elevated minimum RV elastance, leading to increase mPAP
- Further work
  - Using our model to observe patient reactions to exercise
  - Developing a model selection program to better differentiate PH severities
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