BENCHMARK CAHLLENGE BMS 2021

for

Optimization of Anesthetic and Hemodynamic Drug Delivery Problem in Simulated Patient Environment

The benchmark competition is released with the purpose to enable the research community working on **control applications** to provide solutions for this highly interactive and complex system and to test them in a systematic manner. Please consider inviting your doctoral students and senior researchers to contribute papers to this special session.

The files can be downloaded from

BMS2021 website: https://bms2021.ugent.be/BCC.html

Matlab File Exchange platform: <u>https://nl.mathworks.com/matlabcentral/fileexchange/85208-open-source-patient-simulator</u>

When you submit the paper select Open Invited Track and fill in the following code (code: x2k82) paper submission deadline 30 April 2021

SYSTEM DESCRIPTION

The main objective of controller is to maintain the hemodynamic variables (i.e. MAP and CO) while ensuring that the level of depth of anesthesia is at the desired level. MAP is controlled by manipulating the SNP, CO is controlled by manipulating the DPM and the anesthesia level is controlled by manipulating the Propofol infusion. As a function of the patient status one or more of the three drugs are controlled to ensure stability of the hemodynamic variables. Implementation of such a complex control strategy in clinical trial requires detailed simulation studies. Given all the available know-how described above, a benchmark platform has been developed [Ionescu et al, 2020]. The graphic overview of the implemented functions to mimic a complete(r) anesthesia paradigm for drug titration regulatory loops is given in figure 1.

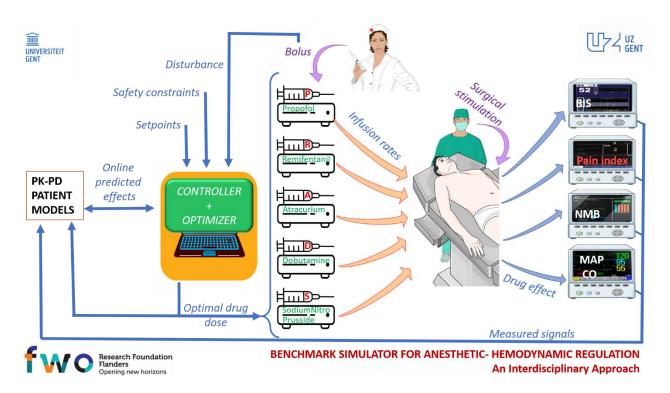


Fig. 1 Conceptual representation of the possible interactions taking place between the sedation and hemodynamic systems involved in the balancing act of optimizing general anesthesia.

The aim of this benchmark challenge is to investigate the feasibility of different control strategies to the regulatory problem of hypnosis-hemodynamic variables. This is novel in the application field and patient characteristics such as drug resistance, sensitivity, adverse effects and drug retention times have to be taken into account.

This is an open-source simulator, and the users has the freedom to modify it according to their research focus. However, there are some recommendations

- Patient safety, meaning that variables are to be controlled variables within the clinical intervals
- Do not exceed the constraints on the input (i.e. min-max values of the pumps for drug delivery)
- Respect the intervals for the output variables (e.g. BIS value between 40-60)
- Ideally a MIMO control is designed to ensure that the entire system (i.e. the patient) remains stable

More details regarding the intervals and constraints can be found in [lonescu et al 2020].

The Benchmark Challenge at BMS2021 allows researchers to approach an important control problem to test their recent developments in the design of **classical and advanced control techniques.** There are no constraints with respect to the control approach, it is fully the choice of the user from PID to advanced methodologies (e.g. MPC). It is important to mention the fact that this is an open-source and the user has the freedom to adapt/change the simulators in terms of models, interaction etc. but the authors will have to motivate the implemented changes in their paper.

Below an indication of the min and max values for the inputs and outputs are given.

| BIS interval: 40-60% | Propofol infusion: 0 – 5 mg/kg*min |
|------------------------|---|
| RASS score: (-5) – 4 | Remifentanil infusion: 0 – 2.5 mcg/kg*min |
| CO: 65 - 110 ml/kg*min | Dopamine infusion: 0 – 10 mcg/kg*min |
| MAP: 65 – 110 mmHg | SNP infusion: 0 – 10 mcg/kg*min |
| NMB: 0 – 100% | Atracurium infusion: 0 – 15 mcg/ml |

KEY REFERENCES

Copot, D., Ionescu, C.-M. (2019). Models for nociception stimulation and memory effects in awake and aware healthy individuals. IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, 66(3), 718–726.

Copot, D., Ionescu, C.-M. (2014). Drug delivery system for general anesthesia: where are we? IEEE International Conference on Systems Man and Cybernetics Conference (pp. 2452–2457). Presented at the IEEE International Conference on Systems, Man, and Cybernetics (SMC).

Copot, D., Chevalier, A., Ionescu, C.-M., De Keyser, R. (2013). A two-compartment fractional derivate model for propofol diffusion in anesthesia. IEEE International Conference on Control Applications (pp. 264–269). Presented at the IEEE Multi-Conference on Systems and Control, IEEE.

De Keyser, R., Copot, D., Ionescu, C.-M. (2015). Estimation of patient sensitivity to drug effect during Propofol hypnosis. IEEE International Conference on Systems Man and Cybernetics Conference Proceedings (pp. 2487–2491). Presented at the IEEE International Conference on Systems, Man, and Cybernetics (SMC).

Ghita, M., Neckebroek, M., Muresan, C., Copot, D. (2020). Closed-loop control of anesthesia : survey on actual trends, challenges and perspectives. IEEE ACCESS, 8, 206264–206279. https://doi.org/10.1109/ACCESS.2020.3037725

Ghita, M., Neckebroek, M., Juchem, J., Copot, D., Muresan, C. I., Ionescu, C.-M. (2020a). Bioimpedance sensor and methodology for acute pain monitoring. SENSORS, 20(23). <u>https://doi.org/10.3390/s20236765</u>

Ionescu C, Neckebroek M, Ghita Mi, Copot D, An Open Source Patient Simulator for Design and Evaluation of Computer Based Multiple Drug Dosing Control for Anesthetic and Hemodynamic Variables IEEE Access; 2021; doi 10.1109/ACCESS.2021.3049880

Ionescu, C.-M., Copot, D., De Keyser, R. (2017). Anesthesiologist in the loop and predictive algorithm to maintain hypnosis while mimicking surgical disturbance. IFAC PAPERSONLINE (Vol. 50, pp. 15080–15085). Presented at the 20th World Congress of the International-Federation-of-Automatic-Control (IFAC).

Ionescu, C.-M., Machado, J. T., De Keyser, R., Decruyenaere, J., Struys, M. (2015). Nonlinear dynamics of the patient's response to drug effect during general anesthesia. COMMUNICATIONS IN NONLINEAR SCIENCE AND NUMERICAL SIMULATION, 20(3), 914–926.

Ionescu, C.-M., Hodrea, R., De Keyser, R. (2011). Variable time-delay estimation for anesthesia control during intensive care. IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, 58(2), 363–369.

Ionescu, C.-M., De Keyser, R., TORRICO, B., DE SMET, T., Struys, M., & NORMEY-RICO, J. (2008). Robust predictive control strategy applied for propofol dosing using BIS as a controlled variable during anesthesia. IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, 55(9), 2161–2170.

Neckebroek, M., Ghita, M., Ghita, M., Copot, D., Ionescu, C.-M. (2020). Pain detection with bioimpedance methodology from 3-dimensional exploration of nociception in a postoperative observational trial. JOURNAL OF CLINICAL MEDICINE, 9(3). https://doi.org/10.3390/jcm9030684

Padula, Fabrizio, Ionescu, C.-M., Latronico, N., Paltenghi, M., Visioli, A., Vivacqua, G. (2017). Optimized PID control of depth of hypnosis in anesthesia. COMPUTER METHODS AND PROGRAMS IN BIOMEDICINE, 144, 21–35.

Padula, F., Ionescu, C.-M., Latronico, N., Paltenghi, M., Visioli, A., & Vivacqua, G. (2016). Inversion-based propofol dosing for intravenous induction of hypnosis. COMMUNICATIONS IN NONLINEAR SCIENCE AND NUMERICAL SIMULATION, 39, 481–494.