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

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Acronyms

1. ECC - European Control Conference
2. IEEE – Institute of Electrical and Electronics Engineers
3. FIRS MIS - Fonds de la Recherche Scientifique Mandat d’impulsion scientific (Incentive grant for scientific research)
4. SAAS - Service d’Automatique et d’Analyse des Syst`emes
5. ULB - Universit´e Libre de Bruxelles
6. UBC – University of British Columbia
7. ERG - Explicit Reference Governor
8. PK – PharmacoKinetic model
9. PD - PharmacoDynamic model
10. DOH – Depth of Hypnosis
11. TIVA - Total intravenous anesthesia
12. PID - proportional–integral–derivative
13. LBM - Lean Body Mass
14. DSM - Dynamic Safety Margin
15. NF - Navigation Field
16. KF - Kalman Filter

Remarks

1. By defining approximation error as *e*(*t*) = *y*(*t*)− ˆ*y*(*t*), the value of δ0 can be determined as δ0 = max*v*2[0,0.5]sup|(e)*t*|
2. Since the states of the system are not directly measured during the experiments, to determine the Lyapunov function *Vi*(·), *i* = 1, · · · ,7 an estimator is needed.
3. To make sure that obtained matrix *Pi* through (31) is valid Lyapunov matrix for all patients, one possible way is to use Kharitonov theory, and replace the constraint *ATPi*+*PiA* \_ 0 with the resulting four Kharitonov’s based constraints.

Abstract Summary

A closed form control scheme is an improved method for the control of the depth of hypnosis.

Introduction Summary

1. Current method of administering anaesthesia dosage is manual feedback control. Closed loop anaesthesia has gained much attention in recent years.
2. Anaesthesia consists of three components. Manipulating infusion rate of propofol to control DOH is proposed.
3. Propofol hypnosis can be divided into three temporal phases. The main challenge is to administer the drug without overdosing them.
4. The need to use constrained control schemes in closed-loop anesthesia to prevent patient’s overdosing has been highlighted.
5. The paper makes use of the recently introduced Explicit Reference Governor (ERG) framework.
6. Organisation of the paper: model description, proposed ERG scheme details, simulations and conclusion

Comparison between Figure 5 and 6

|  |  |
| --- | --- |
| Figure 5  | Figure 6 |
| The DOH percentage drops from 100% to below 40% in the first 10 minutes | The DOH percentage drops from 100% to above 40% in the first 10 minutes and experiences a steady rise. |
| The I (t) [ml/h] value is above 200 for most patients, reaching 400 in the first 20 minutes | Most patients have an I (t) [ml/h] approximately equal to 200 in the first 10 minutes |
| In the Cp [ug/m] plot, the transient region lasts 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 lasts for a time approximately less than 5 min.  | The transient period lasts for about 10 min. |

Key Results

The proposed ERG scheme guarantees 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

Yes, I understand the conclusion

Section II



PK model: It shows the relationship between 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 C1 (in [mg/l]) is the propofol concentration.

PD model: It shows the relationship between the plasma concentration with the pharmacological end-effect. Input variable C1 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.

$$\left[\begin{matrix}C\_{1}\\C\_{2}\\C\_{3}\end{matrix}\right]=\left|\begin{matrix}-(k\_{10}+k\_{12}+k\_{13})&k\_{12}&k\_{13}\\k\_{21}&-k\_{21}&0\\k\_{31}&0&-k\_{31}\end{matrix}\right|\left[\begin{matrix}C\_{1}\\C\_{2}\\C\_{3}\end{matrix}\right]+\left[\begin{matrix}\frac{1}{V\_{1}}\\0\\0\end{matrix}\right]I$$

$$k\_{10}= \frac{Cl\_{1}}{V\_{1}},k\_{12}= \frac{Cl\_{2}}{V\_{1}},k\_{21}= \frac{Cl\_{2}}{V\_{2}},k\_{13}= \frac{Cl\_{3}}{V\_{1}},k\_{31}= \frac{Cl\_{3}}{V\_{3}}$$

C1, C2 and C3 are the propofol concentration in the plasma, fast peripheral compartment, and slow peripheral compartments respectively. 𝑉1, 𝑉2 and 𝑉3 are the volumes for each compartment respectively. Cl1 is the elimination clearance Cl2 and Cl3 are inter-compartmental clearance respectively.

The PD model is expressed as $PD\left(s\right)= \frac{C\_{e}(s)}{C\_{p}(s)}= e^{-T\_{d}\left(s\right).\frac{k\_{d}}{s+ k\_{d}}}$

$C\_{p}\left(t\right)= C\_{1}\left(t\right)=1,$ Td (in [s]) and kd (in [s−1]) are transport delay and rate of propofol distribution between the plasma concentration and the brain.

SECTION III



I have read the PID section of the Experience Controls application.

$$G\_{ff}\left(s\right)=k+ \frac{k\_{i}}{s}$$

$$G\_{c}\left(s\right)= \frac{k\_{d}N\_{s}}{s+N}$$

$$LBM=0.3281×W+0.33929×H-29.5336 $$

Using W=71 kg H=173 cm for male

$$LBM=52.4587$$

$$k=0.0243×LBM, k\_{i}=0.000165×LBM, k\_{d}=1.35×LBM$$

$$k=1.2747, k\_{i}=8.6557×10^{-3}, k\_{d}=70.8192$$

• 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 occurs due to the saturation of an actuator in a system leading to large overshoots in the output response (overdose as used in the paper)

• Equation [13] represents a non-linear system

• Constraint satisfaction prevents overdose.

• The aim of the ERG is to determine an invariant set that would contain the state trajectory if the currently auxiliary reference were to remain constant.

• The ERG generates signal which is the input or reference signal to the system and is independent of the propofol delivery system.