GENERATIVE PHYSIOLOGICAL MODEL-BASED PREDICTION OF PHYSIOLOGICAL CLOSED-LOOP SYSTEM PERFORMANCE

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Motivation:

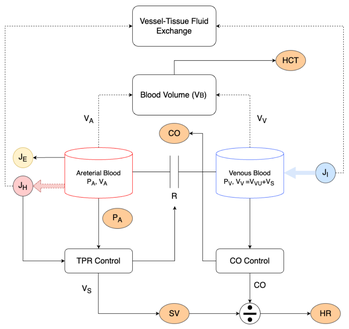
- Physiological closed-loop controlled medical devices has the potential to offer an exciting opportunity to enable automated critical care.
- The evaluation of safety and efficacy profile of these systems remain crucial in regulatory science.
- In silico generative model-based prediction of physiological closed-loop system performance helps us gain better insights about such systems.

Objectives:

- To develop a realistic virtual patient generator (VPG) using experimental data of sheep and pigs undergoing hemorrhage and resuscitation.
- To apply the VPG to predict performance metrics of a known physiological closed-loop control algorithm in unseen dataset.
- To compare the predicted in silico performance metrics with in vivo metrics obtained from experiments.

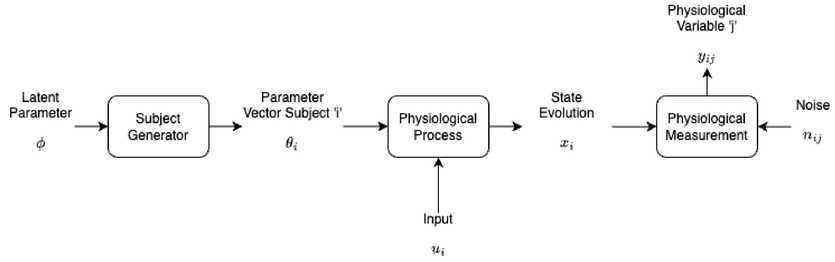
Mathematical Model Development:

- The mathematical model takes hemorrhage rate (J_H) and fluid infusion rate (J_I) as inputs, and predicts hematocrit (HCT), cardiac output (CO), mean arterial blood pressure (P_A), stroke volume (SV), and heart rate (HR) as outputs.



Model-Based Virtual Patient Generator:

- Given the mathematical model, the latent parameters in the probabilistic graphical model φ (VPG), θ, and n are inferred using experimental data.
- In this study, we used in vivo data collected from 27 sheep and 12 pigs undergoing hemorrhagic shock and fluid resuscitation

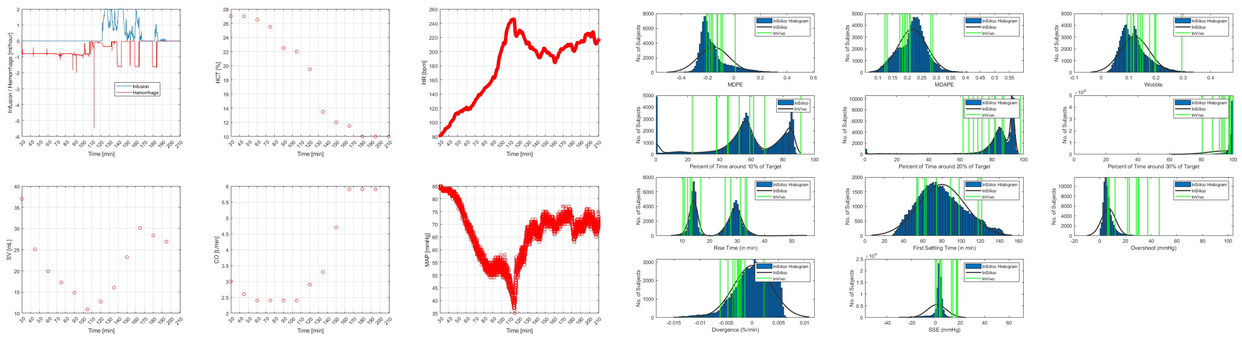


Prediction of Physiological Closed-Loop Control Algorithm Performance:

- An independent experimental data consisting of 13 pigs was used to assess the predictive capability of the VPG. Pigs underwent closed-loop controlled resuscitation using a known 2-DOF PID control algorithm.
- Performance metrics were compared between in silico vs in vivo.

Results and Discussion:

- The left plot shows a representative example of the experimental data.
- The right plot compares the distributions of in silico and in vivo performance metrics.



- The in silico metrics capture the in vivo metrics adequately except overshoot. This can be attributed to the fact that the overshoot in training data is lower than the test dataset.

Conclusion:

- The VPG based on generative physiological modeling can adequately predict the performance metrics of physiological closed-loop control algorithms in unseen experiments. This opens up the possibility of testing various control algorithms in silico to understand their safety and efficacy profile.

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Award ID#: CNS-1748762