Hidden Markov methodology for identifying physiological states of shock in intensive care units

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Introduction

Motivation:

- Detecting hemorrhaging (i.e. internal bleeding) in patients in intensive care units (ICUs) can pose significant challenges for critical care workers because the trauma occurs **subcutaneously**. Clinicians ultimately rely on monitoring vital signs for specific trends indicative of a hemorrhage event.
- Delays in the recognition and treatment of deteriorating patients have consistently been associated with increased mortality.
- In those with trauma-related hemorrhage, **40 percent** of preventable deaths are related to inadequate hemorrhage recognition or control [1, 2].

Objectives:

- Develop an **unsupervised** learning methodology for **early detection** of internal bleeding to reduce the number of deaths witnessed in trauma ICUs.
- Use a **Bayesian regime switching model** (an extension of a hidden Markov model (HMM)), with informed priors to assist in identifying latent states of shock.
- Integrate method into medical software to provide real time probabilistic assessments of bleeding and other shock events.

Electronic Health Record (EHR) Data

Longitudinal data (4 major vitals):

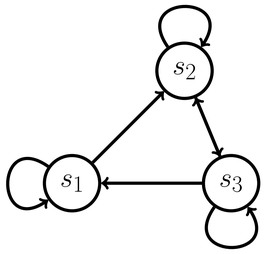
- (1) Heart rate, (2) mean arterial pressure (MAP), (3) hemoglobin, and (4) lactate concentration
- All vitals are discretized on a 15 minute grid.

Other patient information (covariates):

- International Classification of Disease (ICD-10) codes: indicator of patient's medical history
- Lab measurements
- Red blood cell (RBC) transfusion order and administration times (**IMPORTANT**)

Regime Switching Setup

State Transitions



- s_1: Baseline (low risk)
- s_2: Shock event
- s_3: Recovery

HMM Description

- doubly nested stochastic process
- latent state space follows a Markov process where each state affects the distribution of the observed data.
- Time is treated as discrete since vitals are measured every 15 minutes, and the latent state Markov process is defined by a probability transition matrix.
- **Standard Assumption**: the response at a given time point is conditionally independent of all other observations, given the latent state at that instant.

Model Statement

- Bayesian HMM where the physiological state sequence is the latent Markov process.
- Let $\boldsymbol{Y}^{(i)} = (\boldsymbol{y}_1^{(i)}, \ldots, \boldsymbol{y}_{n_i}^{(i)})$ represent the multivariate response for patient $i \in \{1, \ldots, N\}$ with

$$\boldsymbol{y}_k^{(i)} = \left(\text{hemoglobin}_k^{(i)},\ \text{heart rate}_k^{(i)},\ \text{MAP}_k^{(i)},\ \text{lactate}_k^{(i)}\right)^T, k \in \{1, \ldots, n_i\}$$

- Contrary to the conditional independence assumption common in HMMs, the response is modelled using a **vector autoregressive (VAR) process** where

$$\boldsymbol{y}_k^{(i)} = \boldsymbol{\nu}_k^{(i)} + \boldsymbol{A}_1 \cdot (\boldsymbol{y}_{k-1}^{(i)} - \boldsymbol{\nu}_{k-1}^{(i)}) + \boldsymbol{u}_k, \quad \boldsymbol{u}_k \sim N_4(\boldsymbol{0}, \boldsymbol{R}) \tag{1}$$

and

$$(\boldsymbol{\nu}_k^{(i)})^T = \left(1 \ \textstyle\sum_{l=1}^{k} \mathbf{1}\{\boldsymbol{b}_l^{(i)} = 2\} \ \sum_{l=1}^{k} \mathbf{1}\{\boldsymbol{b}_l^{(i)} = 3\}\right) \boldsymbol{\alpha}^{(i)} + \boldsymbol{x}_k^{(i)} \boldsymbol{\beta}.$$

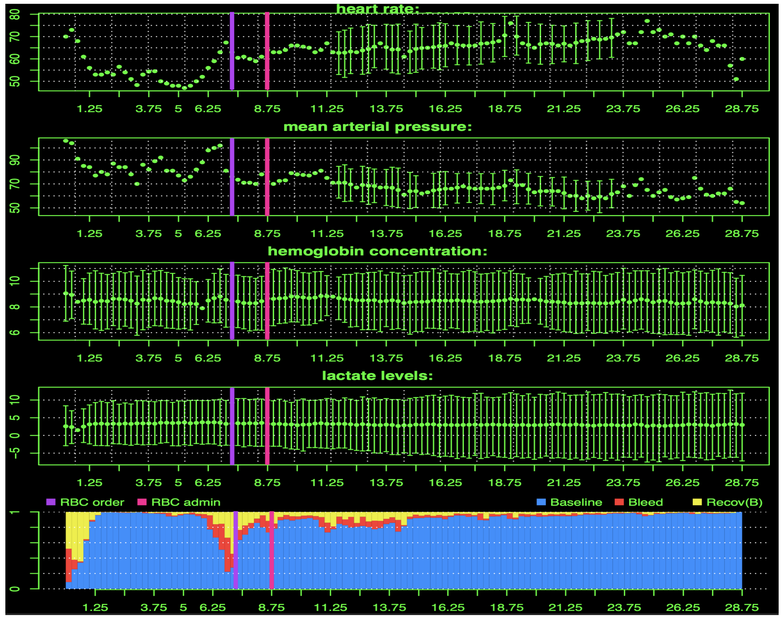
(i) $\boldsymbol{b}^{(i)} = (\boldsymbol{b}_1^{(i)}, \ldots, \boldsymbol{b}_{n_i}^{(i)})$ is the latent physiological state sequence **modelled as a Markov process**
(ii) $\boldsymbol{\alpha}^{(i)}$ is a 3×4 matrix of random effect coefficients corresponding to the states' effects on the mean process.
(iii) $\boldsymbol{x}_k^{(i)}$ is a 1×1 covariate matrix corresponding to the administration of RBC transfusions
(iv) $\boldsymbol{\beta}$ is a 1×4 vector representing the effect of RBC transfusions on the means of the four vital processes.

- The stationary and conditional distributions for the VAR(1) process are

$$\begin{cases} \boldsymbol{y}_1^{(i)} \mid \boldsymbol{b}_1^{(i)}, \boldsymbol{\alpha}^{(i)}, \boldsymbol{\beta}, \boldsymbol{A}_1, \boldsymbol{R} & \sim \mathrm{N}_4\left(\boldsymbol{\nu}_1^{(i)}, \boldsymbol{\Gamma}\right) \\ \boldsymbol{y}_k^{(i)} \mid \boldsymbol{y}_{k-1}^{(i)}, \boldsymbol{b}_k^{(i)}, \boldsymbol{b}_{k-1}^{(i)}, \boldsymbol{\alpha}^{(i)}, \boldsymbol{\beta}, \boldsymbol{A}_1, \boldsymbol{R} & \sim \mathrm{N}_4\left(\boldsymbol{\nu}_k^{(i)} + \boldsymbol{A}_1(\boldsymbol{y}_{k-1}^{(i)} - \boldsymbol{\nu}_{k-1}^{(i)}), \boldsymbol{R}\right) \end{cases}$$

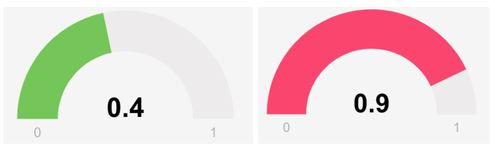
- Parameter estimation is done using Markov chain Monte Carlo (MCMC) sampling.

Probabilistic Assessment of Shock Events



R-Shiny Application

- A crucial piece of this project is how the results from the model are presented in a clinical environment.
- Presenting the posterior probabilities from the charts before is *not* the most intuitive representation of the possibility of shock.
- A better representation answers the question:
  What is the probability that a patient has started bleeding at some point in the last ____ amount of time?
- The probability is presented in a dial system, similar to other medical devices (e.g. *FloTrac*).



Future Developments

- **Assessing model performance**: This paper and methodology is still under development, thus we still have to test this approach outside of the training data. Using medical expertise and other model evaluation techniques, we will assess the performance of our method in early detection of bleeding and other shock events.
- **Adding more states**: Currently this is a three state model which more broadly detects "shock." However, extending the model by adding more states will allow for more refined detection of specific shock states (e.g. hemorrhage, sepsis, etc.).
- **Incorporating patient medicine**: Medication data can seriously affect the vital measurements. This will fine tune the ability to detect shock events because it will allow the model to determine if the vitals are shifting due to medicine, or if some physiological state of shock is occurring.
- **Calibrating the detection of shock events**: When applied in a medical setting, it is important to minimize the number of false-positive alerts. Thus, based on simulated data, a "cutoff" can be determined to serve as an alarm threshold.
- **Cardiac waveform data**: For the data currently, the information about a patient is discretized every 15 minutes. However, using *arterial lines*, physicians can monitor vitals at a nearly continuous rate. Thus, developing the methodology for a functional response HMM could have large application in progressing the research of early shock detection.

References

[1] Holcomb, J. B., Tilley, B. C., Baraniuk, S., Fox, E. E., Wade, C. E., Podbielski, J. M., Del Junco, D. J., Brasel, K. J., Bulger, E. M., Callcut, R. A. et al. [2015], 'Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the proppr randomized clinical trial', *Journal of the American Medical Association* 313(5), 471–482. PMID: 25647203.

[2] Stensballe, J., Henriksen, H. H. and Johansson, P. I. [2017], 'Early haemorrhage control and management of trauma-induced coagulopathy: the importance of goal-directed therapy', *Current Opinion in Critical Care* 23(6), 503–510. PMID: 29059118.

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