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Prediction of Mean Arterial Blood Pressure with Linear Stochastic Models

Sahika Genc

Abstract— **A model-based approach that integrates known portion of the cardiovascular system and unknown portion through a parameter estimation to predict evolution of the mean arterial pressure is considered. The unknown portion corresponds to the neural portion that acts like a controller that takes corrective actions to regulate the arterial blood pressure at a constant level. The input to the neural part is the arterial pressure and output is the sympathetic nerve activity. In this model, heart rate is considered a proxy for sympathetic nerve activity. The neural portion is modeled as a linear discrete-time system with random coefficients. The performance of the model is tested on a case study of acute hypotensive episodes (AHEs) on PhysioNet data. TPRs and FPRs improve as more data becomes available during estimation period.**

I. INTRODUCTION

This study aims to develop a data-driven stochastic algorithm based on physiological model of the cardiovascular system in order to predict the long-term (minutes or hours) evolution of the mean arterial pressure (MAP). A well-regulated systemic arterial pressure is critical for operation of the cardiovascular system. If the systemic arterial pressure is significantly below its normal operating point, then the brain and heart do not receive adequate blood regardless of their vascular resistance by local control mechanisms [1]. Predicting the evolution of the mean arterial pressure can help identify timely and appropriate interventions.

We can categorize the methods to study the changes in the mean arterial pressure into two categories: 1)physiological model-based, and 2) data-driven. Physiological model-based approaches have been very popular in 70s and there has been several attempts to describe the functioning of the cardiovascular system. In order to analyze and predict the critical measures of the cardiovascular system, numerous mathematical models have been developed for hemodynamics, central nervous system (CNS) control, pharmacodynamics, and, at a higher level, the entire closed-loop system [2], [3]. A variety of modeling approaches have been exploited, ranging from fluid dynamics models to electrical circuit analogy, from lumped parameter models to segmental analysis (e.g., [4], [3], [5], [6], [7]). However, no model is a perfect one, but only an approximation of the real dynamics.

Today the most popular approaches are data-driven and based on advances in signal processing such as neural networks and statistical methods such as logistic regression. This is partly because noninvasive technologies for measurement of cardiovascular variables resulted in collection of data sets at ICUs. That in turn resulted in expansion of classification-based methods. In developing these algorithms, the data sets are separated into two categories, training and test. The algorithms are trained on the training data set to identify the patterns or parameters. Then, the performance of the algorithm is tested on the test data set, generally, resulting on a receiver-operator curve (ROC). The success rate of these algorithms is based on the training data set which may not have enough patient variation to develop robust algorithms for a population with large variation.

In this paper, we provide a method combining data-driven and physiological model-based approaches. We consider the complete arterial baroreceptor reflex pathway as a closed-loop control system composed of an *effector* portion that includes heart and peripheral blood vessels and *neural portion* that includes arterial baroreceptors, their afferent nerve fibers, the medullary cardiovascular centers (MCCs), and efferent sympathetic and parasympathetic fibers [1]. Mean arterial pressure is the output of the effector portion and the input to the neural portion while the activity of the sympathetic and parasympathetic nerves is output of the neural portion and input to the effector portion.

In general, the effector part of the control system model is very-well understood; see [8] and references there in. However, there are still gaps in understanding the neural portion. Our cardiovascular system model differs from the one in [8] from various aspects. First, we assume that the closed-loop system is modeled by linear differential equations with random coefficients instead of constant coefficients. In some applications, the constancy of coefficients in successive observations may reasonably be questioned [9].

Our approach is similar to [8] in the sense that the model parameters (mean and standard deviation for the stochastic model) adapt to each subject's data. Thus there is a learning period during which the model parameters are calculated. The duration of the learning period a critical parameter and depends on the type of MAP-reducing disturbances. Also, the learning period is repeated periodically to consider changes in the subject's state resulting from clinical interventions or cardiovascular disturbances. The paper is organized as follows. First, we describe the stochastic predictive assessment model (SPAM). Then, we consider a case study to predict occurrences of AHE using the predicted evolution of the MAP from SPAM. Finally, we provide ideas for improvement of the model and future work.

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Sahika Genc is with the Sensor Informatics and Technologies Laboratory, Software Sciences and Analytics, General Electric Global Research, Niskayuna, NY 12309 USA gencs@research.ge.com

II. STOCHASTIC PREDICTIVE ASSESSMENT MODEL

In the section, we describe the stochastic predictive assessment model (SPAM) in detail. The cardiovascular system is very complex. It is not practical to model the every detail of the system. Our goal is to develop a relatively simple model and incrementally increase the complexity of the model based on its performance at each level. First, we develop the closed-loop control system model for the arterial baroreceptor pathway. Then, we explain a method to estimate the closed-loop control system model parameters from the present and past patient data. Finally, we form an ensemble of MAP time-series data describing the evolution of MAP over the next half an hour to two hours.

A typical closed-loop control system consists of a plant, sensor, and controller [10] as shown in Fig. 1. There are two types of control: 1) Regulation and 2) servo. In regulation, the reference is a set point and the control objective is to minimize the steady-state error between the set point and output. In servo, the objective is to minimize the tracking error between the reference and output. We consider regulation model where the patient-specific MAP is the set point, heart rate (HR) is the control signal, and MAP is the output signal. The plant disturbance is modeled as a single or a combination of MAP-reducing disturbances.

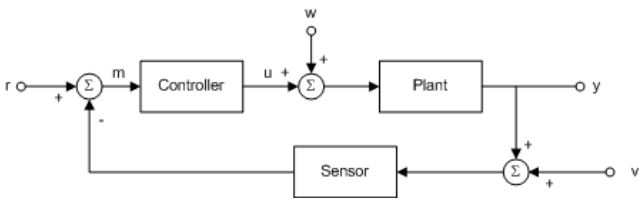

Fig. 1. Closed-loop feedback system: r = reference, u = control, y = output, w = plant disturbance, and v = sensor noise.

We now describe the control system model in detail. The plant corresponds to heart and vessels. The sensor and controller includes arterial baroreceptors, their afferent nerve fibers, the medullary cardiovascular centers (MCCs), and efferent sympathetic and parasympathetic fibers [1]. We consider heart rate (HR) as the output of the controller instead of sympathetic and parasympathetic nerve activity (SNA and PNA). This is because HR responds to the changes in SNA and PNA and more likely to be among the parameters collected at ICU, compared to SNA and PNA. The output of the plant is MAP which is measured by arterial baroreceptors that sense arterial pressure from the magnitude of the stretch of the elastic arterial walls. The reference point depends on various factors. For example during exercise the reference point may be higher than its normal value. Conversely, the set point may be lower with increased central venous pressure (CVP).

We now describe the mathematical model for each control system component. Suppose given input u, output y is defined as follows

$$y[k] = \sum_{i=1}^{n}(a_i + \alpha_i[k])y[k-i] + \sum_{j=1}^{n}(b_j + \beta_j)u[k-j] \quad (1)$$

where $a_1 \dots a_n$ and $b_1 \dots b_n$ are real coefficient, $\alpha_1 \dots \alpha_n$ and $\beta_1 \dots \beta_n$ are mutually independent Gaussian white noise with variance $\sigma > 0$, the input is independent with the random coefficients, n is the order of the system, k is the current discrete-time point, and $k-i$ are the past data points. We construct the differential equation using physiological models of the closed-loop cardiovascular system where the plant is modeled using fluid-dynamic models, the controller is constructed based on the past patient vital sign data observed up until to the prediction point.

In this model, the random coefficients correspond to a combination of compliances, resistances, and contractility. These coefficients are patient specific and may vary over the course of patient monitoring. Since these variations are not observed in ICU, then it is logical to consider the coefficients of the linear system to be random [9]. Thus we consider the model to be as simple as possible yet representative enough to derive suitable estimators for predicting the evolution of the system. Second, in this paper we omit the model for the pulmonary system.

In the following, $h(t), p(t)$, and $v(t)$ denote HR, MAP, and stroke volume (SV). We assume that both the controller and plant are linear systems for their given inputs however input may be function of HR, MAP, and SV. For the controller, $y(t) = h(t)$ and $u(t) = p(t)$. The plant model is two parts (states). The first part models the effects of HR and MAP on SV based on Frank-Starling mechanism. Thus, for the first part, $y(t) = v(t)$ and $u(t) = h(t)/p(t)$. This implies an additional feedback loop that is not explicitly shown in Fig. 1. The second part models the effect of HR and SV on MAP. Thus, for the second part, $y(t) = p(t)$ and $u(t) = h(t) \times v(t)$.

Given a set of observations of input and output, we state our parameter estimation problem as follows

$$\xi = \{y[1] \dots y[N], u[1], \dots, u[N-1]\} \quad (2)$$

where N is a positive integer, estimate the vector of unknown parameters

$$\phi^T = (\alpha_1 \dots \alpha_n \dots \beta_1 \dots \beta_n \sigma) \quad (3)$$

with respect to a cost function. We apply the conditional maximum likelihood estimator method

$$\hat{\phi} = arg[maxP(Y_1|Y_0, U)] \quad (4)$$

where $Y_1 = \{y[n+1] \dots y[n+N]\}$, $Y_0 = \{y[1] \dots y[n]\}$ (initial state of the system), and $U = \{u[1] \dots u[N-1]\}$. A consistent maximum likelihood estimator is derived in [11].

The SPAM algorithm flow chart is provided in Fig. 2. There are two types of inputs to the algorithm: **Parameters:** N: Number of data points for estimation, M: Number of data points for prediction, R: Number of repetitions, n_h: Order of the controller, n_v: Order of the first part (SV) of the plant,

n_p: Order of the second part (MAP) of the plant, and A: Age of the patient (or arterial compliance), and **Waveforms:** HR, MAP, and PP (or SV) We estimate SV as the multiplication of PP and estimated arterial compliance based on age of the subject.

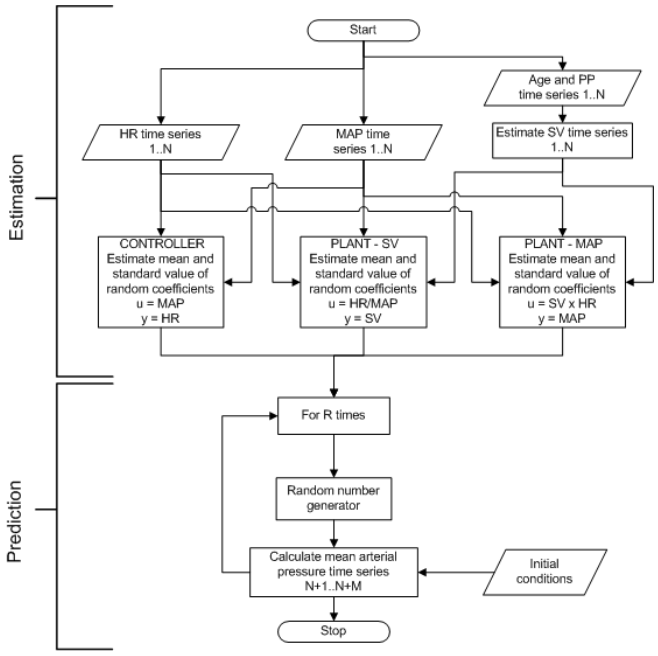

Fig. 2. The flow chart of SPAM.

We estimate the model parameters for each closed-loop control system separately[1]. We calculate the mean and standard deviation of the random coefficients for each block of the control system based on the input-output relations stated above from past N data points. Then we simulate the closed-loop control system model based on estimated mean and standard deviation of the random coefficients and initial conditions to predict the values of the MAP for the next M data points. We repeat the simulation several times because of the random coefficients. Thus, the output of the SPAM algorithm is an ensemble of R MAP time series data of length M.

III. CASE STUDY: PREDICTION OF ACUTE HYPOTENSIVE EPISODES

In this section, we consider a case study to predict the AHEs based on predicted MAP time series data generated by the SPAM algorithm. One recent study underlying the significance of arterial pressure regulation is a statistical study of acute hypotensive episodes (AHEs) on Multiparameter Intelligent Monitoring in Intensive Care (MIMIC) II Database [12][13]. In this paper, an AHE is defined as an interval in which at least 90% of the non-overlapping one-minute averages of the arterial blood pressure waveform (MAP) were in the acute hypotensive range (below 60 mmHg) during any 30-minute window within the interval. According to [12], in December 2008, the MIMIC II Database contained 2320 complete adult patient records (including both recorded physiologic signals and time series, and accompanying clinical data). Arterial blood pressure was recorded in 53% of the patients. In-hospital mortality of patients with AHE (37.8%) was more than twice that of patients whose arterial blood pressure (ABP) was monitored and who did not experience AHEs (17.8%).

In this case study, we use mean, systolic, and diastolic blood pressures and heart rate stored in the numerics records and age of the patient from the clinical records in PhysioNet AHE Challenge training data [14]. Numerics records in [14] contain time series of vital signs sampled once per minute. We preprocess the variables in the numerics data prior to feeding in to the SPAM algorithm because the numerics records contain missing data and we need to account for the sensor noise and artifacts. However, there may still be signal quality issues while numerics data is being generated and in that case we need to refer to the waveform data. In this paper, we have not used the waveform data to confirm the quality of the numerics data.

The flow chart of the AHE prediction with the SPAM algorithm is given in Fig. 3. We run the SPAM algorithm as long as data is available to adapt to the changes in the patient state. There may be changes in the patient state that may result in changes in the model parameters SPAM uses to predict the evolution of MAP. The patient state may change due to medication or clinician intervention and disturbances to the cardiovascular system. The AHE identification logic is applied to all the predicted time series MAP data. If the AHE is identified in majority of the ensemble, then the onset of AHE is declared and the mean onset time is recorded or provided to the user.

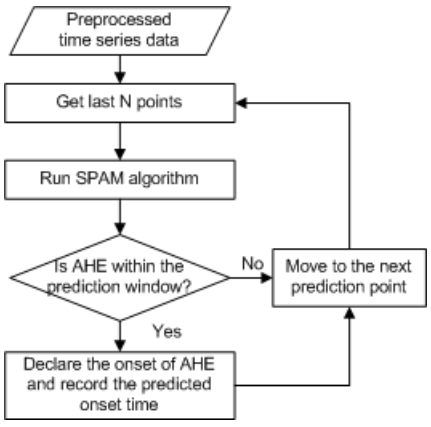

Fig. 3. The SPAM algorithm to predict the onset of AHE.

We test the performance of the SPAM AHE prediction algorithm on two groups in the training data, C1 and H2. Group C1 contains data from ICU patients who do not have the AHE in the records. Group H2 contains data from ICU patients with one or more AHEs and who are not treated with pressors. There are 10 (14) records in Group H2 (C1) that contain all the variables needed to run the SPAM AHE

[1]This simplification can result in an unstable closed-loop system. We discuss the impact of stability in the case study and future work.

prediction algorithm and total of approximately 760 (676) hours of recording for each variable. We run the SPAM AHE prediction every time a new data point is available. Since the training data numerics record contains parameters recorded every minute, the algorithm runs every minute. However, if the time-complexity of the algorithm is too demanding for the software/hardware platform, then the prediction frequency needs to be reduced. In order to calculate the performance of the algorithm, we check whether the AHE onset is correctly predicted or not at every prediction point. In general, we observe that once a prediction is made, the algorithm consistently predicts the onset until the event occurs.

In the following results, we used the following values for the input parameters: $M = 60, R = 20, n_h = n_v = n_p = 2$ and AHE prediction threshold is 0.8, i.e., if 80% of the MAP time-series predictions in the ensemble identify AHE then we declare the onset of AHE. The True Positive Rates (TPRs) and False Positive Rates (FPRs) for Groups H2 and C1 are shown in Tables I and II, respectively. TPRs and FPRs for Group H2 records are above 95% and below 11%, respectively. FPRs for Group C1 are below 3.1%. The rates get better for most of the records as more is available during the estimation period. On the other hand, in general, as the estimation time gets longer, the FPRs improve significantly for both groups. Even though the FPRs and TPRs improve with increased data points during the estimation period, the prediction onset time decreases for several records. The mean prediction onset varied between 15-20 minutes at best.

TABLE I
PERCENT TRUE POSITIVE RATES (TPRS) AND FALSE POSITIVE RATES (FPRS) FOR GROUP H2.

Record	TPR (4 hr)	FPR (4 hr)	TPR (5 hr)	FPR (5 hr)
a40164	NaN	6.71	NaN	9.86
a40099	100.00	10.15	100.00	7.06
a40012	100.00	8.42	100.00	7.50
a40050	100.00	7.63	100.00	5.47
a40119	100.00	7.25	100.00	6.92
a40076	100.00	6.41	100.00	3.44
a40006	100.00	4.65	98.31	2.45
a40051	100.00	4.52	100.00	3.61
a40172	95.00	11.06	95.00	6.73
a40127	66.67	7.73	50.00	6.82

IV. CONCLUSION AND FUTURE WORK

This study provides promising results on predictive assessment of AHEs and can be extended to other MAP patterns without building a new model. The effect of medication is still an interesting topic for further investigation. Also, the model for the neural part can be improved by considering nonlinear nature of the arterial regulation. We may improve our current results by implementing an extended Kalman filter approach to joint state and parameter estimation [15]or dual unscented Kalman filter [16]. The parameter estimation theory can be extended to the entire closed-loop system instead of considering each block separately [17]. In addition, the AHE prediction logic can be improved to consider the previous predictions and observations.

TABLE II
FALSE POSITIVE RATES (FPRS)(%) FOR GROUP C1.

Record	FPR (4 hr)	FPR (5 hr)
a40282	3.01	3.10
a41664	2.86	0.31
a40802	2.25	0.89
a41434	1.61	1.55
a41466	0.91	0.15
a41934	0.79	0.25
a40551	0.78	0.32
a41495	0.42	0.00
a40921	0.20	0.13
a40473	0.12	0.00
a41137	0.00	0.00
a41177	0.00	0.00
a42141	0.00	0.00
a42259	0.00	0.07

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