Performance of robust PID and Q-design controllers for propofol anesthesia

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Abstract: Control of propofol anesthesia is characterized by large variability in individual responses to drug infusion, relatively simple system dynamics and relatively low performance criteria. Robust PID control can be expected to provide adequate control given these characteristics. While feasibility of robust PID control of propofol anesthesia has been shown in clinical trials, controllers that use an explicit model might provide additional valuable characteristics. This paper examines the performance achieved with a manually tuned robust PID controller and a higher-order Q-design controller. The additional degrees of freedom in the Q-design allow an increase in the robustness margin, at the cost of decreased gain at low frequencies and corresponding increased time to induction of anesthesia. These results indicate that the uncertainty introduced by interpatient variability is an important factor limiting closed-loop performance. Performance improvement from increased controller complexity may therefore be limited, unless strategies aimed at reducing the uncertainty are implemented.

Keywords: PID control, Robust control, Anesthesia, Q-design.

1. INTRODUCTION

General anesthesia as routinely used in the operating room is induced by administering a combination of drugs. The anesthesiologist, who is responsible for the patient's safety while in the operating room, carefully doses these drugs based on knowledge of the drug effect and the observed response of the patient. Due to the dynamics of the drug effects and large inter-patient variability, this requires repeated manual adjustments. Closed-loop technology can provide performance and safety improvements, by taking over low-level repetitive tasks of drug dosing adjustments, while the anesthesiologist can focus on the high-level tasks (Bibian et al. (2005)). Feasibility of closed-loop propofol infusion has been shown in various trials (e.g. Liu et al. (2006); Sawaguchi et al. (2008); Gentilini et al. (2001); Puri et al. (2015)). Closed-loop control was shown to outperform manual control in terms of time in range of adequate anesthesia (Liu et al. (2006); Puri et al. (2015); Brogi et al. (2016); Pasin et al. (2016)).

Control of anesthesia is characterized by uncertain but relatively simple dynamics (stable, minimum phase, non-oscillatory) and relatively low performance criteria (standard practice corresponds to manual control). A well designed PID controller can be expected to provide adequate robust control for a system with these characteristics. We have shown feasibility of robust PID control of propofol anesthesia in simulation (Dumont et al. (2009)) and in clinical trials in adults and children (Dumont et al. (2011); West et al. (2017); van Heusden et al. (2014)).

⋆ This work was supported by NSERC (Discovery grant 157106-13)

Robust PID control has been shown to provide adequate control performance for propofol anesthesia, however, higher-order controllers might improve performance and control techniques based on explicit models might provide valuable additional characteristics. Model predictive control (MPC) for example provides straightforward extensions for multi-drug systems and safety constraints. Furthermore, additional degrees of freedom introduced by higher-order controllers may improve controller performance. MPC has been suggested for control of anesthesia in simulation, with limited uncertainty (Ionescu et al. (2008)). Sawaguchi et al. (2008) used an adaptive version of MPC in a clinical trial.

The goal of this paper is to compare the performance of a manually-tuned higher-order model-based controller to the performance of a PID controller that we have evaluated in clinical trials. Controller tuning in MPC is not straightforward, and the effect of the choice of a nominal model cannot easily be distinguished from the effect of the controller tuning. We therefore evaluate the performance of a model-based design using the affine parametrization (Goodwin et al. (2001)). This technique, also known as Q-design of Internal Model Control, is closely related to unconstrained MPC (Garcia et al. (1989)), however, the design trade-off and robustness criteria are explicit functions of the model uncertainty. The robust PID controller for propofol anesthesia in children as described by van Heusden et al. (2014) is compared to a Q-design based on the model set described by van Heusden et al. (2013).

Section 2 describes the control setup and objectives. The robust PID design is summarized in Section 2.3. Q-design

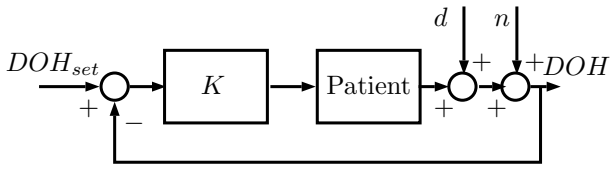

Fig. 1. Block diagram representing closed-loop propofol anesthesia.

is described in Section 3 and used in Section 4 to design a model-based controller for propofol anesthesia. The nominal model and uncertainty description required for this design are described in Section 4.1. Control performance of the PID and Q-design controllers is evaluated in Section 5. The results are discussed in Section 6.

2. ROBUST PID DESIGN FOR PROPOFOL ANESTHESIA

2.1 Control of propofol anesthesia

Consider the simplified closed-loop setup for propofol anesthesia shown in Fig. 2.1. The user defined setpoint DOH_{set} is compared to the measured depth of hypnosis (DOH), and drug infusion to the patient is determined by a 1 degree-of-freedom feedback controller K. The measured DOH is affected by disturbances $d(t)$ and measurement noise $n(t)$. In this simplified setup, any dynamics introduced by the DOH monitor are assumed to equal unity, and a feedforward term or 2 degree-of-freedom controller implementation that uses a filtered setpoint DOH_{set} are not taken into account. This simplified setup is used to compare PID and model-based control. Any performance improvements provided by feedforward or setpoint filtering can be applied to either controller.

Processed electroencephalography (EEG) DOH monitors provide a measure on a scale from 0-100, where 0 corresponds to iso-electric EEG, and values between 90-100 correspond to awake EEG. Indices between 40-60 are associated with adequate anesthesia. During induction of anesthesia, the patient DOH index is lowered from ≈ 90 to 40-60, corresponding to a step response. Disturbances d as a result of surgical stimulation increase the DOH index.

Patient responses to propofol anesthesia can be modeled using pharmacokinetic-pharmacodynamic (PKPD) models. Propofol PK is commonly modeled using a three-compartment model. Propofol PD can be described by a first-order model with a time delay, followed by a nonlinear response function. In this study, the model set described by van Heusden et al. (2013) is used where the PD model is linearized for induction of anesthesia.

2.2 Control objectives

Closed-loop control for propofol anesthesia needs to provide sufficiently fast induction of anesthesia, while limiting the overshoot. Slow induction of anesthesia may delay securing of the airway, and compromise patient safety. It could also delay the start of the procedure, which is clinically undesirable and could delay the operating room. A large overshoot in DOH following induction of anesthesia is associated with significant blood pressure decreases, particularly in adults. In children, blood pressure changes are less pronounced and more overshoot can be tolerated to increase speed of induction of anesthesia and reduce patient discomfort. During maintenance of anesthesia, the controller needs to provide fast disturbance rejection without introducing significant overshoot.

2.3 Robust PID control for propofol anesthesia in children

A robust PID controller was designed for propofol anesthesia in children by van Heusden et al. (2014), and this controller was evaluated in a clinical study including 71 cases. This controller was designed using a subset of the model set described by van Heusden et al. (2013). The controller was manually tuned.

This manual design was based on 28 patient models, linearized for induction of anesthesia. Robustness was evaluated in the frequency domain, using the corresponding frequency response functions, and the controller was designed to achieve sufficient phase and gain margins. Performance was evaluated based on the time-domain response of the linear and nonlinear models, during induction of anesthesia and following disturbances. During clinical evaluation in 71 cases, the time to achieve induction of anesthesia was (median (min, max)) 3.6 (1.3, 6.1) minutes [1]. The time spent within 10 units of the setpoint was (median (min, max)) 89 (52, 100) %.

An optimization based PID tuning method was proposed for propofol anesthesia by Soltesz et al. (2016). This method aims to maximize the integral gain of the controller, which corresponds to minimizing the integral error following a load step disturbance. Robustness is guaranteed by limiting the peak of the sensitivity function, given either a multi-model uncertainty or a nominal model with unstructured uncertainty. The optimal controllers described by Soltesz et al. (2016) showed strong similarity with the manually tuned PID controller, both in the frequency response function and the closed-loop time responses. While the robust PID controller assessed in this paper is manually tuned, this manual design is close to optimal, considering maximization of the integral gain while limiting the peak sensitivity.

3. ROBUST MODEL-BASED DESIGN USING AFFINE PARAMETRIZATION

Assume that the uncertain plant $G_p(z)$ is described by a multiplicative uncertainty description;

$$G_p(z) = G_o(z)(1 + w_I(z)\Delta(z)),$$

where the unstructured uncertainty is bounded $|\Delta(j\omega)| \leqslant 1, \forall\omega$, $G_o(z)$ represents the nominal model and $w_I(z)$ the multiplicative uncertainty weight. Assume that the user-defined robust performance objective is defined as $w_P(z)$.

3.1 Robust Q-design

Q-design is based on the following affine controller parametrization:

[1] Time to induction of anesthesia was defined as the time from the start of propofol infusion, to the moment the DOH reaches 60 and remains below 60 for 30 seconds.

$$Q(z) = \frac{C(z)}{1 + C(z)G_o(z)}. \quad (1)$$

The controller that is indirectly defined by (1) stabilizes a stable, linear, time-invariant nominal plant $G_o(z)$ if and only if $Q(z)$ is stable and proper. Furthermore, this parametrization describes all stabilizing controllers (Goodwin et al. (2001), ch. 15). The sensitivity function S_o and the complementary sensitivity function T_o of the controlled nominal plant G_o are linear in $Q(z)$;

$$T_o(z) = Q(z)G_o(z),$$
$$S_o(z) = 1 - Q(z)G_o(z).$$

Controller design is reduced to the design of $Q(z)$, which can be used to shape one sensitivity function.

In the presence of multiplicative uncertainty, robust performance is guaranteed if (Skogestad and Postlethwaite (2007))

$$\max_{\omega}(|w_P(z)S_o(z)| + |w_I(z)T_o(z)|) < 1.$$

Using the affine parametrization, this robustness criterion is given by

$$\max_{\omega}(|w_P(z)(1 - Q(z)G_o(z))| + |w_I(z)Q(z)G_o(z)|) < 1.$$

Controller design is then reduced to the design of $Q(z)$ to achieve a desired sensitivity function, while meeting this robustness constraint.

3.2 Robust Q-design in the presence of a time delay

Q-design can easily be extended to stable, minimum phase systems with a time delay (Goodwin et al. (2001)). Define

$$G_o(z) = z^{-d}\overline{G_o}(z),$$

where d is the time delay, and $\overline{G_o}(z)$ represents the nominal model without time delay. $Q(z)$ can then be evaluated as

$$Q(z) = \frac{C(z)}{1 + C(z)\overline{G_o}(z)}$$

(Goodwin et al. (2001), ch. 15.5), which leads to a Smith controller form. In this case, the nominal complementary sensitivity is given by

$$T_o(z) = z^{-d}Q(z)\overline{G_o}(z)$$

and the sensitivity by

$$S_o(z) = 1 - z^{-d}Q(z)\overline{G_o}(z).$$

Since $\overline{G_o}(z)$ and its inverse are stable, any stable proper $Q(z)$ defines a stabilizing controller and $Q(z)$ can be chosen as

$$Q(z) = F_Q(z)[\overline{G_o}(z)]^{-1}. \quad (2)$$

The nominal sensitivity and complementary sensitivity then simplify to

$$S_o(z) = 1 - z^{-d}F_Q(z)$$

and

$$T_o(z) = z^{-d}F_Q(z).$$

Design of a controller that achieves robust performance simplifies to designing $F_Q(z)$ such that

$$\max_{\omega}(|w_P(z)(1 - z^{-d}F_Q(z))| + |w_I(z)z^{-d}F_Q(z)|) < 1. \quad (3)$$

Note that the limitations due to the uncertainty are explicit in this design, and directly linked to the design variable F_Q. The only limitations to the achievable performance are the time delay and the uncertainty weight $w_I(z)$. In the following, this condition will be approximated on a finite frequency grid.

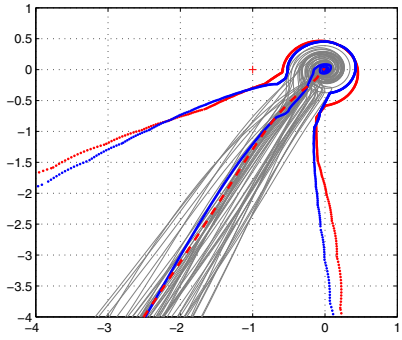

Fig. 2. Nyquist plot of the loop function with K_{PID} for the 47 individual pediatric models (grey), the optimal nonparametric nominal model $G_{np_{ped}}$ (blue) and the fourth order parametric model G_o (red dashed). The bounds of the unstructured uncertainty description of the loop function are shown for both $G_{np_{ped}}$ and G_o in blue and red respectively.

4. Q-DESIGN FOR PROPOFOL ANESTHESIA

4.1 Nominal model and uncertainty description

The Q-design controller in this paper is based on the model set described by van Heusden et al. (2013). This set includes the models used to design the PID controller described in Section 2, as well as additional models identified from data from a clinical study evaluating this PID controller. The inter-patient variability is characterized by a multi-model description. There are numerous ways to define a nominal model from this description. In Bibian et al. (2006), the uncertainty region was approximated by the smallest circle in the Nyquist plot that encompassed the lowest and highest gains combined with the lowest and highest phase at each frequency. A full order frequency domain model minimizing the uncertainty was identified. A rational function was then identified from this frequency domain model. In Dumont et al. (2009), a low-order nominal model was identified directly using non-convex gradient based constrained optimization.

In this study, we identify the optimal full order nominal model using convex optimization. In a second step a low-order parametric model is identified. This method allows for the evaluation of optimality; the nonparametric model is optimal and conservatism introduced by the low-order approximation can be evaluated.

Consider the additive uncertainty description

$$G_p(e^{-j\omega_k}) = G_{np}(e^{-j\omega_k}) + w_{A_{np}}(e^{-j\omega_k})\Delta_A(e^{-j\omega_k});$$
$$|\Delta_A(e^{-j\omega_k})| \leqslant 1, \omega_k \in \Omega, \quad (4)$$

where G_p, for $p \in [1, n_P]$ describe the individual patient models for n_P patients, the number of models in the set. $G_{np}(e^{-j\omega_k})$ is the optimal frequency domain model, $w_{A_{np}}(e^{-j\omega_k})$ is the uncertainty weight at frequency ω_k and Δ_A describes the unstructured uncertainty.

Identification of $G_{np}(e^{-j\omega_k})$ at frequency ω_k that minimizes $w_{A_{np}}$ is a convex optimization problem (Hindi et al. (2002)) and can be solved efficiently for a large number of frequencies (Löfberg (2004)). Given the model set G_p, the optimal nonparametric nominal model optimizes the

following problem at each frequency $\omega_k \in \Omega$:

$$\begin{aligned} &\min_{w_{A_{np}}, G_{np}} w_{A_{np}}(e^{-j\omega_k}) \\ &s.t. \\ &|G_p(e^{-j\omega_k}) - G_{np}(e^{-j\omega_k})| \leqslant w_{A_{np}}(e^{-j\omega_k}). \end{aligned} \tag{5}$$

In the second step, a low-order discrete parametric nominal model $G_o(z)$ with a sampling interval of $T_s = 5$ seconds is identified from G_{np}. The corresponding multiplicative uncertainty weights are calculated according to

$$\begin{aligned} G_p(e^{-j\omega_k}) = G_o(e^{-j\omega_k})(1 + w_I(e^{-j\omega_k})\Delta_I(e^{-j\omega_k})); \\ |\Delta_I(e^{-j\omega})| \leqslant 1, \omega_k \in \Omega. \end{aligned} \tag{6}$$

The model set described by van Heusden et al. (2013) contains 47 individual responses from children age 6 - 16 years. The models are linearized for induction of anesthesia. The model input is scaled to body weight. The output is scaled to $1 - WAV_{CNS}/100$. The frequency response data for each model are generated on a finite frequency grid for a sampling time $T_s = 5$s:

$$\omega_k = \frac{\pi}{T_s}\frac{k}{2048}, k \in [0, 2048], \tag{7}$$

At each frequency ω_k, $G_{np}(e^{-j\omega_k})$ optimizing (5) is calculated.

The individual patient models G_p contain time delays. For the second step, the time delay for the low-order nominal model is estimated from the impulse response of G_{np}, calculated through its inverse Fourier transform. The delay is estimated to be 5 seconds. A discrete model with $T_s = 5$ and $\tau_d = 1$ is estimated from the frequency domain model using the output error approach. Different initial conditions were used, the stable model G_o that achieved the best fit is given in equation (8).

Adequacy and conservatism of the unstructured uncertainty model are evaluated using the loop function with the clinically evaluated robust PID controller K_{PID}. Fig. 2 shows the individual loop functions $K_{PID}G_p$, as well as the loop function $K_{PID}G_{np}$ with the optimal nonparametric nominal model G_{np}, and the loop function $K_{PID}G_o$ with the nominal model and their corresponding unstructured uncertainty.

The predicted margins of K_{PID} are significantly smaller for the unstructured uncertainty models than for the multi-model approach. Most of the conservatism is introduced by the unstructured uncertainty rather than by the low-order approximation. The assumption of unstructured uncertainty introduces an overestimation of M, the maximum amplitude of the sensitivity function, as reflected by the reduced distance to the critical point -1; the predicted M increased from ≈ 2 for the multi-model representation to ≈ 3.5 for the unstructured uncertainty.

4.2 Controller design

The performance objective is formulated according to Skogestad and Postlethwaite (2007), Ch. 2.7 as

$$w_P(s) = \frac{s/M + \omega_B}{s + \omega_B A},$$

and evaluated at ω_k as defined in Section 4.1. M corresponds to the worst case maximum amplitude of the sensitivity function, ω_B represents the minimum bandwidth and A the maximum steady-state tracking error.

To achieve the clinical control objectives discussed in Section 2.2, the bandwidth of the closed-loop system is maximized while limiting the maximum amplitude of the sensitivity function. The controller is designed using a manual approach; w_P and a low-order filter F_Q are designed iteratively to maximize the bandwidth while satisfying the robust performance criteria (3). In addition to this robust performance criterion, performance was evaluated in the time domain by evaluating the response during induction of anesthesia of all models in the multi-model description.

Following this iterative procedure, $w_P(z)$ was defined as $\omega_B = 0.0015$, $A = 0.01$ and $M = 3.5$, similar to the margin achieved by the pediatric PID controller. F_Q was chosen as a fourth order filter with unity steady-state gain, two real and two complex poles. To achieve a sufficiently fast induction of anesthesia, the nominal complimentary sensitivity function allows for significant overshoot; the complex poles of F_Q were placed at $\omega = 0.0079$ with a damping factor of 0.62. The real poles were placed at 0.6 and 0.7. A zero was added at 0.9 to reduce the roll-off around the bandwidth and reduce the peak of the sensitivity function. The resulting controller is given by $C_{Ped}(z^{-1})$ in equation (8).

Fig. 3 shows the designed nominal complementary sensitivity function T_o as well as T for the nominal model achieved with the PID controller. The peak value of T_o is reduced in the Q-design compared to the PID design. The frequency domain characteristics of the Q-design controller C_{Ped} and PID controller are similar between $\approx 0.005 - 0.2$ rad/s, see Fig. 4. At low frequencies, the gain of C_{Ped} is lower than the PID gain, while the roll-off at high frequencies is smaller; the PID controller contains a noise filter that is not taken into account in this Q-design.

5. RESULTS: CLOSED-LOOP PERFORMANCE

The characteristics of the two design methods are summarized in Table 1. Fig. 5 shows the response of the set of linearized pediatric models controlled by the Q-design (C_{Ped}) and PID controller (K_{PID}) to a step change in the reference signal of 50, corresponding to induction of anesthesia. C_{Ped} reduces the overshoot, but induction of anesthesia is slower. Several subjects have an induction time of more than 5 minutes, which is clinically not desired. Note that the nominal response does not reflect the average response for the population. The speed of the designed response is therefore not achieved for the majority of individual models. Fig. 6 shows the performance criteria as well as the achieved performance for the nominal models and the original multi-model sets. While the bandwidth of the nominal design is sufficient, the achieved bandwidth for most subjects is smaller than the nominal design. Furthermore, ω_B, the minimum bandwidth used for design, strongly underestimates the nominal bandwidth as well as the bandwidth achieved for the multi-model set. The maximal amplitude of the sensitivity function evaluated over the multi-model set is much smaller than $M = 3.5$ as used in the design, reflecting the conservatism introduced by the unstructured uncertainty.

$$G_o(z^{-1}) = \frac{0.00122z^{-1}(1-0.9995z^{-1})(1-0.9916z^{-1})}{(1-0.9997z^{-1})(1-0.9960z^{-1})(1-(0.9737+0.0159i)z^{-1})(1-(0.9737-0.0159i)z^{-1})}. \quad (8)$$

$$C_{Ped}(z^{-1}) = \frac{1.4945(1-0.90z^{-1})(1-0.9997z^{-1})(1-0.9960z^{-1})(1-(0.9737+0.0159i)z^{-1})(1-(0.9737-0.0159i)z^{-1})}{(1-z^{-1})(1-0.9995z^{-1})(1-0.9916z^{-1})(1-0.9617z^{-1})(1-0.6718z^{-1})(1-0.6190z^{-1})} \quad (9)$$

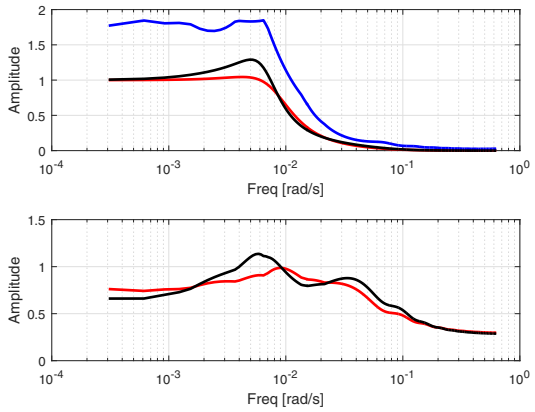

Fig. 3. Top: Controller design for the nominal pediatric model and uncertainty. The nominal complementary sensitivity T_o as designed using Q-design is shown in red, T for the nominal model achieved with the PID controller in black, the inverse of the uncertainty weights W_I is shown in blue. Bottom: Robust performance criteria (3) as a function of frequency, for the PID controller (black) and the Q-design (red).

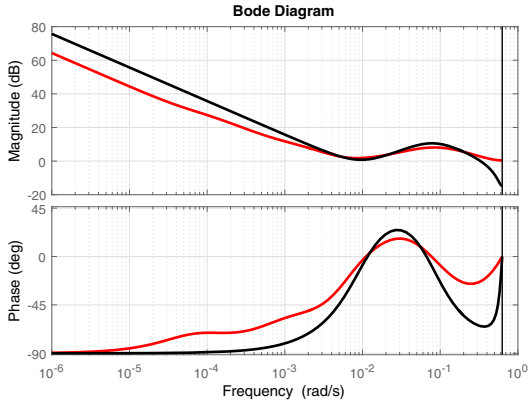

Fig. 4. Bode diagrams of the Q-design controller (red) and the PID controller (black).

	PID	Q-Design
Tuning	Manual	Manual
Parameters	2-DOF PID parameters and filter	ω_p and F_Q
Uncertainty	Multi-model	Unstructured
Design criteria	Maximize integral gain, limit peak sensitivity	Maximize bandwidth, robust performance
Performance evaluation	Time domain response	Robust performance, time domain response

Table 1. Summary of design methods

6. DISCUSSION

Control of anesthesia is characterized by large uncertainty. Robust PID control can therefore be expected to provide

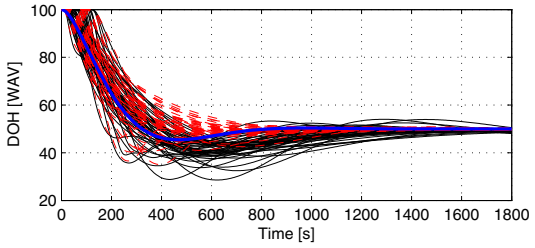

Fig. 5. Response to induction of anesthesia of the 47 linearized pediatric models controlled by K_{PID} (black) and the Q-design controller (red dashed). The nominal response of the Q-design controller is indicated in blue.

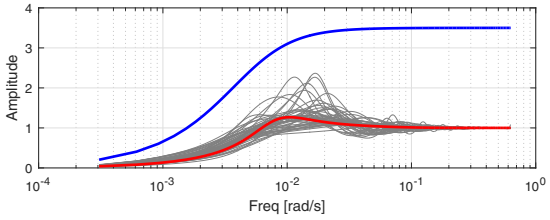

Fig. 6. Achieved sensitivity with Q-design: nominal performance (red), $1/w_P$ (blue), and the achieved performance for the multi-model set (grey).

adequate robust control. In this paper, the performance of a robust PID controller, which has been shown to be close to optimal, was compared to a manually tuned sixth-order model-based controller. The behaviour of these controllers was similar at higher frequencies. At lower frequencies, the PID gain was higher than the gain of the model-based controller. The additional degrees of freedom in the higher-order model-based controller allow an increase in robustness margins by increasing the phase margin, at the cost of decreased gain at low frequencies. Simulated time-domain responses to induction of anesthesia show a corresponding reduction in overshoot, at the cost of increased time to induction. These results indicate that the uncertainty introduced by interpatient variability is indeed an important factor limiting the achievable closed-loop performance, and that performance improvement from additional controller complexity may be limited. Model-based methods such as MPC may be beneficial for extensions to multi-drug systems or the inclusion of safety constraints.

It should be noted that both the PID controller and the model-based controller were manually tuned, based on the same design objective but different design criteria. An optimization based approach would provide a more accurate comparison, however, this would require a PID and a model-based design method that aim to optimize the exact same criteria.

The PID controller was tuned using a multi-model uncertainty description, while the model-based controller

required an unstructured uncertainty description, which introduced conservatism. A model-based design that uses unstructured uncertainty to evaluate robust stability, but that evaluates robust performance using a multi-model approach may reduce the conservatism. Alternative strategies aimed to reduce the uncertainty, for example using patient demographics (Bibian et al. (2006)), may allow for improved performance.

The choice of a nominal model is essential for model-based design. The designed nominal closed-loop was not reflective of the response of the model set. Although the nominal model used in this paper minimizes the modeling error, model-based design might be simplified when using a nominal model that minimizes a closed-loop error rather than the modeling error (Douma and Van den Hof (2005); Oomen and Bosgra (2012)).

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