Name: Fadare Rasaq Omotunde

Matric no: 16/ENG04/066

Course Title: Introduction to Biomedical Engineering (EEE 578)

Assignment Title: Analysis of “ERG scheme for closed-loop Anesthesia”.

1. **Title of paper**
   An Explicit Reference Governor Scheme for Closed-Loop Anesthesia
2. **Authors and affiliation**
   Mehdi Hosseinzadeh – Université Libre de Bruxelles, Brussels, Belgium
   Klaske van Heusden – The University of British Columbia, Vancouver, Canada
   Guy A. Dumont – The University of British Columbia, Vancouver, Canada
   Emanuele Garone – Université Libre de Bruxelles, Brussels, Belgium
3. **Structure of Paper**
   Abstract
   Introduction
   Modeling of the system
   Fig 1: PKPD model block diagram
   Control Architecture
   Pre-stabilizing the Propofol Delivery System
   Fig 2: The iControl closed-loop anesthesia system
   Fig 3: Block diagram of the propofol control system
   Enforcing Constraints Handling Capability
   Fig 4: Approximation error for different hypnosis levels.
   Results and Discussion
   Fig 5: The unconstrained simulated responses of the 44 patients
   Table 1: COMPARISON OF THE OBTAINED INDUCTION TIME.
   Conclusion
   Fig 6: The simulated responses of the 44 patients with the ERG scheme
   References
4. **Abbreviations**
   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

5. **Remarks**
    a. By defining approximation error as $e(t) = y(t) - \hat{} y(t)$, the value of $\delta 0$ can be determined as $\delta 0 = \max v \in [0,0.5] \sup t |e(t)|$.
    b. 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.
    c. To make sure that obtained matrix P_i is valid Lyapunov matrix for all patients, one possible way is to use Kharitonov theory, and replace the constraint $A^T P_i + P_i A \leq 0$ with the resulting four Kharitonov's based constraints.
6. **Abstract**

A constrained control scheme for the control of depth of hypnosis in clinical anesthesia while obeying all imposed clinical constraints.

7. **Introduction**
    a. Meaning of anesthesia and why it is used on people undergoing surgery, and manual feedback control is the current practice.
    b. The components of anesthesia, and the proposal of a propofol delivery system to control the depth of hypnosis.
    c. The phases of propofol hypnosis and the challenge of safely administering the drug during the induction phase and the proposed solutions.
    d. The overdosing problem as well as other safety issues can be solved by defining some suitable safety constraints.
    e. The use of Explicit Reference Governor (ERG) framework because it requires very limited computational capability.
    f. The organization of the rest of the paper as broken down into sections.

8. **Differences between figure 5 and 6**

Figure 5	**Figure 6**
The DOH% goes below 40% during the first 10 mins of the DOH|time plot	The DOH% does not go below 40% during the entire plot
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 Cp [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 Ce [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.
Induction Time mean ± STD^2 [min, max] = 3.11 ± 0.38 [2.53, 4.46]	Induction Time mean ± STD^2 [min, max] = 6.24 ± 7.51 [4.98, 8.96]

Table 1: comparison of Figure 5 & 6

Key results

a. The proposed ERG scheme provides results that guarantee constraint satisfaction.
b. A DOH of 50% was achieved for all patients.
c. The ERG scheme gives a slower induction time mean.
d. The ERG scheme automatically converges to the desired level of hypnosis using the auxiliary reference.

9. **Conclusion**
    a. I see the organization of the conclusion section.
    b. Yes, I understand the conclusion.
10. **Section II**

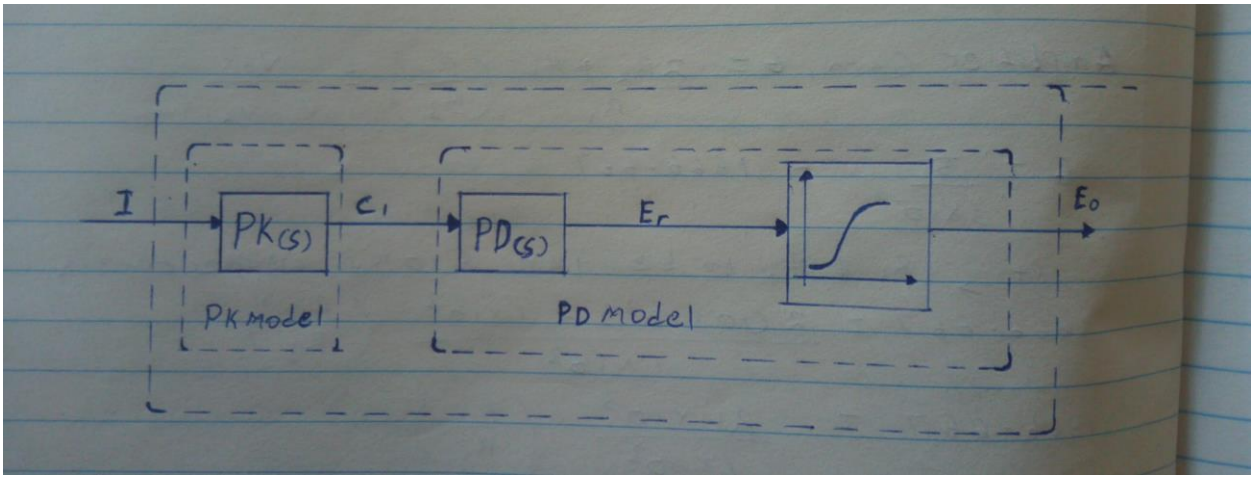

Figure 1: PKPD Model

• 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.

Output variable: C1 (in [mg/l]) is the propofol concentration.

• PD model: It relates the plasma concentration with the pharmacological end-effect.

Input variable: C1 is the propofol concentration.

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.

Output variable: Eo (t) is the clinical hypnotic effect.

PK Model equation.

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

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

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.

PD Model equation.

$$PD(s) = \frac{C_e(s)}{C_p(s)} = e^{-T_d s} \frac{k_d}{s + k_d}$$

Where Cp(t) = C1(t), and Td (in [s]) and kd (in [s−1]) are transport delay and rate of propofol distribution between the plasma concentration and the brain.

11. Section III

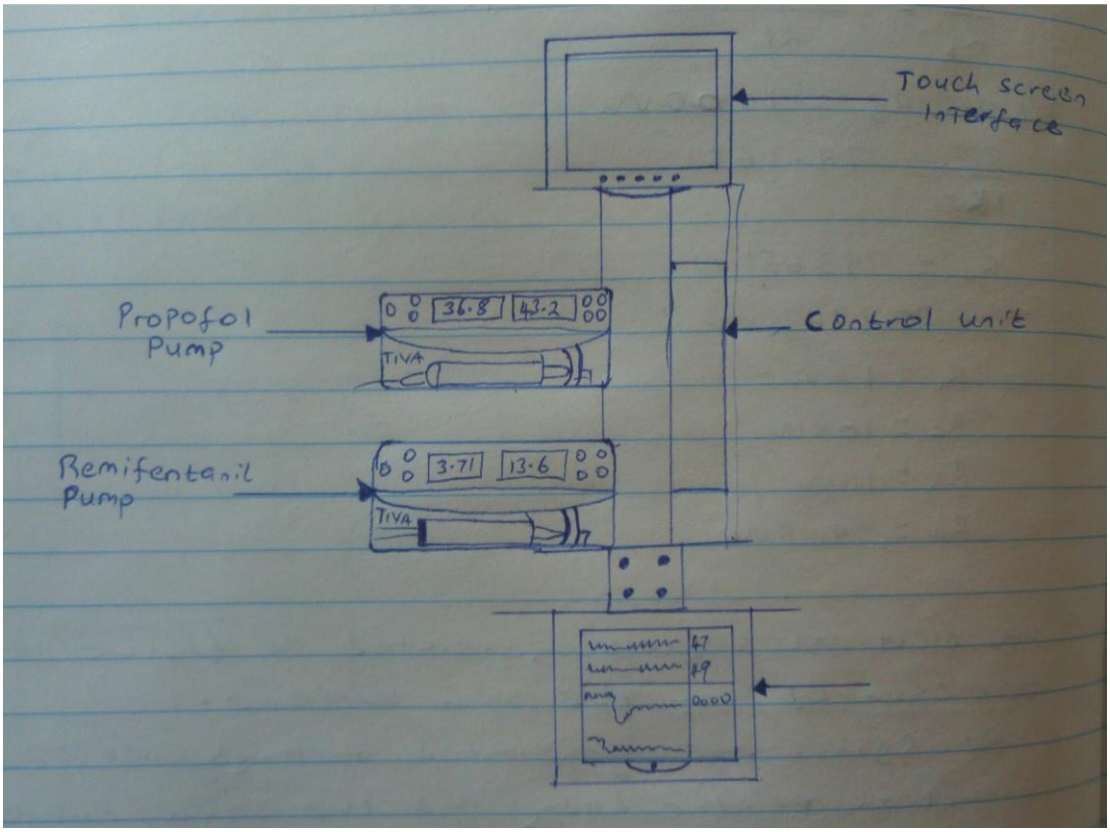

Figure 2: The iControl closed-loop anesthesia system

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

Design of a PID controller

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

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

$LBM = 0.3281.W + 0.33929.H - 29.5336$ – for male

$LBM = 0.29569.W + 0.41813.H - 43.2933$ – for female

Using W = 69Kg and H = 188cm for male LBM

$$LBM = (0.3281 \times 69) + (0.33929 \times 188) - 29.5336$$

$$LBM = 56.89182$$

$$k = 0.0243LBM, k_1 = 0.000165LBM, k_d = 1.35LBM$$

$$k = 1.382471226$$

$$k_i = 0.0093871503$$

$$k_d = 76.803957$$

- 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 refers to a scenario in a PID feedback controller where a large change in setpoint occurs and the integral term accumulates a significant error during the rise.
- Equation (13) represents a non-linear system.
- Constraints satisfaction prevents integral windup which in the case is overdose.
- The aim of the ERG framework is to determine an invariant set (in particular, a Lyapunov level set) that would contain the state trajectory if the currently auxiliary reference were to remain constant.
- The ERG generates a signal which is used as a reference signal to the system.