MODEL IDENTIFICATION FOR CLOSED-LOOP CONTROL OF PROPOFOL IN CHILDREN

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Background: The effect of intravenous anesthetic drugs is traditionally modeled using pharmacokinetic (PK) and pharmacodynamic (PD) models. However, a physiological meaningful set of PD parameters is not required for controller design and is not essential for prediction of closed-loop performance provided that the experimental conditions for identification and closed-loop control are similar[1]. In this study, a set of models describing the effect of propofol in children is identified specifically for the design of a robust linear closed-loop controller.

Methods: Following approval of the institutional ethics board, data was analyzed for thirty children, ASA category I/II undergoing elective general surgery using total intravenous anesthesia (TIVA). The WAVcns index[2] as measure of the depth of hypnosis (DOH) was recorded during induction and maintenance of anesthesia. Corresponding propofol infusion rates were recorded manually. Sixteen recordings were discarded due to corrupted data (6), missing data (8) or a strong reaction to tracheal intubation (2) as reflected in the measure of DOH. Data for the first 8 min following the start of the propofol infusion were used for model identification. The Paedfusor[2] PK model was used to predict the propofol plasma concentration. Three different methods were employed for patient model identification: i). Single-step PD model[4]: The PD model was identified using an extensive search of k_{e0} and time-delay combined with constrained least-squares estimation of γ and EC_{50}; ii) Two-step PD model: In the first step, the linear part of the PD model plus time-delay was identified. In the next step, a search algorithm determined the hill parameter that minimizes the root mean squared of the residual; iii). Black-box model: Parameters of a first-order time-delayed model, directly relating the infusion profile to clinical effect were identified. Closed-loop performance of a robust linear controller, designed based on the Black-box model, was verified for the three model sets.

Results: Similar modeling errors can be obtained with the three different sets of parameters. The predicted mean (SD) EC_{50} and γ were 4.5(1.4) and 5.5(1.8) μg/ml and 2.1(0.8) and 1.7(0.2) for the Single-Step PD model and the Two-Step PD model, respectively. The Two-step PD model contained a significantly larger delay 31(24) seconds, compared with the Single-Step PD model 14(20) seconds. Predicted closed-loop performance with a robust linear controller was similar for all three model sets, despite the parametric or structural differences. Clinical evaluation of the controllers in a pilot study[5] confirms the reliability of the models for the design of linear controllers.

Conclusions: Data from induction of anesthesia is not sufficiently rich to independently identify all PD model parameters but is adequately exciting to identify a linear first-order time delay model. Although the identified PD models do not necessarily provide physiologically relevant parameters, the identified models are appropriate for model-based controller design.

References

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