MARYLAND

Model-Based Non-Invasive Hemorrhage Detection:



Observer-Based and Parameter Estimation-Based Approaches

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Motivation, Novelty, & Challenges

- Motivation: Early detection of hemorrhage is critical to clinical decision making and interventions for hemorrhaging patients. This work concerns model-based hemorrhage detection. It compares two alternative algorithms in their efficacy to detect hemorrhage using continuous SpHb measurements.
- Novelty: We pursue model-based state and parameter estimation approaches as opposed to data-driven routes widely explored in the literature.
- Challenges: (i) The algorithm must detect hemorrhage against a wide range of model parameter variability. (ii) The system is nonlinear in its output equation.

Methodology

- A lumped-parameter blood volume kinetics model is used as the plant dynamics in which rates of hemorrhage (H) and resuscitation (I) are the inputs and fractional change in blood volume is the output.
- If there is hemorrhage, the output equation becomes nonlinear. One approach to handle the nonlinearity is to use nonlinear state estimation. The other approach is to approximate the output equation to linear and derive signatures of hemorrhage via extensive estimation error analysis. We explored the latter option in this work.
- Extensive in silico testing of both the algorithms was evaluated using virtual subjects created using collective variational inference from the dataset of 23 sheep subjects undergoing acute hemorrhage and volume resuscitation.

Blood Volume Kinetics Model

Blood Volume (BV) Kinetics Model



 The plant dynamics can be represented in state-space representation as below:

$$\begin{split} \begin{bmatrix} x_1 \\ \dot{x}_2 \end{bmatrix} &= \begin{bmatrix} -k & 1 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + \begin{bmatrix} \frac{k}{1} \\ 1 + \alpha_u \end{bmatrix} u - \begin{bmatrix} \frac{k}{1} \\ \frac{k}{1 + \alpha_h} \end{bmatrix} u \\ z &= \frac{1}{V_{B0}} x_1 = \frac{\sigma(0) - \sigma(t)}{\sigma(t)} - \frac{\int_0^t h(\tau)\sigma(\tau)d\tau}{V_{B0}\sigma(t)} \end{split}$$

where x_1 is change in BV from initial BV, x_2 is interstitial fluid shift volume, V_{B0} pre-resuscitation/hemorrhage BV, $\alpha_u \& \alpha_h$ are volume split ratios due to fluid gain and loss in the steady state, k is fluid shift rate constant, $\sigma(t)$ is continuous SpHb measurement, u and h are rate of fluid resuscitation (I) and hemorrhage (H), respectively.

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Hemorrhage Detection Algorithms

 Hemorrhage is modelled as state variable x₃, and then an observer is designed neglecting the unknown term related to hemorrhage in measurement equation.

$$\dot{\mathbf{x}} = \begin{bmatrix} -\mathbf{k} & 1 & -\frac{1}{k} \\ 0 & 0 & -\frac{\mathbf{k}}{1+\alpha_{h}} \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \mathbf{x}_{1} \\ \mathbf{x}_{2} \\ \mathbf{x}_{3} \end{bmatrix} + \begin{bmatrix} \frac{1}{k} \\ \frac{1}{1+\alpha_{u}} \\ 0 \end{bmatrix} \mathbf{u}$$

<u>Observer</u>: $\dot{\hat{\mathbf{x}}} = A\hat{\mathbf{x}} + B\mathbf{u} + L\left[\left(\frac{x_1}{v_{B_0}} + \frac{\int_0^t h(\tau)\sigma(\tau)d\tau}{v_{B_0}\sigma(t)}\right) - \frac{\hat{x_1}}{v_{B_0}}\right]$

* <u>Algorithm1</u> (A1): Carrying out the error dynamics analysis on the observer design and assuming that hemorrhage h(t) is slowly varying and approximated to a step signal, we can derive $\hat{x}_3(t) < \bar{x}_3(t)$

with $\bar{x}_3(t)$ being the lower bound of nominal $x_3(t)$ values when h(t) = 0.

• The linear parametric model and parameter adaptation law are given by: $\dot{z} + kz = \frac{1}{V_{E0}} \left(u + \frac{k}{1 + \alpha_u} \int_0^t u(c) dc \right)$

$$\dot{\hat{\theta}} = \Gamma \varepsilon \phi = \Gamma \left(\dot{z} - \left[\hat{k} \ \frac{\widehat{1}}{V_{B0}} \ \frac{\widehat{k}}{V_{B0}(1 + \alpha_u)} \right] \begin{bmatrix} -z \\ u \\ v \end{bmatrix} \right) \begin{bmatrix} -z \\ u \\ v \end{bmatrix}$$

* <u>Algorithm2</u> (A2): If the patient is resuscitating then it can be derived that hemorrhage can be detected if $\widehat{\theta_3} > \theta_3$

Results

- Normalized time (NT = Time to detect hemorrhage/Time to lose 25% BV) is less than 1, then we safely detected hemorrhage and using this F1 score was calculated for a range of H-I scenarios on 200 virtual subjects.
- The contour plots below show the F1 score for a wide range of H-I scenarios across the virtual subjects for A1 & A2.
- The table below summarizes the overall performance (average) and it shows that A1 outperforms A2.



Conclusion

0.58

Δ2

0.72

0.61

0.58

The results of this study suggest that both the observer-based and parameter estimation-based methods show potential in detecting hemorrhage, but the performance degraded during high hemorrhage rates and low infusion rates.