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**Smart Multidrug Delivery for Anesthesia**

**Introduction and Model**

Anesthesia is a medical treatment that prevents patients from feeling pain during procedures like surgery, certain screenings, and diagnostic tests. General anesthesia affects the whole body, making patients unconscious and unable to move. In particular, the clinical procedure consists of inducing 3 conditions: hypnosis, analgesia, and neuromuscular blockade. The first condition is ensured by the injection of Propofol, the second by the Remifentanil and the last by the Atracurium. The obtained outputs are respectively: Bispectral Index (BIS), Richmond Agitation-Sedation Score (RASS) and NeuroMuscolar Blockde (NBM).

BIS processes the EEG signals in order to obtain a value, which is an integer number, that reflects the level of consciousness of the patient on a scale 0 to 100, where 100 means the patient is completely awake and 0 means that there’s no brain activity recorded. During the surgery the BIS target value is 50 (general anesthesia).

RASS is a 10-point scale of integer numbers that goes from -5 (unarousable) to +4 (combative) and describes the agitation or sedation of the patient; during the surgery the goal is to maintain RASS around level -4 (deep sedation).

NBM defines the lack of movement, and the aims is to maintain an adequate level of paralysis during the surgery; the value range goes from 0 up to 100% where 0 means total paralysis and 100% means total muscular activity. For surgery the preferred level of NBM is 15%.

Because we are two-person group we consider only two inputs: Propofol (drug 1) and the Remifentanil (drug 2) and we want to reach and maintain a steady state of BIS = 50 10 and of RASS = -4 1 in less than 60s via a closed-loop delivery. In particular the inputs of the system are the dose of Propofol and Remifentanil injected, while the outputs are respectively the BIS and RASS signals as reported in the following schema[[1]](#footnote-1).



Figure : Schema of the control system.

The Simulink Non-Linear model is reported below. After the input block there is a saturation block both for the Propofol and the Remifentanil, this is used in order define an upper and a lower limit for the injection:

* [0 - 5] mg/(kg\*min) for Propofol;
* [0 - 2.5] mg/(kg\*min) for Remifentanil.

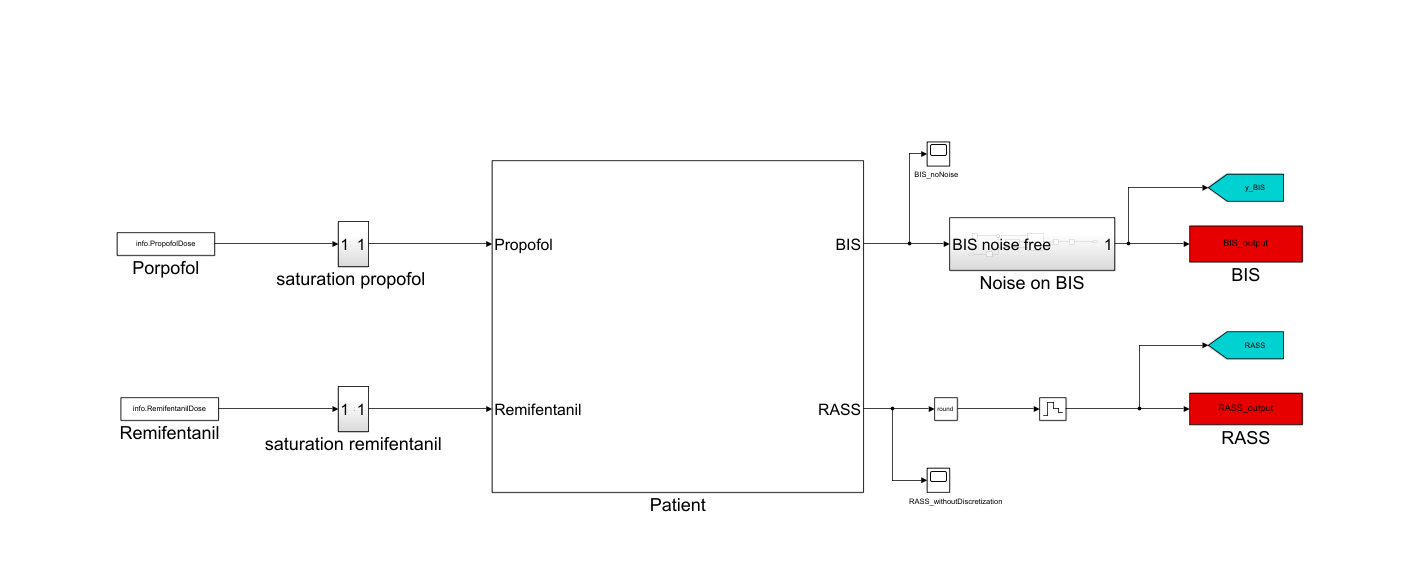


Figure : Non-Linear Simulink model.

We have available biological parameters of 24 different subjects and one set of biological parameters calculated as the mean value among all the subjects.

The outputs of this system for the average patient are reported in the graphs below.

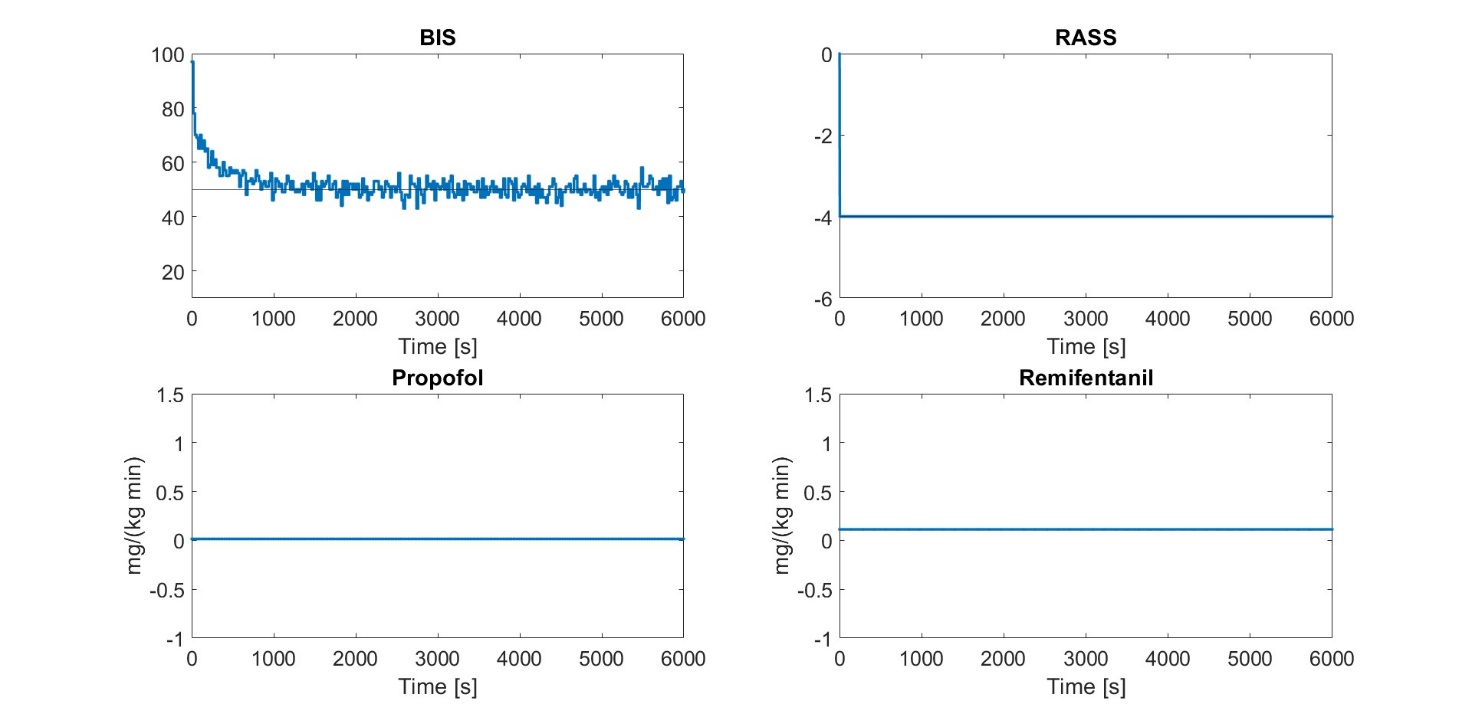


Figure : Inputs and outputs of the non-linear system.

**Task 1: Model Linearization Average Patient and Validation**

In order to linearize a non-linear system model, we need to calculate the equilibrium point around which we can do the linearization. We used Simulink's Model Linearizer to obtain the operating point required by the linearization, knowing the outputs that we were aiming for. The first attempt, trying to trim the model knowing the desired outputs didn't yield any solution because the constraints made it unfeasible. Then, we tried trimming the model considering not the desired outputs, but the starting doses of the drugs, as given by the homework instructions. This yielded viable results, and the computed outputs were comparable to the desired outputs. We then used the states that were computed for this operating point to estimate a new operating point with unknown inputs and the desired outputs. This last attempt was successful, and we used the latest operating point as parameters for the Model Linearizer to linearize our system model.

The linearize model is described through four matrices A, B, C and D which can be used in a Simulink scheme using State Space block as can be seen in Figure 4.

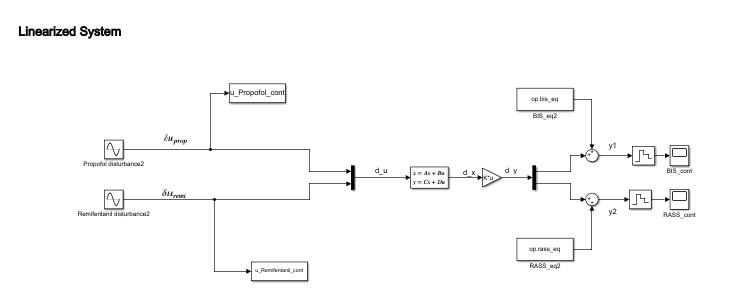


Figure 4: Linear model in Simulink.

Through a Matlab function (*c2d*) we can easily discretize the linearized model. The Simulink scheme for the discrete model is the same as the previous but uses a Discrete State Space block and sampling when needed.

The non-linear model works with actual values of input and output. On the other hand, the linearized model accepts in input the variation of the input from the equilibrium points and gives in output the variation of BIS and RASS from the desired output.

We compared the performance of the three models when the inputs present a sinusoidal 30% perturbation of the operating point.

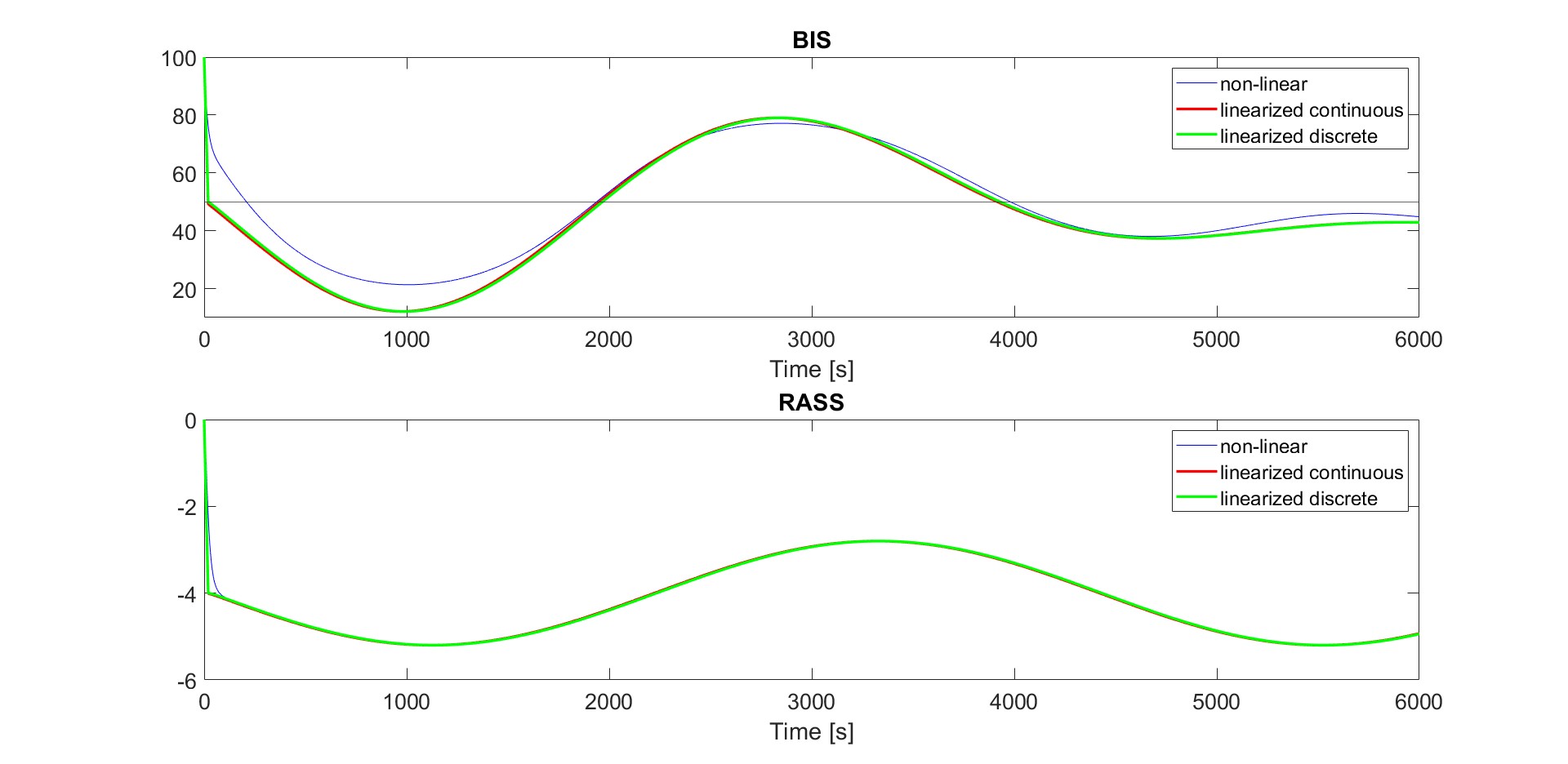


Figure : Comparison between Non-Linear, Linear continuous and Linear discrete models.

From the comparison of the three models, we can see that the linearized system faithfully follows the non-linear system aside from a slight difference at the beginning.

**Task 2: MPC for the Linearized Average Patient, Accessible**

We try now to control our linearized system to obtain the performance described before, by applying the Model Predictive Control strategy. In this case, the MPC requires in input the current state of the system. We consider the state as accessible, and we employed a simple escamotage to access the state as the output of the linear system. The actual outputs are computed at a later step using a gain block where the gain is the matrix C computed in the linearization.

Since this is a biological system we couldn’t withdraw injected drugs, therefor we set the constraints that input as computed by MPC couldn’t be negative.

We tune the MPC to value more the output rather than the input by setting low values of r matrix and by regulating the aggressiveness of the controller with the matrix q.

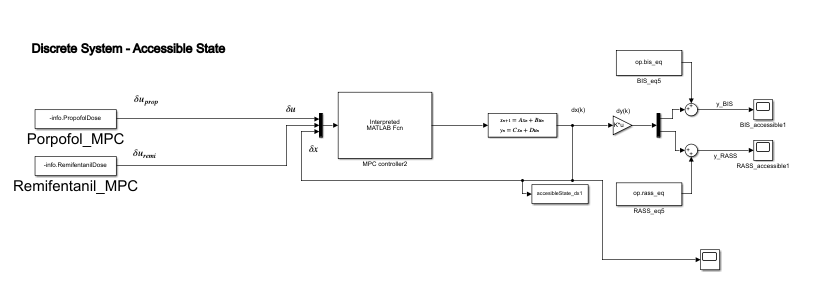


Figure : Simulink Model with the MPC.

We notice that there’s a perfect match and response from the controlled system with MPC, this is expected since we are applying an MPC build around the linear system that it is controlling, therefore there's an exact match with the plant.

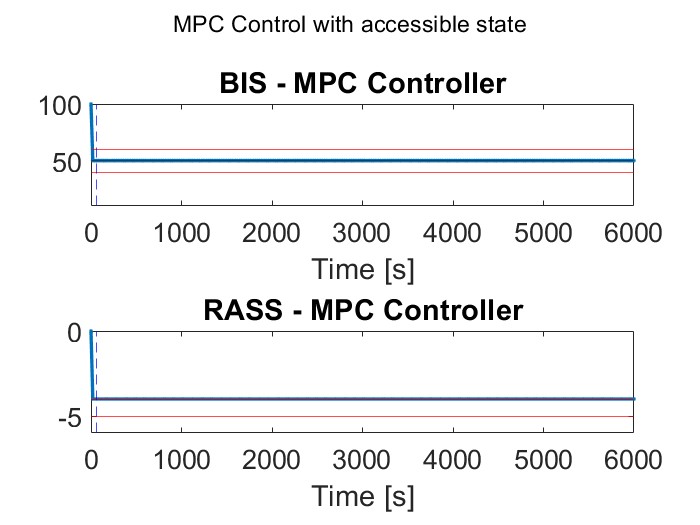


Figure : Output from the MPC controlled system.

1. Final Project Anesthesia, prof. Del Favero [↑](#footnote-ref-1)