A Physiological Mathematical Model of Heart Rate Response to Fluid Perturbation

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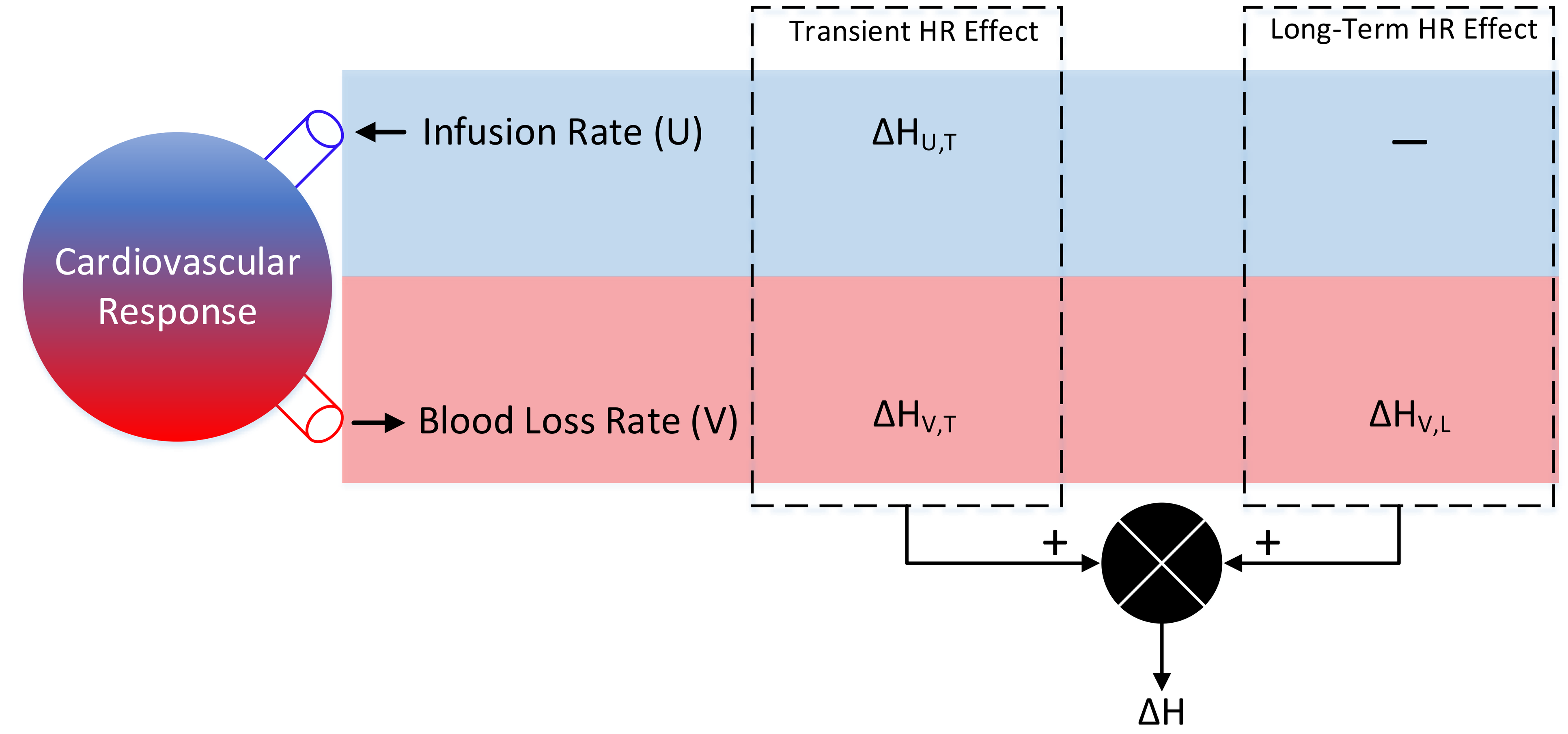
Background: Physiological closed-loop controlled (PCLC) medical devices are a rapidly advancing type of technology that can control a measured physiological variable in a closed-loop manner.
Assessment of PCLC medical devices through comprehensive clinical trials is often costly. Thus, in conjunction with smaller clinical trials, mathematical models can be leveraged to evaluate a device's performance under different physiological conditions.

Method: To create the mathematical model of Heart Rate (HR) response to blood loss and fluid infusion, two types of responses need to be studied.

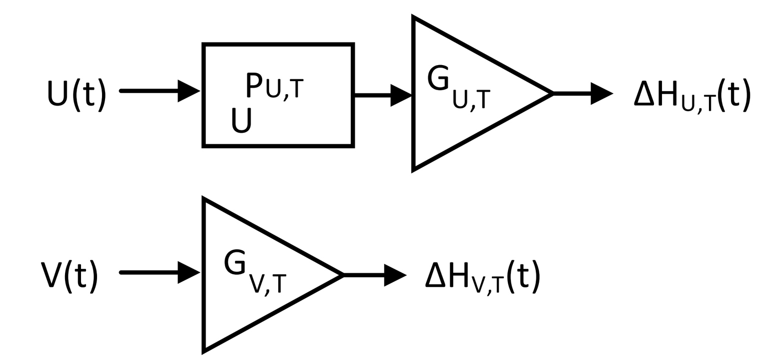
- Transient Response: describes the instantaneous change in HR due to fluid perturbation
- Long-term response: The change in the steady-state value of HR response due to the perturbation.

A severe hemorrhage causes a transient increase in HR. Moreover, due to the loss in blood volume and arterial pressure, there may be a long-term increase in HR within a few hours after the hemorrhage till it reaches a plateau. Fluid infusion also transiently alleviates HR response, as reported in prior studies. A control-oriented mathematical model of HR is developed in this research. To capture the long-term HR response due to the blood loss, a proportional-integral controller is implemented into the model, which enforces the change in HR to follow the expected long-term effect of blood loss.

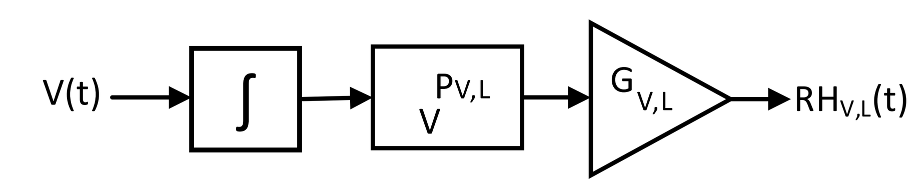
Result: In this research, a model to predict the change in HR due to hemorrhage and fluid infusion was presented. This model applies a control-oriented approach where the rate of hemorrhage greatly influences the change in HR. Using a maximum likelihood optimization and averaged between 21 sheep subjects, the fitting performance showed a normalized root mean square error of 7+/-3%. This model can be incorporated into existing hemodynamic models to create a virtual cohort of patients for testing PCLC devices for hemorrhagic applications.



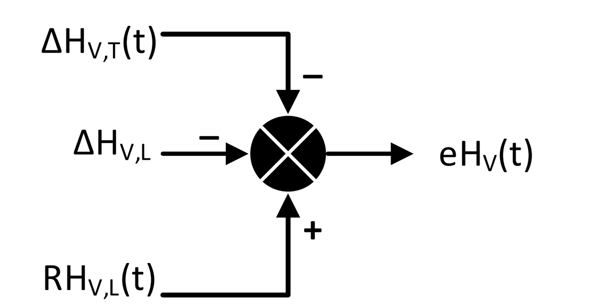
(A) Heart rate (H) model structure determined by transient and long-term effects to fluid perturbation



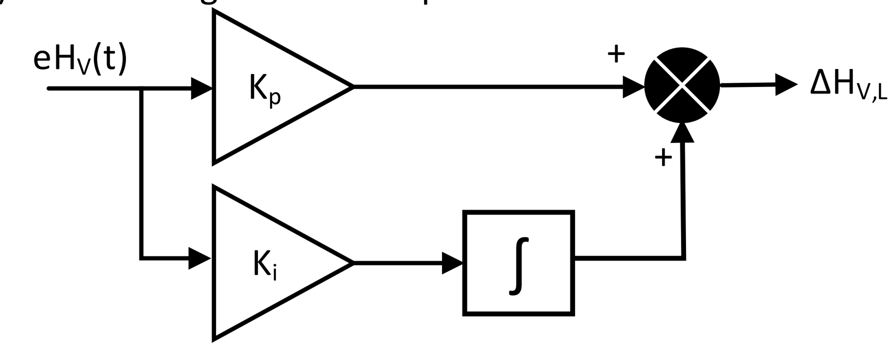
(B) Transient HR response to fluid perturbation



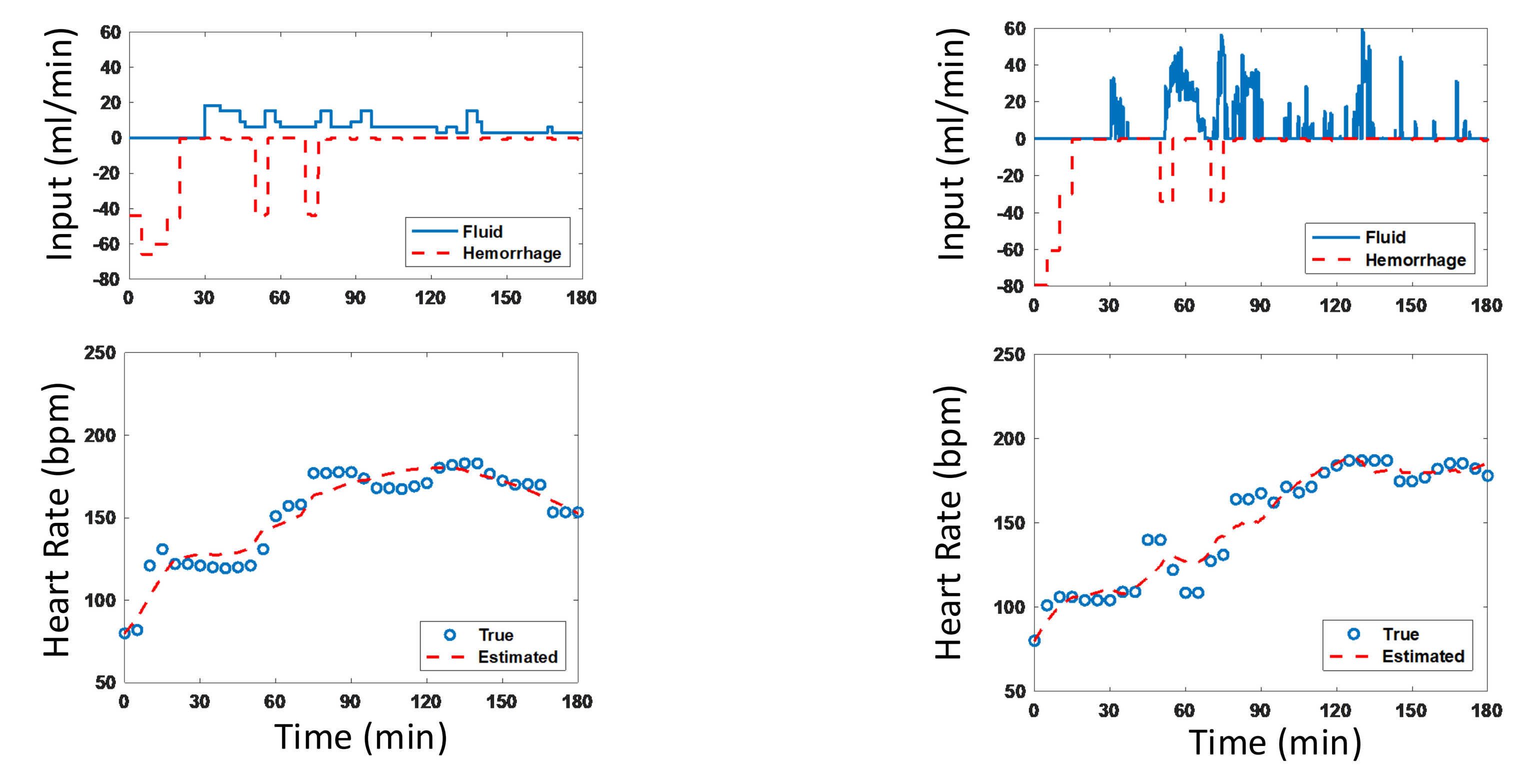
(C) Desired long-term HR response to blood loss



(D) Error in HR for long-term closed-loop feedback effect



(E) Control-oriented long-term HR response to blood loss



(F) Heart rate response estimation to fluid perturbation in two representative subjects

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