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Matric no: 16/ENG04/063

Assignment Title: Paper analysis of "ERG scheme for closed-loop Anesthesia".

Title: An Explicit Reference Governor Scheme for Closed-Loop Anesthesia

Authors: Mehdi Hosseinzadeh, Member, IEEE, Klaske van Heusden, Guy A. Dumont, Life Fellow, IEEE, and Emanuele Garone, Member, IEEE

Structure of the paper:

Acronyms

- ECE - European Control Conference
- IEEE – Institute of Electrical and Electronics Engineers
- FNRS MIS – Fond de la Recherche Scientifique Mandat d'impulsion scientific

- SAAS - Service d'Automatiqueet d'Analyse des Syst`emes
- ERG – Explicit Reference Governor
- PK – PharmacoKinetic
- PD – PharmacoDynamic
- PKPD – PharmacoKinetic PharmacoDynamic
- DOH – Depth of hypnosis
- PID – Proportional Integral Derivative
- LBM – Lean Body Mass
- DSM – Dynamic Safety Margin
- NF – Navigational Field
- KF – Kalman Filter

Remarks

1. By defining approximation error as $e(t) = y(t) - \hat{y}(t)$, the value of $\delta 0$ can be determined as $\delta 0 = \max \sup |e(t)|$.
2. Since the states of the system are not directly measured during the experiments, to determine the Lyapunov function $Vi(\cdot)$, $i = 1, \cdots, 7$ an estimator is needed.
3. To make sure that the obtained matrix Pi through (31) is valid Lyapunov matrix for all patients, one possible way is to use Kharitonov theory [29], and replace the constraint $ATPi+PiA \_ 0$ with the resulting four Kharitonov'sbased constraints.

Abstract summarised

A constrained control scheme based on an explicit governor can prevent the overdose of anesthesia in patients.

Introduction summarised

- Definition of anesthesia, Current clinical practice as a manual feedback control and improvement using a closed-loop anesthesia system.
- Components of anesthesia: Hypnosis, Analgesia, and neuromuscular blockade. Paper's goal of controlling hypnosis using a propofol delivery system.

- Division of propofol hypnosis: Induction, Maintenance, and emergence. Overdose because of unbalancing between the anaesthetic regime and the patient's pharmacological need.
- Formulating overdosing problem and safety issues by defining suitable safety constraints based on the therapeutic window of propofol.
- Methodology for the scheme using the Explicit Reference Governor as a framework to determine an invariant set containing state trajectory.
- The organization of the paper: Models used, Details of the control system and proposed ERG scheme and simulations carried out using the proposed scheme.

Results based on figure comparison

- **Differences between corresponding plots**

Figure 5	Figure 6
For the DOH plot, most patients have a DOH % of less than 50 between 0 – 10 min, with a sufficient amount susceptible to overdosing (DOH % less than 40)	Every patient has a DOH % of approximately 50 between 0 – 10 min
The I (t) [ml/h] value is above 200 for most patients, reaching 400 at the initial time of 0 – 10 min	Most patients have an I (t) [ml/h] approximately equal to 200 between 0- 10 min
In the C_p [ug/m] plot, the transient region last for a short period (less than 5 min)	The transient period lasts for about 10 min for most patients.
In the C_e [ug/m] plot, the transient region is very steep lasting for a time approximately less than 5 min.	The transient period less steep lasts for about 10 min.

Table 1: Difference between figure 5 and figure 6 of the reviewed paper

- **Key results**
    - The proposed ERG scheme guarantee constraints satisfaction
    - A DOH of 50 % was achieved for all patients
    - The ERG scheme automatically converges to the desired level of hypnosis using the auxiliary reference.

- The ERG scheme leads to slower induction for patients.

Conclusion

- I see the organization of the 'conclusion' section
- I understand the conclusion

Section II

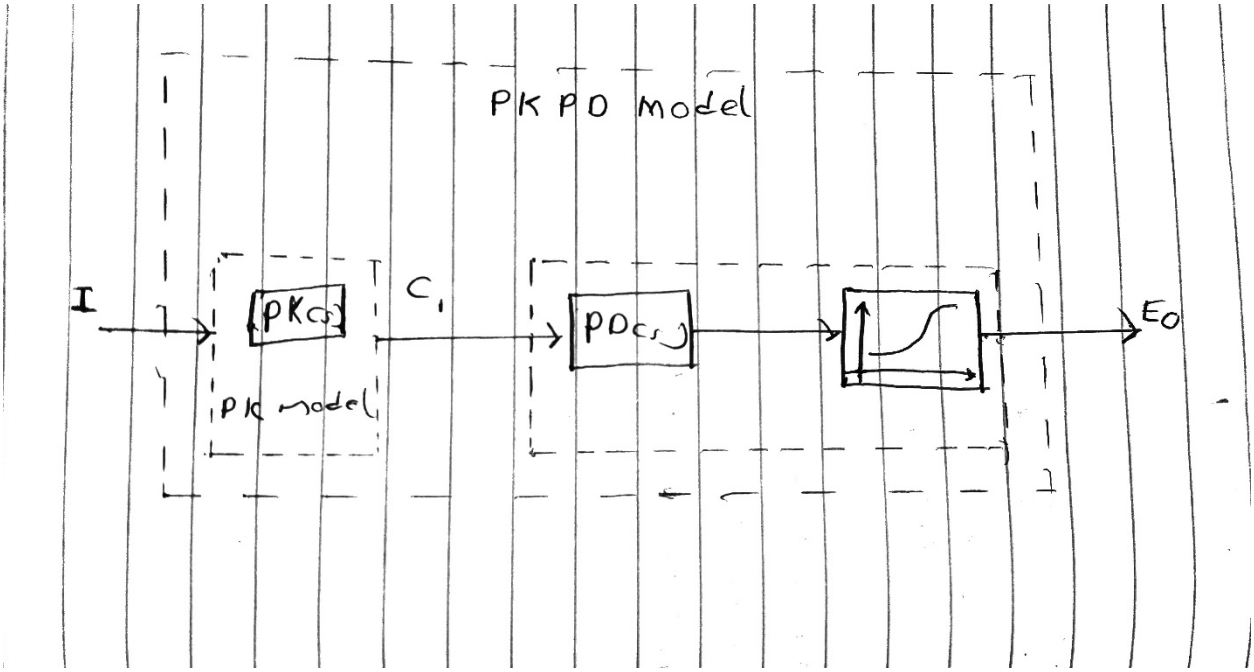

Figure 1: PKPD model block diagram

- PK model: It relates the drug plasma concentration with the administered dose. It considers three compartments: plasma compartment, shallow peripheral compartment and the deep peripheral compartment. Input variable: I (t) (in [mg/s]) is the infusion rate and output variable C_1 (in [mg/l]) is the propofol concentration.
- PD model: It relates the plasma concentration with the pharmacological end-effect. Input variable C_1 is the propofol concentration and output variable Eo (t) is the clinical hypnotic effect.
- PKPD model: It gives a drug-response relationship of the propofol. Input variable: I (t) (in [mg/s]) is the infusion rate and output variable Eo (t) is the clinical hypnotic effect.

The PK model is expressed using the state-space representation below.

$$\begin{bmatrix}\dot{C}_1\\ \dot{C}_2\\ \dot{C}_3\end{bmatrix} = \begin{bmatrix}-(k_{10}+k_{12}+k_{13}) & k_{12} & k_{13}\\ k_{21} & -k_{21} & 0\\ k_{31} & 0 & -k_{31}\end{bmatrix}\begin{bmatrix}C_1\\ C_2\\ C_3\end{bmatrix} + \begin{bmatrix}\frac{1}{V_1}\\ 0\\ 0\end{bmatrix} I$$

$$k_{10} = \frac{Cl_1}{V_1}, k_{12} = \frac{Cl_2}{V_1}, k_{21} = \frac{Cl_2}{V_2}, k_{13} = \frac{Cl_3}{V_1}, k_{31} = \frac{Cl_3}{V_3}$$

$C_1, C_2, and\ C_3$ are the propofol concentration in the plasma, fast peripheral compartment, and slow peripheral compartments respectively. $V_1, V_2, and\ V_3$ are the volumes for each compartment respectively. Cl_1 is the elimination clearance $Cl_2\ and\ Cl_3$ are inter-compartmental clearance respectively.

The PD model is expressed as $PD(s) = \frac{C_e\,(s)}{C_p\,(s)} = e^{-T_d s}\,\frac{k_d}{s+k_d}$

$C_p\,(t) = C_1\,(t) = 1,$

$T_d\ (in\ [s])is\ the\ transport\ delay\ and\ k_d\ (in\ [s^{-1}])is\ the\ rate\ of\ propofol\ distribution\ the\ plasma\ concentration\ and\ the\ brain.$

Section III

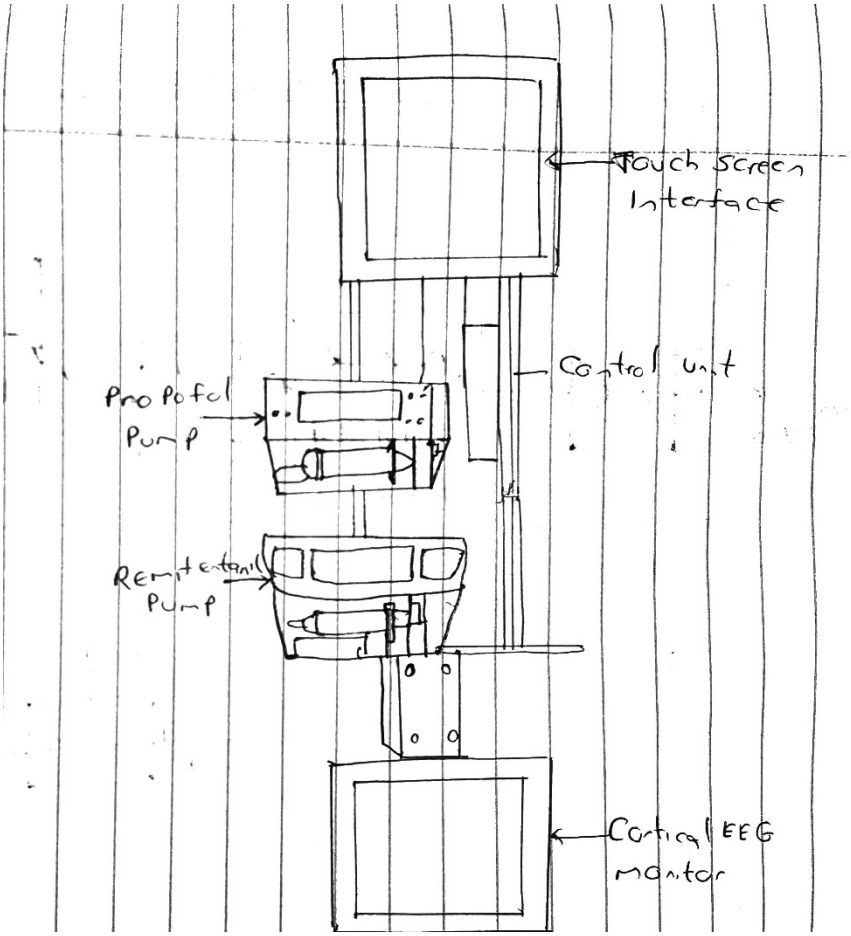

Figure 2: The iControl closed-loop anesthesia system

- I have read the PID section of the 'experience controls' app.
- PID controller design

$$G_{ff}(s) = k + \frac{k_i}{s}$$

$$G_c(s) = \frac{k_d N s}{s + N}$$

$$LBM = 0.3281W + 0.33929H - 29.5336 \; for \; male$$

Using W = 61 kg and H = 167 cm

$$LBM = 0.3281(61) + 0.33929(167) - 29.5336$$

$$LBM = 47.14193$$

$$k = 0.0243LBM, k_i = 0.000165LBM, k_d = 1.35LBM$$

$$k = 0.0243(47.14193), k_i = 0.000165(47.14193), k_d = 1.35(47.14193)$$

$$k = 1.1455, k_i = 0.0078, k_d = 63.6416$$

- The iControl system is used for the clinical evaluation of the controller design. It stabilizes the propofol delivery system using a robust PID controller.
- Integrator windup is a phenomenon that occurs due to the saturation of an actuator in a system (saturation of control signal) leading to large overshoots in the output response. In the case of the system discussed in this paper, it will lead to overdose.
- Equation [13] represents a non-linear system
- Constraint satisfaction ascertains overdose prevention.
- The ERG aims at adding the constraint-handling capability to the iControl system by generating auxiliary reference v (t) to contain the trajectories of the pre-stabilized propofol delivery system in a suitable invariant set.
- The ERG generates an output, which is used as the input or reference signal to the system. It is independent of the propofol delivery system.