

TSP

# Project and Development of a Decision Support System for Anesthesia Based on Data Fusion and PK/PD models.

<sup>1</sup>Bruno Bestle Turrin; <sup>2</sup>Fuad Kassab Jr.; <sup>3</sup>Joaquim E. Vieira <sup>1, 2</sup>Escola Politécnica da Universidade de São Paulo; <sup>3</sup>Faculdade de Medicina da Universdade de São Paulo

The 7th edition of the INFIERI School series, held at USP, August 28 to September 9, 2023



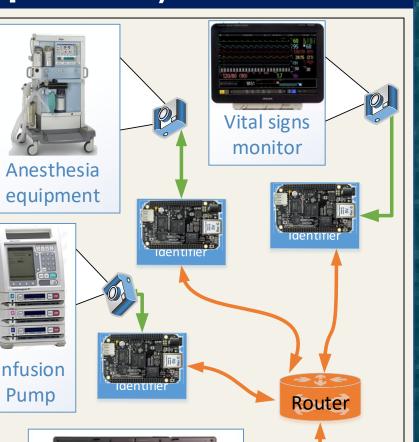
# Abstract

The balanced anesthesia process contains three main parts: the control of hypnosis, analgesia, and neuromuscular blockage. For the induction phase, the anesthesiologist performs protocols based on prior planning specific to each patient and usually performs these controls by monitoring the classic vital signs and other clinical signs for the maintenance phase. In a way, this professional is the controller in a control system that acts on the plant (the patient) through the infusion of hypnotic drugs, analgesics, and neuromuscular blockers. In addition, the anesthesiologist estimates the state of consciousness, the level of analgesia and the level neuromuscular blockage through other indirect measures, as well as a state observer.

# Methods and Materials (Data Acquisition)

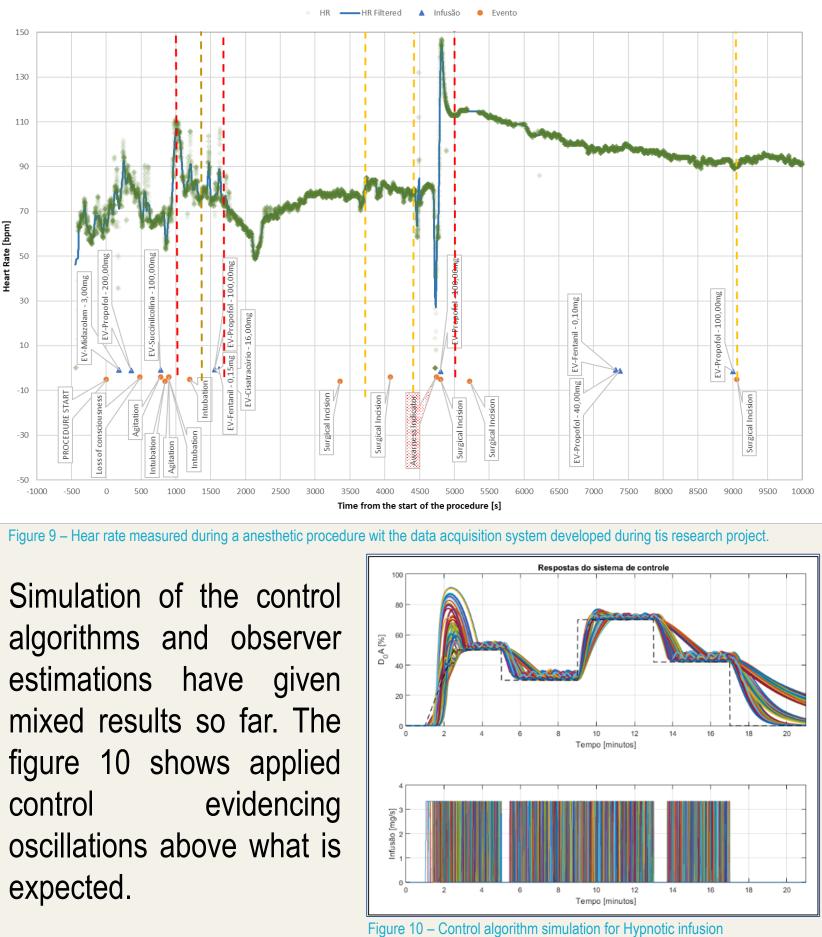
Unfortunately, most of the equipment available at the surgical center do not provide an opened communication protocol. Some of the equipment do not even have a communication port. To circumvent this problem in a standardized manner for every equipment, we have developed a data acquisition system based on image treatment and classification.

In front of every equipment of importance to this research, a camera and a processing unit where carefully positioned to extract images form the equipment's displays (figure 3). The processing unit runs a software, developed in this project, to process and identify the measurements shown by the equipment (figure 4). Once it is processed, the data is stored locally and sent to a central system, which combines data form different identifiers in a single database.



# Results

Currently, data acquisition is still going in the Hospital das Clínicas de São Paulo. We have collected data from more than 40 anesthetic procedures, combining over 20Gb of information. Most of the expected phenomena described by the PK/PD models were observed during the data acquisition, as is shown in the figure 9.



There are different techniques for direct monitoring of these three anesthesia variables (DoA, NMB and NoL), such as BIS and Narcotrend, but all have some disadvantages, especially when the anesthesia process combines different drugs.

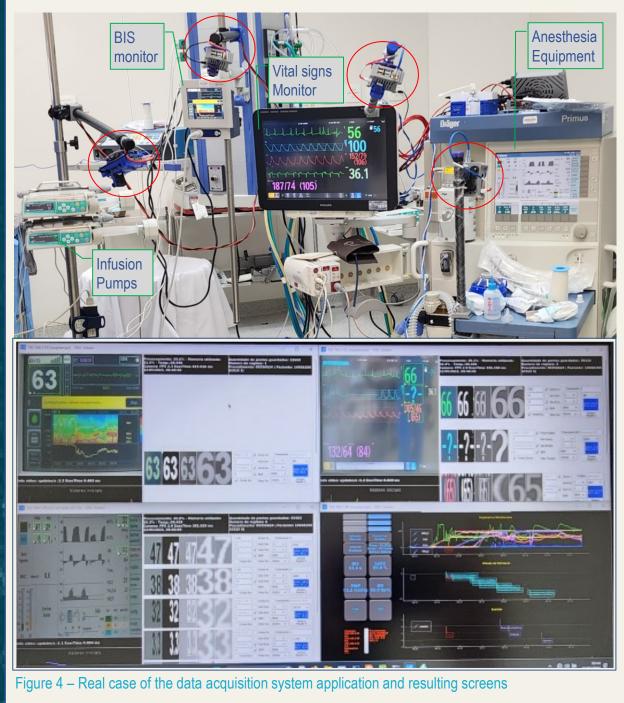
This work proposes a new way of evaluating DoA, NMB and NoL using data fusion techniques to combine classical clinical signs with advanced EEG monitoring techniques to provide a decision support system for the anesthesiologist.

A great part of the work done in this research project was aimed at the development of the data acquisition system used in the operating rooms at Hospital das Clínicas in São Paulo, Brazil.

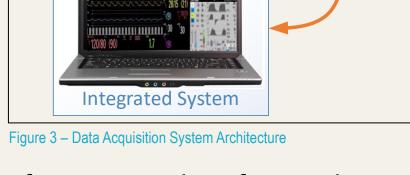
# Introduction

During a general anesthesia procedure, the anesthesiologists act similarly to a pair of state observer and controller [1]. The professional must control and maintain a certain level of hypnoses, nociception and neuromuscular blockade, administering a set of different drugs in three main temporal phases (figure 2), while minimizing the effects on the metabolic, hemodynamic and respiratory workings of the patient [2].

Hypnoses 1 inimizing effects on  $(D_oA(NdC) - Hypnoses)$ Hemodynamics  $N_oL$  – Analgesia Temperature Metabolic NMBL – NM Block



The selected classifier was used for its simplicity, relatively fast training process and implementation, but certainly other algorithms such as convolutional neural networks could have been used for this purpose.



The identifier software searches for contiguous regions inside each area of interest in the image to isolate the algorisms, and then passes each one through a classifier (Support Vector Machine SVM). The resulting identification is combined into the monitored parameter in the screen of the equipment (figure 5).

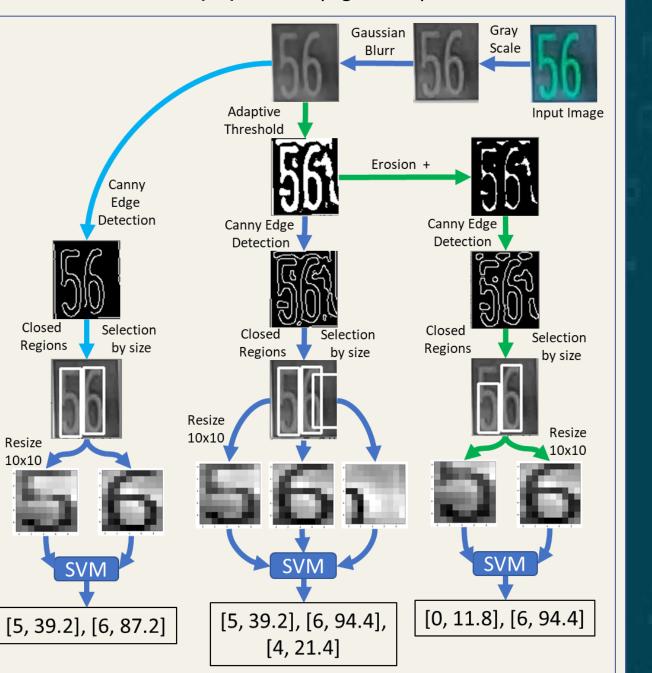


Figure 5 – Image treatment process and resulting classification of algorisms

# Conclusion

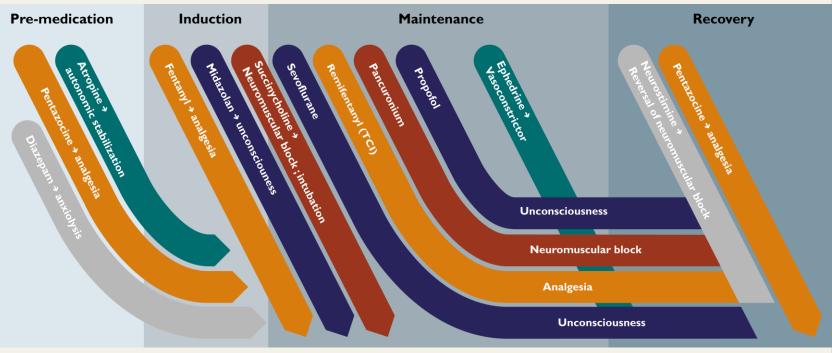
Despite the complicated workaround developed exclusively to acquire needed data, this chosen method has proven to be very effective and especially useful when applied to equipment that do not have a communications port. The required development and experiments preparations effort has been compensated with good and reliable data.

At this point in the development research project, the amount of data collected is almost enough to draw a few conclusions, but the proposed solution implementations requires still a few months of development, however we are excited with the prospect of the results.



### Figure 1 – Main variables of general anesthesia procedure

To be able to attain this objectives, the anesthesiologists rely on previous knowledge and training, the patient's clinical signs, and, most importantly, on a set of monitoring equipment and actuators. Unfortunately, in most cases a direct monitoring of the main variables is not available, and when it is there are some accuracy problems [3].



### Figure 2 – Different drugs used on each phase of the anesthetic procedure

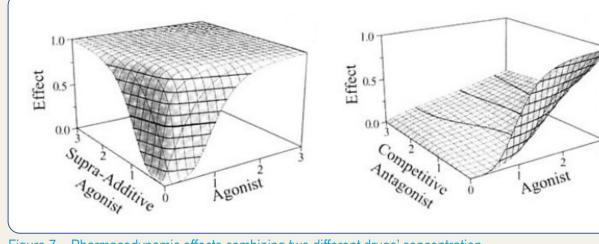
Furthermore, an overdosage or a hypo dosage represents several risk factors (table 1) for the patient that must be considered during the procedure, leading to a great motivation for this research effort.

Table 1 – Risk factors associated with each drug type		
Drug Type	Overdose	Hypodosage
Hypnotic (DoA)	<ul> <li>Recovery time increase</li> <li>Post chirurgical complications Irreversible coma</li> <li>Increased morbidity or Death [5]</li> </ul>	<ul> <li>Intraoperative awareness [4]</li> <li>Recall</li> <li>PTSD</li> </ul>
Analgesic (NoL)	<ul><li>Increased DoA</li><li>Coma, Death</li><li>Chemical addiction</li></ul>	<ul> <li>Intraoperative pain         <ul> <li>(even in an unconscious level)</li> </ul> </li> <li>Hemodynamics alterations</li> </ul>
Neuromuscular Blocker (NMB)	<ul> <li>Prolonged numbness of the limbs</li> <li>Increased difficulty in recovering limb movement</li> </ul>	Involuntary movement during the procedure

# Methods and Materials (Data Fusion)

The mathematical model used are a set of pharmacokinetics (PK) and pharmacodynamics (PD) for each individual drug. The PK model describes [6] how the drug is absorbed, distributed, metabolized and excreted in the human body (figure 6). Depending on the drug, a different  $D_0 A = E_{max} \cdot \frac{C_e^{\gamma}}{C_e^{\gamma} - EC_{50}}$ number of compartments (different types of tissue and organs) is considered, but normally there are 4 each one with the respective differential equation. The input of PK models is the infusion rate of the drug.

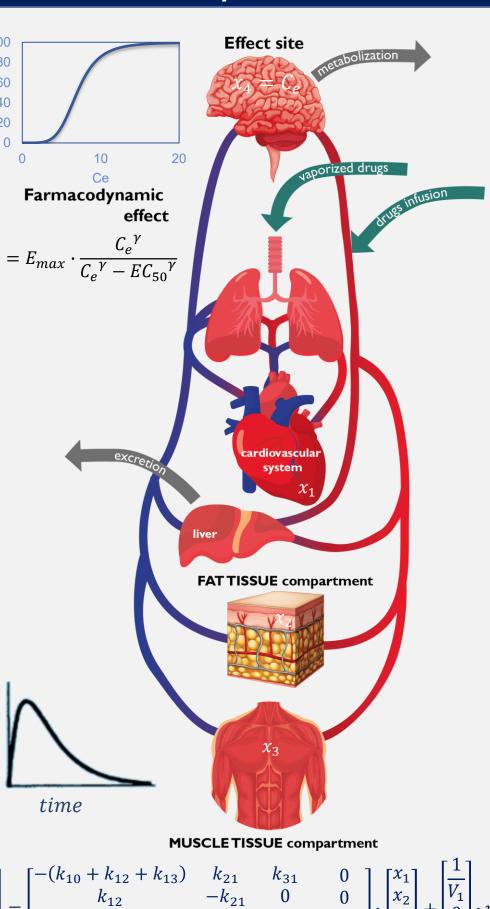
The PD model describes the relation between the concentration of a drug in the effect compartment (Ce) and its effect on the patient [7]. This model is also able to consider different drug concentrations to describe their combined effect (figure 7).





The proposed architecture and functions is shown in the diagram of the figure 8, combining algorithms such as Kalman Filtering, dynamical systems identification and machine learning.

Figure 6 – PK and PD models for one drug.



# References

[1] - BIBIAN, S. et al. Introduction to Automated Drug Delivery in Clinical Anesthesia. European Journal of Control, v. 11, n. September, p. 535–557, 2005.

[2] - MANICA, J. Anestesiologia: Princípios e técnicas. [S.I.]: Artmed Editora, 2009. Disponível em: <https://books.google.com.br/books?id=gPHdhQDkgzgC>.

[3] - AVIDAN, M. S. et al. Anesthesia awareness and the bispectral index. New England Journal of Medicine, v. 358, n. 11, p. 1097–1108, out. 2008

[4] - SACKEL, D. J. Anesthesia awareness: an analysis of its incidence, the risk factors involved, and prevention. Journal of Clinical Anesthesia, v. 18, n. 7, p. 483-485, 2006.

[5] - NUNES, C. S. Towards automation in anaesthesia: A review. IEEE MeMeA 2014 - IEEE International Symposium on Medical Measurements and Applications, Proceedings. Anais...2014

[6] – DUMONT, Guy A. e ANSERMINO, J. Mark. Closed-loop control of anesthesia: A primer for anesthesiologists. Anesthesia and Analgesia, NULL, v. 117, n. 5, p. 1130–1138, 2013.

[7] - MINTO, Charles F.; SCHNIDER, Thomas W.; SHORT, Timothy G.; GREGG, Keith M.; GENTILINI, Andrea; SHAFER, Steven L. Response surface model for anesthetic drug interactions. Anesthesiology, [S. I.], v. 92, n. 6, p. 1603-1616, 2000. DOI: 10.1097/00000542-200006000-00017.

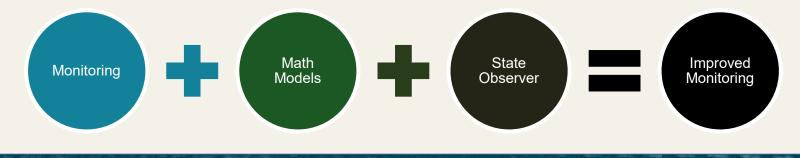
# Acknowledgements

A special thanks to my PhD supervisors:

- Prof. Dr. Fuad Kassab Jr.
- Prof. Dr. Joaquim E. Vieira
- Prof. Dr. Koichi Samechima

This research project is registered at Plataforma Brasil under the code 03424918.6.0000.0068 and was approved by the research ethics committee. It is also registered at the ClinicalTrials.gov under registration code 04079036. In addition, the developments described here were made possible thanks to the support and research grants provided by FAPESP and CAPES:

For this research project, we proposed that combining the existing monitoring, including the physical signs of the patient and the infusions made by the anesthesiologist, with a set of mathematical models and state observers, it will be possible to improve the accuracy of the monitorization, and perform a decision support for the anesthesiologist.





i ng ting tin

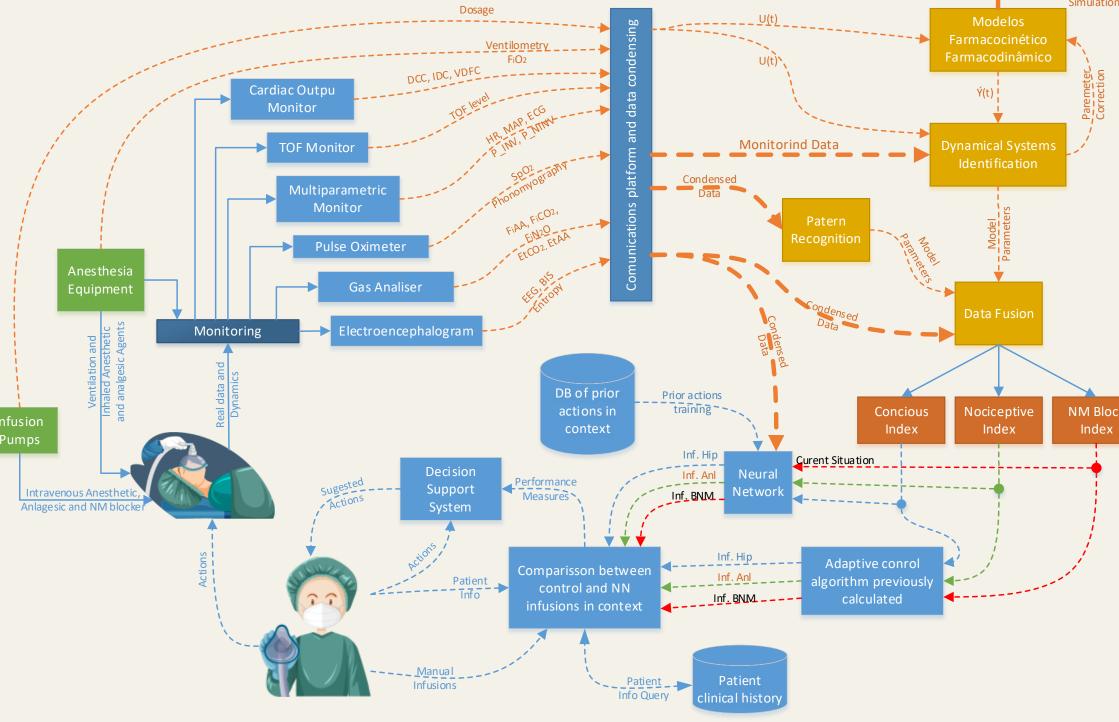


Figure 8 – Proposed architecture for the Decision support syst

- PIPE FAPESP project number **2017/22185-7**
- CAPES PROEX number 88887.488067/2020-00.

# **Contact Information**

# **Bruno Bestle Turrin**

**Control And Automation Engineer M.Sc. Electrical Engineering PhD student at EPUSP** 

## Email: bbturrin@usp.br

Linkdin: https://www.linkedin.com/in/bruno-bestle-turrin-3a413129/ Lattes: lattes.cnpq.br/1438138464113809

FAPESP: https://bv.fapesp.br/en/pesquisador/703557/bruno-bestle-turrin/