

Automated Hemodynamic Regulation with Model Predictive Control

Brian Aufderheide, Ramesh R. Rao and B. Wayne Bequette

Isermann Department of Chemical Engineering
Rensselaer Polytechnic Institute
Troy NY 12180-3590

Abstract-A multiple model adaptive predictive controller is designed to regulate mean arterial pressure and cardiac output in critical care subjects using inotropic and vasoactive drugs. The algorithm uses a multiple model adaptive approach in a model predictive control framework to account for inter- and intra-patient variability and explicitly handle drug rate constraints. The controller is evaluated on canines that were pharmacologically altered to exhibit symptoms of hypertension and depressed cardiac output.

I. INTRODUCTION

Critical care physicians maintain certain patient state variables within acceptable operating ranges by infusing several drugs and/or intravenous fluids. Constant monitoring and manual regulation of the physiological variables can be tedious. Hence, it is desirable to have an automated system to perform such tasks. Reference [1] provides a comprehensive review of research in control of drug infusion.

Model predictive controllers (MPC) are a class of controllers that employ an identifiable model to predict the future behavior of the system over an extended prediction horizon [2]. A cost function (based on setpoint tracking error over a prediction horizon of P steps) is minimized by adjusting a set of future manipulated variable moves (M steps), subject to constraints on the manipulated inputs and controlled outputs. Optimal closed-loop feedback is achieved by implementing only the first control move and repeating the complete sequence of steps at subsequent sample times in a receding horizon fashion. An important issue in the design of drug infusion systems is the need to impose bounds on dosages and infusion rates to avoid overdosing or drug toxicity. For example, sodium nitroprusside (SNP) used in reducing hypertension should be infused less than $10 \mu\text{g kg}^{-1} \text{min}^{-1}$. Alternatively, the physician may want to specify an operating range of the mean arterial pressure instead of a specific setpoint. While most control strategies handle such constraints in an ad hoc manner, the primary advantage to MPC is its ability to handle constraints explicitly. Its optimization-based framework allows computation of the optimal infusion rates subject to input and output constraints. However, this approach relies on the availability and accuracy of the prediction models and requires on-line adaptation to account for patient variability.

In multiple model adaptive control (MMAC), the basic idea is to use a bank of models to capture the possible input-output response behavior. The control parallel is to use a bank of controllers, to achieve a desired closed-loop performance from a wide variety of possible patients; controller k is designed based on model k from the model bank. Using a Bayesian approach, the probability of each model representing the patient response is computed and the resultant control action is the probability-weighted average of control moves of each controller. The model probabilities get altered as the drug sensitivities change in inter/intra patient variations. The primary advantage to this approach is that no a priori model identification is necessary during initial stages of drug

administration. The controller is initialized with a predefined, usually equal, probability and adapted using subsequent measurements.

In this work we present a novel approach combining the MPC and MMAC strategies for regulation of hemodynamic variables in canines. A probability-weighted average of output predictions from a bank of models is used in a MPC framework to calculate drug infusion rates for regulation of mean arterial pressure and cardiac output. This approach has the combined advantage of model adaptation according to patient variations and the ability to handle explicit input and output constraint specifications often desired by the critical physicians.

II. SYSTEM DESCRIPTION

The overall control objective is to maintain two hemodynamic variables, mean arterial pressure (MAP) and cardiac output (CO), at desired setpoints by automated infusion of inotropic and vasoactive drugs. SNP is administered for arterial vasodilation. Dopamine (DPM) is used as an inotrope to enhance cardiac performance; Phenylephrine (PNP) is used for arterial vaso-constriction.

The model bank constitutes of ten linear first order + dead-time or second order models with different gains and time constant values corresponding to each drug and its hemodynamic response. The parameters are chosen to bound nominal drug responses. The controller was initially evaluated and tuned in closed loop simulations using an elaborate non-linear canine circulatory model ([3], [4]) as the "patient" before moving to the experimental phase.

III. EXPERIMENTAL SETUP

The controller was evaluated on three mongrel dogs under IACUC approved protocol. Following induction of a surgical plane of anesthesia, the animal was intubated and mechanically ventilated (Siemens-Elena 900C Servo-Ventilator) with isoflurane or halothane anesthesia. An arterial line was placed in the femoral artery to provide continuous arterial pressure tracings on a Mennen Horizon monitor. A Swan-Ganz catheter (Baxter Edwards Swan Ganz Intellicath CCO/VIP Thermodilution), connected to a Baxter Vigilance monitor, was introduced in the pulmonary arterial tree to provide continuous cardiac output measurement. Control calculations were performed on a Dell Pentium II PC running a custom built Windows based GUI. The pressure and flow measurements were received from the monitors through RS-232 ports. The control loop was closed with rotary infusion pumps (Critikon Simplicity 2100A) modified to accept digital inputs via a digital output card.

IV. RESULTS

The responses to the drugs administered varied greatly depending on the anesthetic used as well as which canine received them. Isoflurane lowers systemic vascular resistance yet the contractility of the heart and the baroreceptor reflex remain relatively strong. With

isoflurane, the MAP setpoint chosen will determine the baroreceptor response either towards the setpoint or against it strongly perturbing the drug effects on the canine. For halothane with 50% nitrous oxide, systemic vascular resistance, baroreceptor reflex and the heart's contractility are all compromised. Because halothane depresses CO values the pharmacodynamics are very slow, having time delays and time constants in some experiments more than double the values on the same canine under isoflurane.

For MAP control, the experimental results were very good with typical setpoint tracking of ± 10 mm Hg at settling times of under 10 to 15 minutes. Figure 1 illustrates the fairly tight control of MAP on a female 19 kg canine under isoflurane. Phenylephrine is infused to mimic a hypertensive patient. Sodium nitroprusside is the controlled input to lower MAP. MAP setpoints are maintained within ± 5 mm Hg with settling times of less than 7 minutes after each setpoint change. The controller also rejects well the disturbance of lowering phenylephrine from 5 to 3 $\mu\text{g kg}^{-1} \text{min}^{-1}$. CO and heart rate (HR) both increase throughout as the baroreceptor reflex fights to increase MAP above the setpoints chosen of 80 mm Hg and 75 mm Hg.

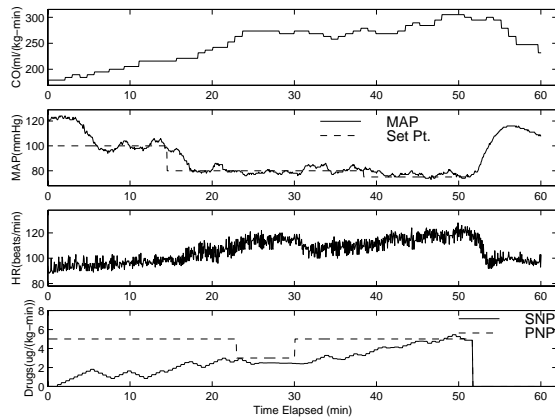


Fig.1. MAP control of hypertensive canine under isoflurane using sodium nitroprusside (SNP). Phenylephrine (PNP) used to induce hypertension.

Controlling MAP and CO is a much more difficult problem. The two hemodynamic variables are highly correlated and interdependent. Choosing a realizable setpoint for CO such that dopamine can be kept in its inotropic infusion range of 3 to 7 $\mu\text{g kg}^{-1} \text{min}^{-1}$ is not trivial. CO response to dopamine can be roughly modeled as a first order system plus time delay. Infusing halothane at levels to mimic congestive heart failure, canine responses to dopamine had time delays of 2-3 minutes and a time constant of 6-8 minutes. Therefore any overshoot in CO due to dopamine takes a long time to settle down. It is critical that not only gains, but also time constants and delays be well estimated, since any model mismatch in dopamine will result in poor CO control. In Figure 2, MAP and CO are controlled on a male 17.8 kg canine under halothane with the infusion of dopamine and sodium nitroprusside. Both reach setpoint in 12 minutes. MAP stays within ± 10 mm Hg throughout the run. CO stays on or near the setpoint for 10 minutes until the canine responded to the slight overshoot in dopamine. It takes over 5 minutes for the overshoot in CO to start returning towards the setpoint. The overshoot in CO is directly related to the increase in HR (noise spike at 13 min. not withstanding). As HR begins to regress to a baseline value of 103 beats/min CO starts to return to setpoint.

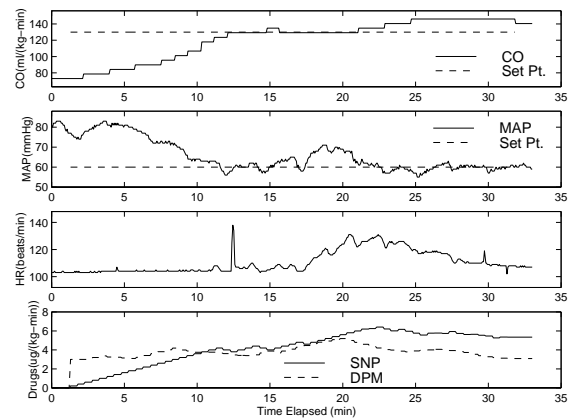


Fig.2. MAP and CO control of depressed CO canine under halothane. Dopamine (DPM) and sodium nitroprusside (SNP) are controlled inputs.

V. DISCUSSION & CONCLUSIONS

Interpatient and inpatient variability are the most significant problems to any controller for drug infusion. This variability is compounded by the different anesthetics used in practice and their greatly varying effects on baseline heart contractility, systemic vascular resistance and the strength of the baroreceptor reflex. The weighted model bank can account for the variability in the drug infusion system, providing a flexible and bounded prediction model for the online constrained optimization problem. Permissible drug infusion rates are explicitly handled and relative importance between controlling MAP and controlling CO can be specified. This control design has demonstrated its efficacy in canine experiments for both hypertensive and depressed cardiac output cases for two different maintenance anesthetics.

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