Hemodynamic Monitoring Using Switching Autoregressive Dynamics of Multivariate Vital Sign Time Series

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Abstract

In a critical care setting, shock and resuscitation endpoints are often defined based on arterial blood pressure values. Patient-specific fluctuations and interactions between heart rate (HR) and blood pressure (BP), however, may provide additional prognostic value to stratify individual patients' risks for adverse outcomes at different blood pressure targets. In this work, we use the switching autoregressive (SVAR) dynamics inferred from the multivariate vital sign time series to stratify mortality risks of intensive care units (ICUs) patients receiving vasopressor treatment. We model vital sign observations as generated from latent states from an autoregressive Hidden Markov Model (AR-HMM) process, and use the proportion of time patients stayed in different latent states to predict outcome. We evaluate the performance of our approach using minute-by-minute HR and mean arterial BP (MAP) of an ICU patient cohort while on vasopressor treatment. Our results indicate that the bivariate HR/MAP dynamics (AUC 0.74 [0.64, 0.84]) contain additional prognostic information beyond the MAP values (AUC 0.53 [0.42, 0.63]) in mortality prediction. Further, HR/MAP dynamics achieved better performance among a subgroup of patients in a low MAP range (median MAP < 65 mmHg) while on pressors. A realtime implementation of our approach may provide clinicians a tool to quantify the effectiveness of interventions and to inform treatment decisions.

1. Introduction

Patients in the intensive care units (ICUs) are critically ill and physiologically unstable, requiring constant monitoring in their vital sign signals, such as heart rate (HR) and blood pressure (BP). Arterial blood pressure, in particular, is closely monitored for patients who are hemodynamically unstable. When patients' mean arterial blood pressure (MAP) values fall below a critical threshold, immediate medical attention is required; fluid resuscitation and vasopressor treatment are administered to bring patients' blood pressure back to a normal range. Surviving sepsis campaign, for example, recommends targeting a mean arterial blood pressure of at least 65 mmHg [1].

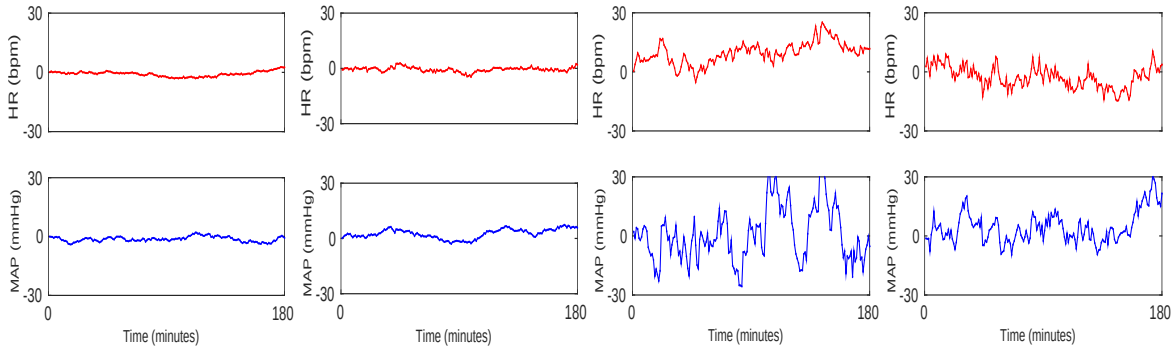
While clinicians often adopt specific blood pressure target for diagnosis and treatment strategies (e.g., titration of pressor dosage), tracking the patient-specific fluctuations and interaction between heart rate (HR) and blood pressure (BP) may provide additional insights on physiological states of a patient. In this work, we use switching autoregressive dynamics of vital sign time series to stratify mortality risk of patients at different blood pressure levels while on vasopressor treatment. The underlying premise of our approach is that subtle changes in the dynamics of vital sign time series reflect patients' hemodynamic responses to the vasopressor treatment, and therefore can potentially provide prognostic information for outcome prediction.

A framework based on autoregressive Hidden Markov Model (AR-HMM) process [2], or switching autoregressive (SVAR) process, was adopted to discover the shared dynamic behaviors exhibited in HR/BP time series of a patient cohort. Specifically, we model observations as generated from a latent state space of an HMM; each latent state characterizes observations as a linear dynamical system (or dynamic mode), parameterized by an autoregressive process. Our previous work demonstrated the utility of such a framework in discovering dynamic behaviors with prognostic values in predicting hospital mortality[3].

In this work, we used the proportion of time patients stayed in different latent states to predict mortality risks of patients at different blood pressure levels while on vasopressor treatment. We evaluated the classification performance of our approach using minute-by-minute HR and BP time series from a cohort of ICU patients in the MIMIC II database [4]

2. Materials and Methods

This study utilized data from 453 ICU patients from the MIMIC II waveform database (version 2), with at least 8 hours of continuous HR and BP measurements during the first 24 hours in the ICU. Approximately 15% (67 out of 453) of patients in this cohort died in the hospital. Analysis focused on a subgroup of 224 patients with at least 3 hours



(a)Mode 1 (b)Mode 9 (c)Mode 7 (d)Mode 15

Figure 1. Example high-risk (1 and 9) vs. low-risk (7 and 15) dynamic modes with prognostic information among patients on pressors.

of pressor treatment (levophed, neo-synephrine, dopamine, epinephrine, vasopressin) during the first 24 hours in the ICUs were used for the analysis. The median/IQR number of hours on pressors during the first day in the ICU were 17.4 [12.3, 20.5] hours for this cohort. The hospital mortality is 15% (34 out of 224 died before hospital discharge).

We employed a switching vector autoregressive process framework to model physiological time series via Markov transitions between a collection of simpler linear dynamical systems [2]. For the n-th patient ($n = 1 \cdots N$), let $y_t^{(n)}$ be a $M \times 1$ vector of observed values of the vital signs at time t ($t = 1 \cdots T^{(n)}$). We assume that there exists a library of K possible dynamics or *modes*, a set of multivariate autoregressive model coefficient matrices $\{A_p^{(k)}\}_{k=1}^K$ of size $M \times M$, with maximal time lag $p = 1 \cdots P$, and the corresponding noise covariances $\{Q^{(k)}\}_{k=1}^K$. Let s_t be a switching variable, indicating the active dynamic mode at time t, and evolving according to a Markovian dynamic with initial distribution $\pi^{(n)}$ and a $K \times K$ transition matrix Z. Following these definitions, an AR-HMM is defined by $y_t = \sum_{p=1}^P A_p^{(z_t)} y_{t-p} + Q^{(z_t)}$. A collection of related time series can be modeled as switching among these dynamic behaviors which describe a locally coherent linear model that persists over a segment of time. Minute-by-minute HR and mean arterial blood pressure (MAP) time series from MIMIC II were modeled as a switching AR(5) process with 25 modes.

We characterized each time series with the proportion of time in different dynamic modes. A logistic regression classifier (with Lasso regularization) was used to predict hospital mortality using mode proportions from the top 20 most common dynamic modes as features. We report 10-fold cross validated AUCs and 95% confidence intervals [5]. For subgroup analysis with cohort size N $<$ 50, features were from the top 10 modes, and performance was based on leave-one-out cross validation. Modes were characterized as high-risk vs. low-risk modes based on odds ratios from logistic regression analysis. Odds ratios (OR) and their 95% confidence intervals were reported.

3. Results

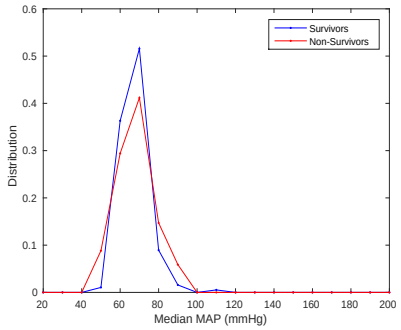
3.1. Dynamic Modes with Prognostic Value at Different BP Ranges

Figure 1 shows example high-risk (1 and 9) vs. low-risk (7 and 15) dynamic modes with prognostic information among patients on pressors. Applying univariate logistic regression on the entire 224 patient cohort (regardless of their MAP levels), high-risk mode 1 ($p < 0.001$, OR 1.44 [1.16, 1.78]) and low-risk mode 15 ($p < 0.01$, OR 0.01 [0.00, 0.21]) are significantly associated with hospital mortality. Note that the high-risk modes often correspond to less variable dynamical patterns.

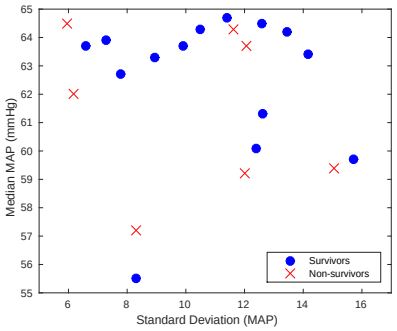
We then performed a sub-group analysis to identify dynamic modes with prognostic values for patients at different MAP ranges. Our results indicate that when median MAP $\leq$ 65 mmHg (N=21, mortality 33%), high-risk modes 1, 9 and low-risk mode 24 achieved (leave-one-out) cross validated AUC of 0.72, 0.69, 0.77 respectively. When median MAP is in the range of [65, 75) mmHg, mode 6 has the highest predictive performance, achieving an AUC of 0.66. When median MAP $\geq$ 75 mmHg while on pressors, mode 12 alone achieved an AUC of 0.62 using 10-fold cross validation.

3.2. Bivariate HR/MAP Dynamics: Survivors vs. Non-Survivors

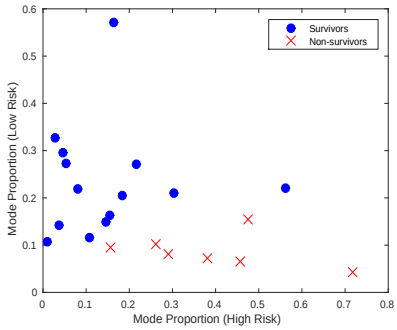
Figure 2 (a) shows the median MAP distribution of the survivors vs the non-survivors while on pressors. Note that the two groups have similar MAP distributions. Population median/IQR for the non-survivors and survivors are 73 [66, 78] mmHg and 72 [68, 76] mmHg respectively.



(a)Median MAP of patients while on pressors (N=224).



(b)Standard deviation and median MAP of the hypotensive subgroup, N=21.



(c)Dynamic mode proportions of the hypotensive subgroup, N=21.

Figure 2. Comparison between survivors vs. non-survivors. Figure (a) shows distribution of median MAP while patients were on pressors (N=224). Median MAP distributions of the survivors vs. the non-survivors are not statistically different based on the ranksum test. Figure (b) plots the standard deviation and median MAP of patients in the hypotensive subgroup (median MAP $<$ 65 mmHg while on pressors), N=21. Figure (c) plots mode proportions of HR/MAP dynamics of patients of the same hypotensive subgroup while on pressors, N=21.

The differences are not statistically significant ($p = 0.73$).

Figure 2 (b) shows the median and standard deviation of MAP for 21 patients with median MAP $<$ 65mmHg while on pressors. Figure 2 (c) shows the dynamic mode proportions for the same 21 patients with median MAP $<$ 65mmHg while on pressors; the high-risk (x-axis) and low-risk mode proportions are calculated from summing over the mode proportions from the top ten modes with smallest p-values in univariate logistic regression analysis. Note the separation between the survivors and non-survivors in their mode proportions: the non-survivors tended to spend more time in the high-risk dynamics rather than the low-risk modes, whereas the survivors spent more time in the low-risk dynamics.

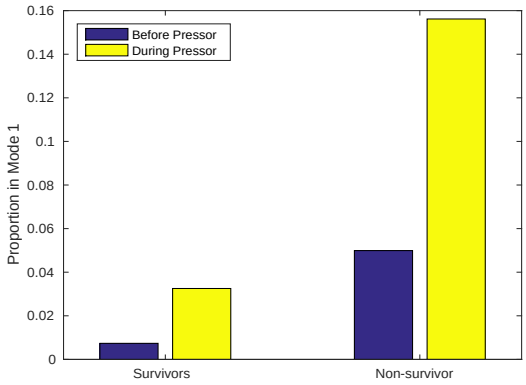


Figure 3. Survivors vs. Non-survivors: changes in mode proportions (population median) for high-risk mode 1 before and after pressor onset.

3.3. Prediction Performance

Table 1 summarizes the prediction performance. Within the pressor subgroup, the bi-variate HR/BP dynamics alone achieved an AUC of 0.74 (95% confidence interval of 0.64, 0.84), out-performing the baseline median MAP performance, 0.53 (0.42 to 0.63). Bivariate dynamics of HR/MAP time series combined with the median MAP levels, achieved an AUC of 0.75 (0.65 to 0.85). Pressure-dependent analysis for pressor subgroups A and B are based on blood pressure samples while patients are on pressors. Bivariate HR/MAP dynamics perform better among the hypotensive subgroup (median MAP $<$ 65 mmHg), achieving an AUC of 0.83 [0.63, 1.00].

3.4. Comparison of Dynamics Before and After Pressor Onset

In this section, we compare HR/MAP dynamics of the survivors and the non-survivors before and after pressor initiation. We focused on 55 patients with at least 30 minutes of MAP before pressor onset; 11 of the 55 patients died (mortality 20%). The median number of HR/MAP minute-by-minute samples available for analysis before pressor onset was 164 (or approximately 2.7 hours). Figure 3 shows the population median of mode proportion for high-risk dynamic mode 1 before and after the pressor onset. The survivor group spent less than 1% of their time (median 0.7% [0.2%, 2.8%]) in the high-risk mode before pressor onset, and increased to 3% [0.5%, 14%] afterwards. Non-survivors spent a larger proportion of time

Features	Cohort (Subgroup)	N	Mortality	AUC
STD MAP + Median MAP Level	All	453	15%	0.52 [0.44, 0.59]
HR/MAP Dynamics	All	453	15%	**0.68 [0.60, 0.75]**
Median MAP level	Pressor	224	15%	0.53 [0.42, 0.63]
STD MAP	Pressor	224	15%	0.53 [0.43, 0.64]
Median + STD MAP	Pressor	224	15%	0.58 [0.47, 0.68]
HR/MAP Dynamics	Pressor	224	15%	**0.74 [0.64, 0.84]**
HR/MAP Dynamics + MAP	Pressor	224	15%	**0.75 [0.65, 0.85]**
HR/MAP Dynamics	Pressor Group A (MAP $<$ 65 mmHg)	21	33%	**0.83 [0.63, 1.00]**
HR/MAP Dynamics	Pressor Group B (MAP [65, 75) mmHg)	131	9%	**0.76 [0.59, 0.92]**

Table 1. Classification performance in predicting hospital mortality in ICU patients using bi-variate HR/MAP dynamics. The pressor group consists of patients on pressor treatment for at least 3 hours during the first 24 hours in the ICU. AUCs and 95% confidence intervals are shown. Pressor group A and B are defined based on median MAP at different thresholds.

(5% [1.8%, 26%]) in the high-risk mode 1 than survivors even before the pressor onset; after the pressor initiation, their proportion of time in high-risk mode 1 increased significantly to 15.6% [6.7%, 37.7%].

4. Discussion and Conclusions

Our results indicate that HR/MAP dynamics contain prognostic information, especially in the low BP range (median MAP $\leq$ 75 mmHg), and can potentially be used to stratify individual patients' risks for adverse outcomes at different blood pressure targets. One potential application of our technique is in patient monitoring, where transitions to high risk dynamical modes could be used to trigger alarms. Recent studies suggest that therapeutic interventions not only should aim at maintaining the mean BP within an acceptable range, but also should direct the patients' trajectory toward healthy dynamical regimes with enhanced variability [6]. A real-time implementation of our technique (e.g., reporting hourly risk scores as described in [7]) may provide clinicians with a tool to quantify the effectiveness of such interventions in the ICU. Future work will extend analysis to stratify risks of other adverse outcomes (e.g. acute kidney injuries) in response to vasopressor treatment, and other interventions in the ICU (such as fluid resuscitation, and ventilation settings). Ultimately, our goal is to provide clinicians a tool to inform treatment strategies by combining the dynamics in high-resolution vital sign time series with all other available physiological and clinical data (lab tests, medication, nursing notes, etc.).

Acknowledgments

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