Project: IEEE P802.15 Working Group for Wireless Personal Area Networks (WPANs)

Submission Title: [IG DEP An Adaptive Control System for Anesthesia during Surgery Operation Using Model Predictive Control of Anesthetic Effects]

Date Submitted: [6 March 2018]

Source: [Yoshitomo Sakuma1, Ryuji Kohno1,2,3] [1;Yokohama National University, 2;Centre for Wireless Communications(CWC), University of Oulu, 3;University of Oulu Research Institute Japan CWC-Nippon]
Address [1; 79-5 Tokiwadai, Hodogaya-ku, Yokohama, Japan 240-8501
2; Linnanmaa, P.O. Box 4500, FIN-90570 Oulu, Finland FI-90014
3; Yokohama Mitsui Bldg. 15F, 1-1-2 Takashima, Nishi-ku,Yokohama, Japan 220-0011]
Voice:[1; +81-45-339-4115, 2:+358-8-553-2849], FAX: [+81-45-338-1157],
Email:[1: kohno@ynu.ac.jp, 2: Ryuji.Kohno@oulu.fi, 3: ryuji.kohno@cwc-nippon.co.jp] Re: []

Re: []

Abstract: [As a use case of dependable wireless networks, an adaptive control system for anesthesia during surgery operation is introduced.]

Purpose: [information]

An Adaptive Control System for Anesthesia during Surgery Operation Using Model Predictive Control of Anesthetic Effects

Yoshitomo Sakuma*, Ryuji Kohno*†

＊Graduate School of Engineering Yokohama National University
† University of Oulu Research Institute Japan – CWC-Nippon, Co. Ltd.

Agenda

1. Background
2. System Model
3. Estimation scheme of the anesthetic effect using Recurrent Neural Network
4. An adaptive control scheme for anesthesia using Model Predictive Control
5. Conclusion and future works

1.1 Background

Present situation in medical practice:
Shortage of the Medical staff

Dependable Medicine using M2M & IoT：Ubiqutous Medicine and welfare

[Example] Total Intravenous Anesthesia(TIVA)

- Controlling anesthesia based vital sign
- Advantage: **Reduce burden of the anesthesiologist**

Problem

- Control scheme considering individual of each patient
- Control scheme based on constraints and demands

Yoshitomo Sakuma(YNU),
Ryuji Kohno(YNU/CWC-Nippon)

1.2 Objects of the control anesthesia

□ Limitation of the dosage

- **Single dosage**
- **Total dosage during surgery**

□ Demands about anesthetic effects

➢ **BIS(Bispectral Index)**

- **Maintain BIS into desired range during surgery**
- **Shortening introduction period**
- **Shortening required time to awake**

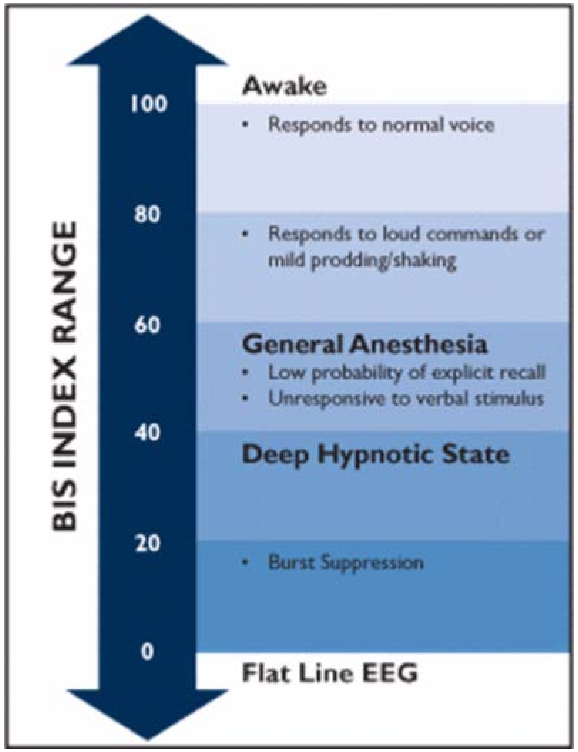
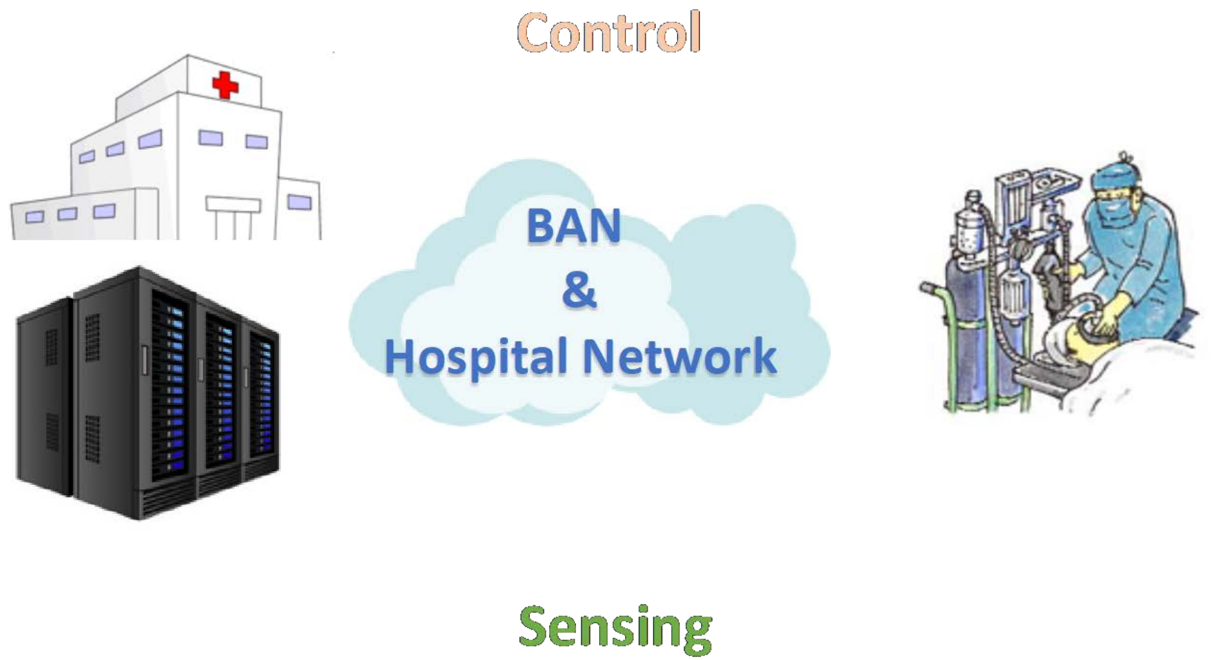


Fig.1 :BIS and anesthetic depth[1]

□ individual in each patient

- Estimate time variation of BIS considering individual

1.3 Overview of our proposal



Final object of our proposal:

Remote sensing & Dependable Closed Feedback Control of TIVA

- **Objects**

1. Reduce burden of the anesthesiologist
2. Remote management of multiple surgery room by one anesthesiologist

Agenda

1. Background
2. System Model
3. Estimation scheme of the anesthetic effect using Recurrent Neural Network
4. An adaptive control scheme for anesthesia using Model Predictive Control
5. Conclusion and future works

2.1. PK-PD Model

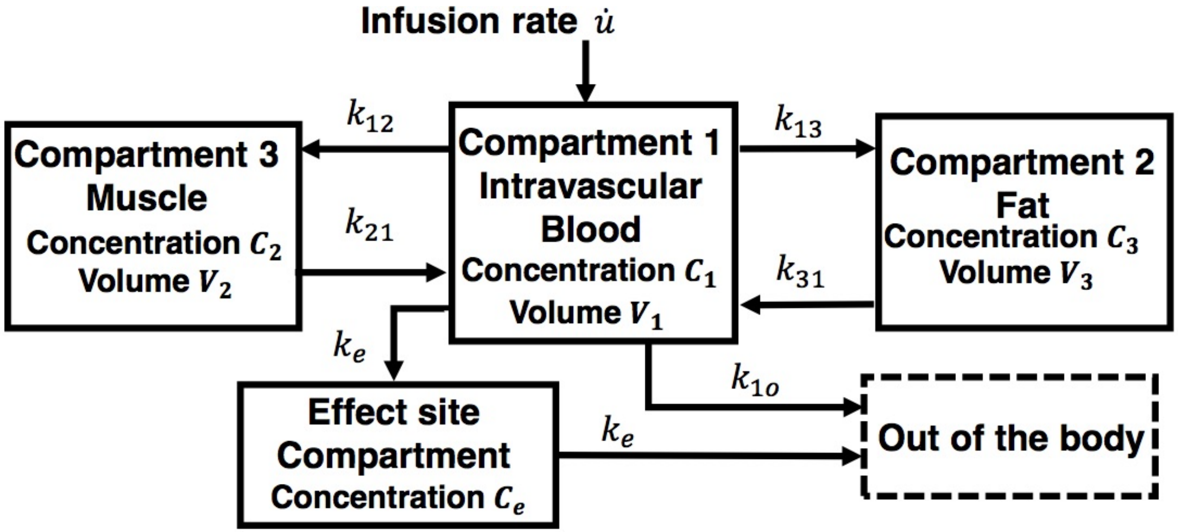


Fig. 2 : PK-PD Model of the Propofol® (*Schnider-Minto* Model)

- State equation of the PK-PD model(Desecrate time)

$$\mathbf{x}[k+1] = \mathbf{A_d}\mathbf{x}[k] + \mathbf{B_d}u[k]$$

$$\mathbf{x}[k] = [C_1[k], C_2[k], C_3[k], C_e[k]]^T$$

$$\mathbf{A_d} = \begin{bmatrix} -k_{1o} - k_{12} - k_{13} & k_{21} & k_{31} & 0 \\ k_{12} & -k_{21} & 0 & 0 \\ k_{13} & 0 & -k_{31} & 0 \\ k_e & 0 & 0 & -k_e \end{bmatrix}$$

$$\mathbf{A_d} = e^{\mathbf{A}T_s} = \mathcal{L}^{-1}[(s\mathbf{I} - \mathbf{A})^{-1}], \mathbf{B_d} = \int_0^{T_s} e^{\mathbf{A}(T_s - \tau)} d\tau \mathbf{B} \qquad \mathbf{B_d} = [\frac{1}{V_1 T_s}, 0, 0, 0]^T$$

2.2. Hill Equation

- Hill equation of the BIS value

$$BIS[k] = E_0\{1 - \frac{(C_e[k])^{\gamma}}{(C_e[k])^{\gamma} + EC_{50}{}^{\gamma}}\}$$

Table1: Average parameter of the Hill equation

Parameter	Average value(SD)
E_0	97.3(0.8)
EC_{50}[g/L]	$3.90\times10^{-3}(1.05\times10^{-3})$
γ	1.81(0.67)

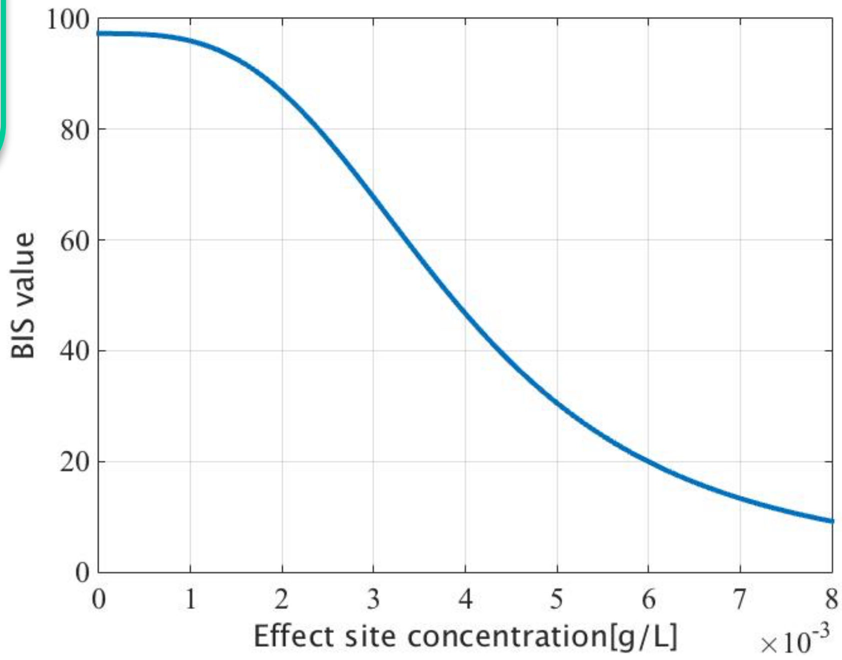


Fig. 3 : Numerical example of the Hill equation

2.3. Whole System model

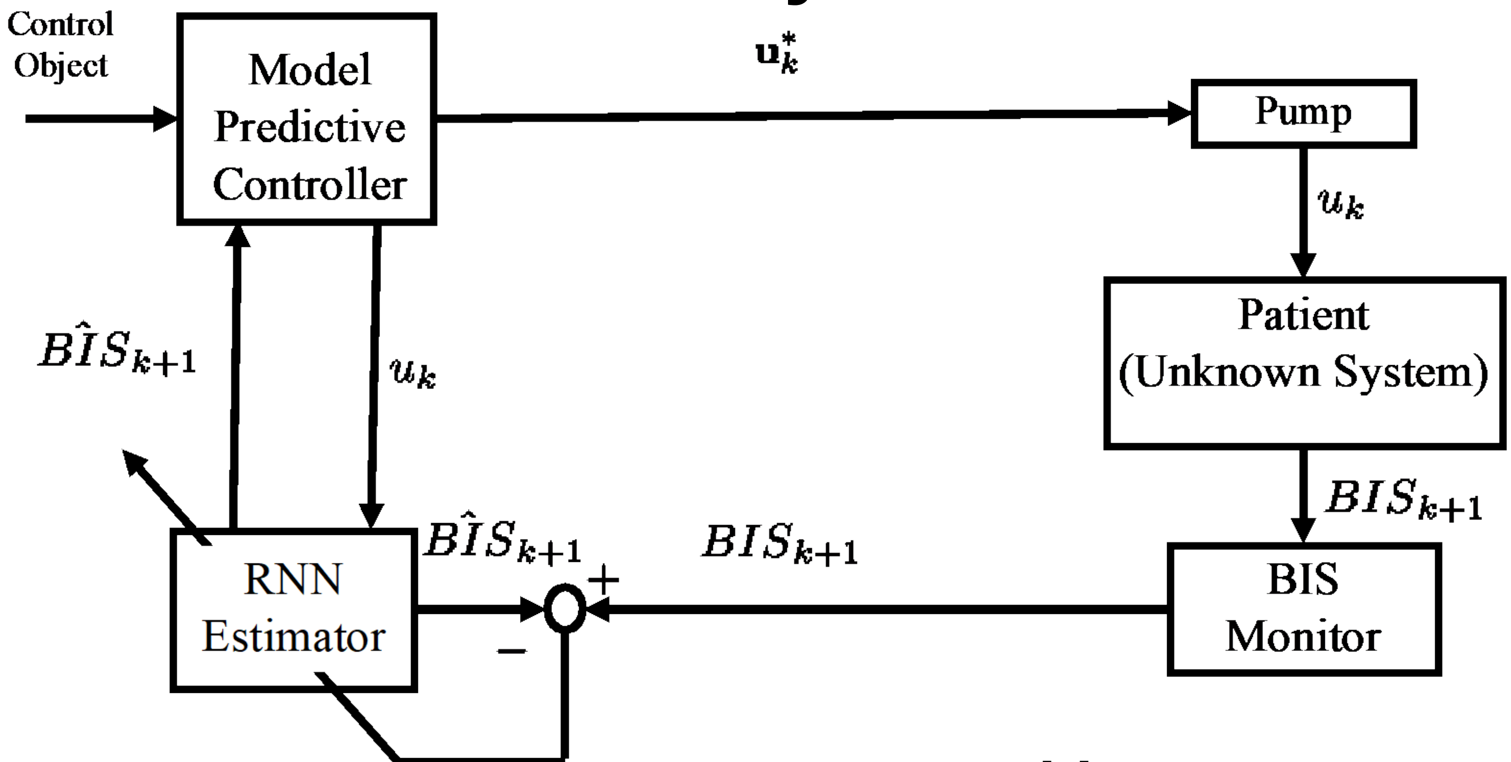


Fig. 4: System model

- Proposed system

1. **<u>Predict anesthetic effect</u> using Recurrent Neural Network**
2. **<u>Model Predictive</u> Control using RNN Estimator**
3. **<u>Update RNN Estimator</u> using sensed BIS value**

Agenda

1. Background
2. System Model
3. Estimation scheme of the anesthetic effect using Recurrent Neural Network
4. An adaptive control scheme for anesthesia using Model Predictive Control
5. Conclusion and future works

Yoshitomo Sakuma(YNU),
Ryuji Kohno(YNU/CWC-Nippon)

3.1 Overview of the estimation scheme

- **RNN: Reccurnt Neural Network**
- **Estimate time series variation**
- **Estimate nonlinear model**

Poposal of the anesthetic effect using RNN

[Problem]Structurer of RNN
Number of hidden layer ・ Units ・ Activation function

Decide structure of Neural Network based on theoretical analysis of Model equation

3.2 Theoretical analysis

- BIS value in the step time k+1

$$BIS_{k+1} = E_0\{1 - \frac{(C_{e,k+1})^\gamma}{(C_{e,k+1})^\gamma + EC_{50}^\gamma}\}$$

$$= E_0\{1 - \frac{1}{1 + (\frac{C_{e,k+1}}{EC_{50}})^{-\gamma}}\}$$

- Define y_{k+1}

$$y_{k+1} = \frac{1}{1 + (\frac{C_{e,k+1}}{EC_{50}})^{-\gamma}} = \frac{1}{1 + \exp(-\gamma \ln(\frac{C_{e,k+1}}{EC_{50}}))}$$

- Taylor's series approximation around $C_{e,k+1} = EC_{50}$

$$\ln(\frac{C_{e,k}}{EC_{50}}) \simeq \frac{1}{EC_{50}} C_{e,k} - 1$$

- **Approximated Hill equation**

$$BIS_k \simeq E_0(1 - \sigma(w_1 C_{e,k} + w_0))$$

Sigmoid function

$$\sigma(x) = \frac{1}{1 + \exp(-x)}, w_0 = -\gamma, w_1 = \frac{\gamma}{EC_{50}}$$

Yoshitomo Sakuma(YNU), Ryuji Kohno(YNU/CWC-Nippon)

3.2 Theoretical analysis(Cont'd)

- Numerical example: comparison between Hill equation and approximated equation

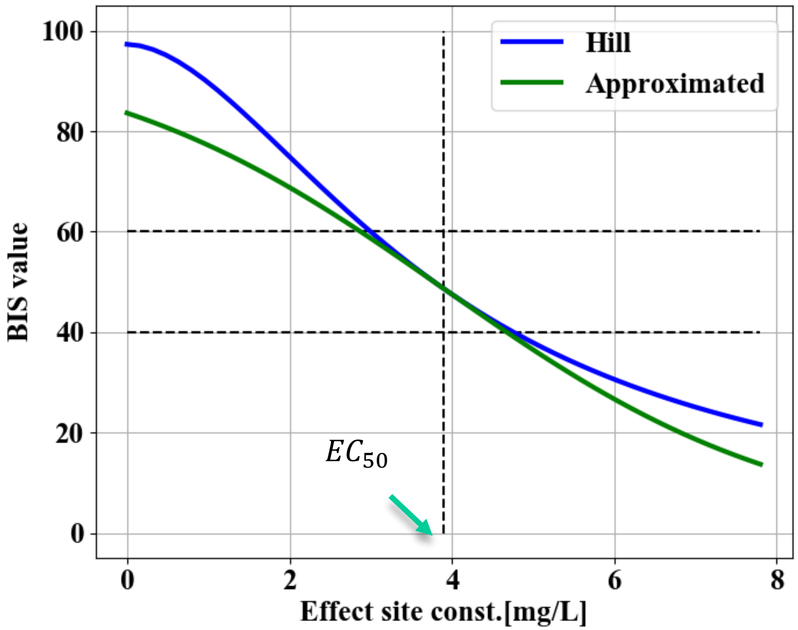


Fig. 5 : comparison between Hill equation and approximated equation

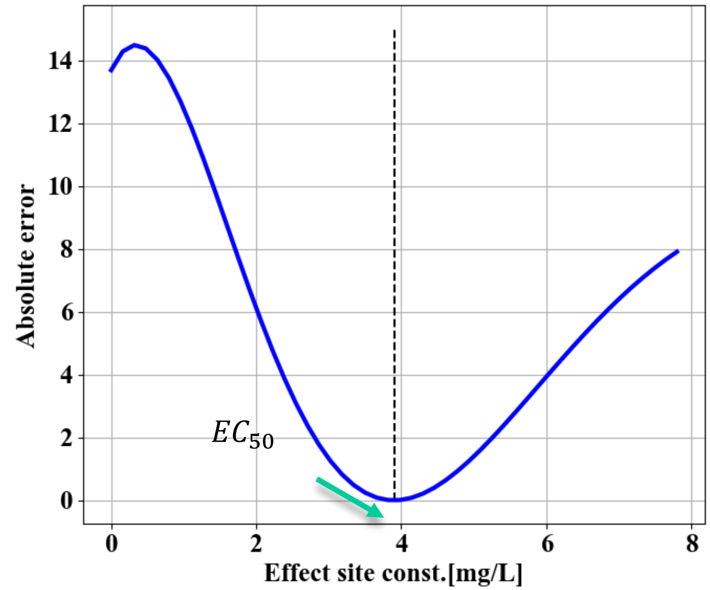


Fig. 6 : Absolute error between Hill equation and approximated equation

The nearer effect site concentration become around EC_{50}, the higher approximate accuracy became

Yoshitomo Sakuma(YNU), Ryuji Kohno(YNU/CWC-Nippon)

3.2 Theoretical analysis (Cont'd)

- Drug concentration of each compartments(from state equation)

$$\begin{bmatrix} C_{1,k+1} \\ C_{2,k+1} \\ C_{3,k+1} \\ C_{e,k+1} \end{bmatrix} = \mathbf{A_d} \begin{bmatrix} C_{1,k} \\ C_{2,k} \\ C_{3,k} \\ C_{e,k} \end{bmatrix} + \mathbf{B_d} u_k$$

- Summary of the Theoretical analysis

- **Approximated Hill equation**

$$BIS_k \simeq E_0(1 - \sigma(w_1 C_{e,k} + w_0))$$

Sigmoid function

✓ Time variation of the drug const.

$$\begin{bmatrix} C_{1,k+1} \\ C_{2,k+1} \\ C_{3,k+1} \\ C_{e,k+1} \end{bmatrix} = \mathbf{A_d} \begin{bmatrix} C_{1,k} \\ C_{2,k} \\ C_{3,k} \\ C_{e,k} \end{bmatrix} + \mathbf{B_d} u_k$$

Yoshitomo Sakuma(YNU), Ryuji Kohno(YNU/CWC-Nippon)

3.3. Proposal of Recurrent Neural Network (RNN)

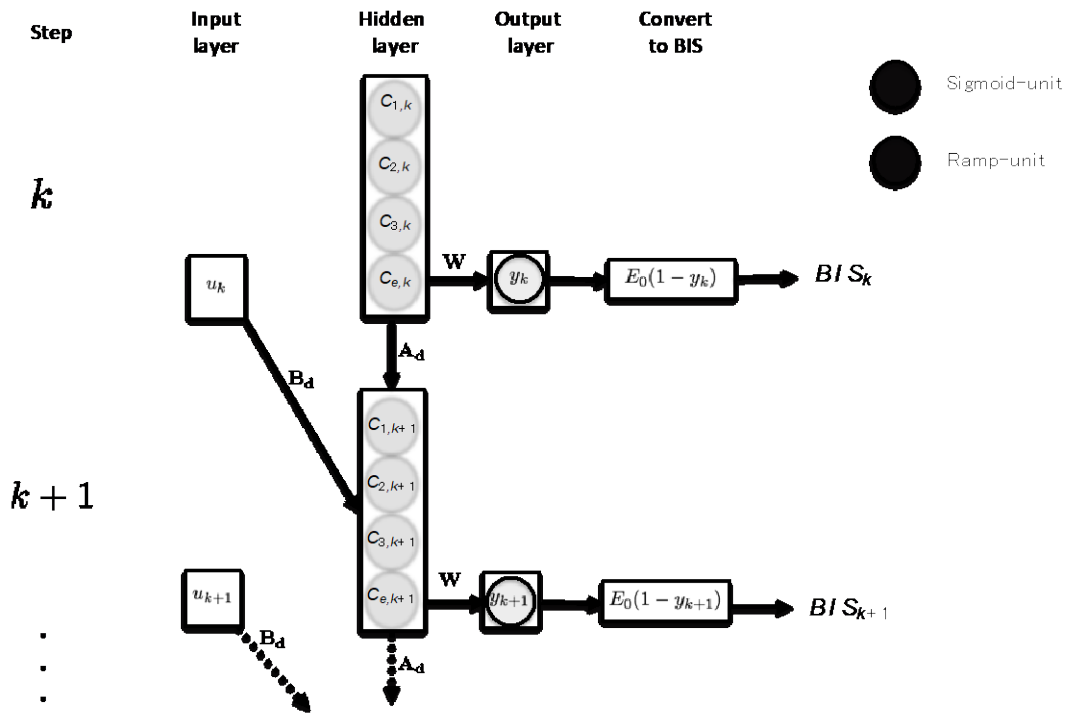


Fig. 7: Proposed RNN

- Proposed RNN: **Predict time series variation of BIS value by the dosing**
- ✓ Input : dosages in each step time
- ✓ Hidden layer: Drug concentration in each step time
- ✓ Output: Predicted BIS value

Agenda

1. Background
2. System Model
3. Estimation scheme of the anesthetic effect using Recurrent Neural Network
4. An adaptive control scheme for anesthesia using Model Predictive Control
5. Conclusion and future works

4.1 Optimization of dosages

- Control adaptively based on prediction by our proposed RNN

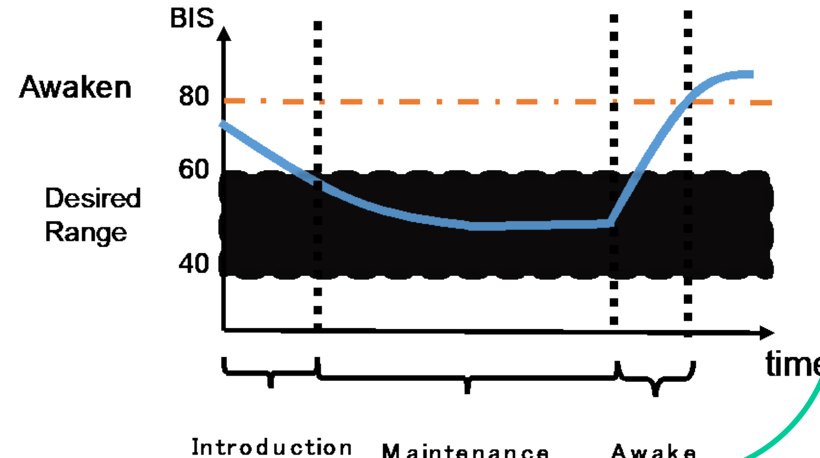
- Objective
  - **<u>Maintain BIS into desired range during surgery</u>**
  - **<u>Shortening introduction period</u>**
  - **<u>Shortening required time to awake</u>**

- Constraints: total dosage

$$0 \leq \sum_{i=0}^{K} u_{k+i} \leq U_{lim}$$

Single dosage

$$0 \leq u_{k+i} \leq u_{lim}$$



Yoshitomo Sakuma(YNU), Ryuji Kohno(YNU/CWC-Nippon)

4.2 Flowchart of our proposal

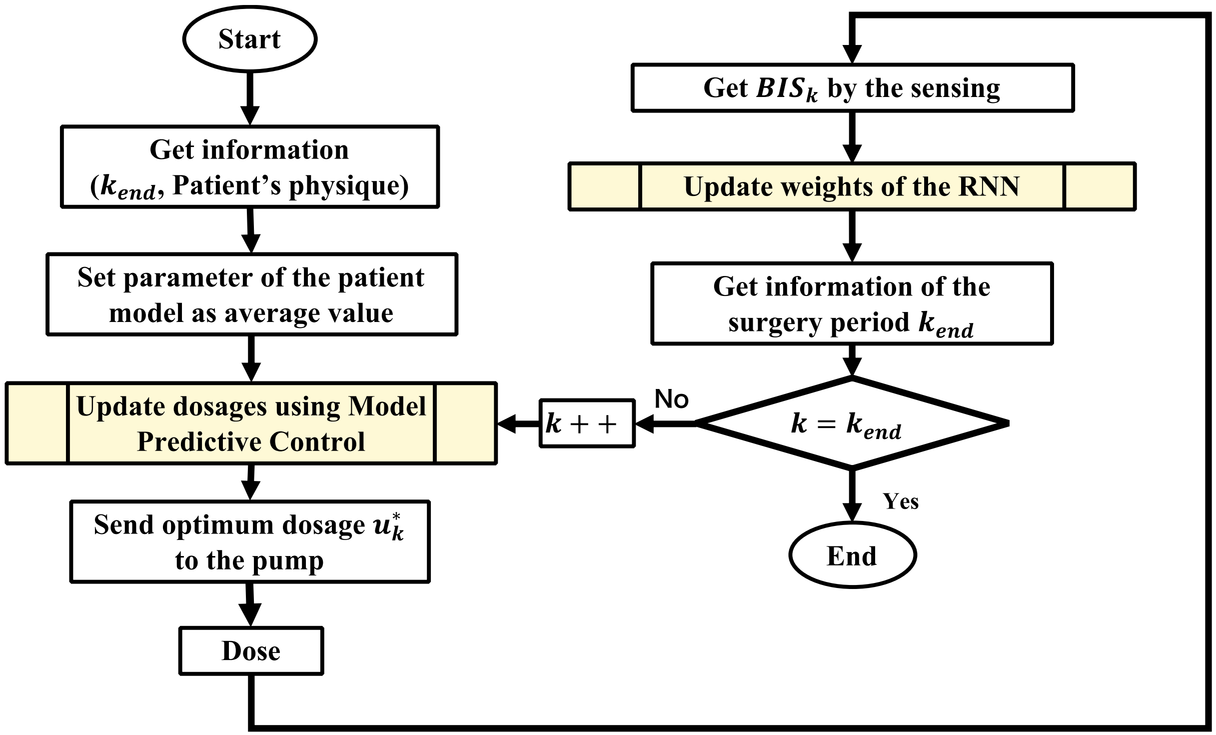


Fig. 8: Flowchart of our proposed scheme

1. **Predict anesthetic effect using Recurrent Neural Network**
2. **Model Predictive Control using RNN Estimator**
3. **Update RNN Estimator using sensed BIS value**

4.3 Evaluation by the computer simulation

- Evaluation index : BIS value in each cases

- Case1: Patient is sensitive to the Propofol
- Case2: The anesthesia doesn’t work readily to the patient
- Case3: Patient are hard to become wakefulness after the surgery

✓ Evaluate Introduction , Maintenance and required time to awake

✓ Bench marker : PID control[3]

Table 2: Parameter of the Hill equation in each cases

Case	EC_{50}[g/L]	γ
Case1	1.8×10^{-3}	3.15
Case2	6.0×10^{-3}	3.15
Case3	2.3×10^{-3}	0.80

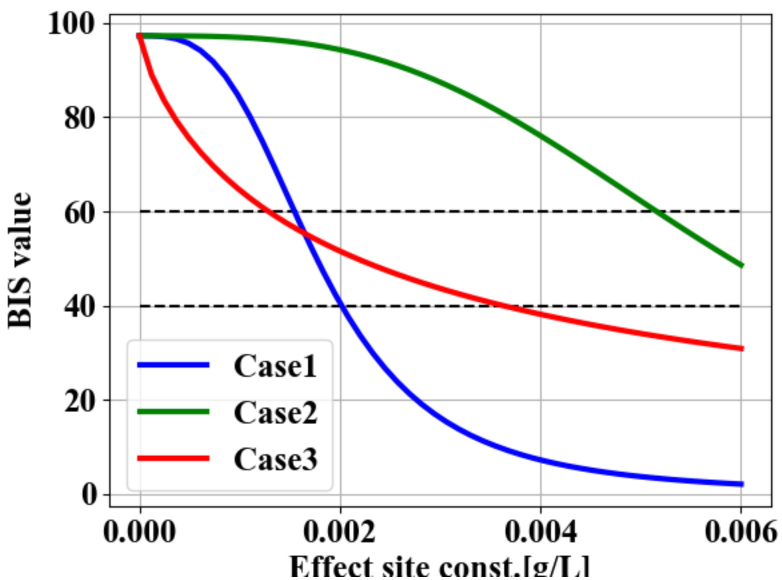


Fig. 10 :Hill equation in each cases

4.4 Simulation parameters

Table 3: PID gain in the bench maker[3]

Index	Value
P(Proportion) Gain	0.65
I(Integration) Gain	0.055
D(Differential) Gain	0.0

Table 4: Simulation parameters

Index	Value
Simulation time[min.]	180
Surgery period [min.]	120
Upper limit of the total dosage per hour[g]	0.84
Upper limit of the single dosage[mg]	0.9
Sampling interval of the control[sec.]	1.0

4.5 Simulation results

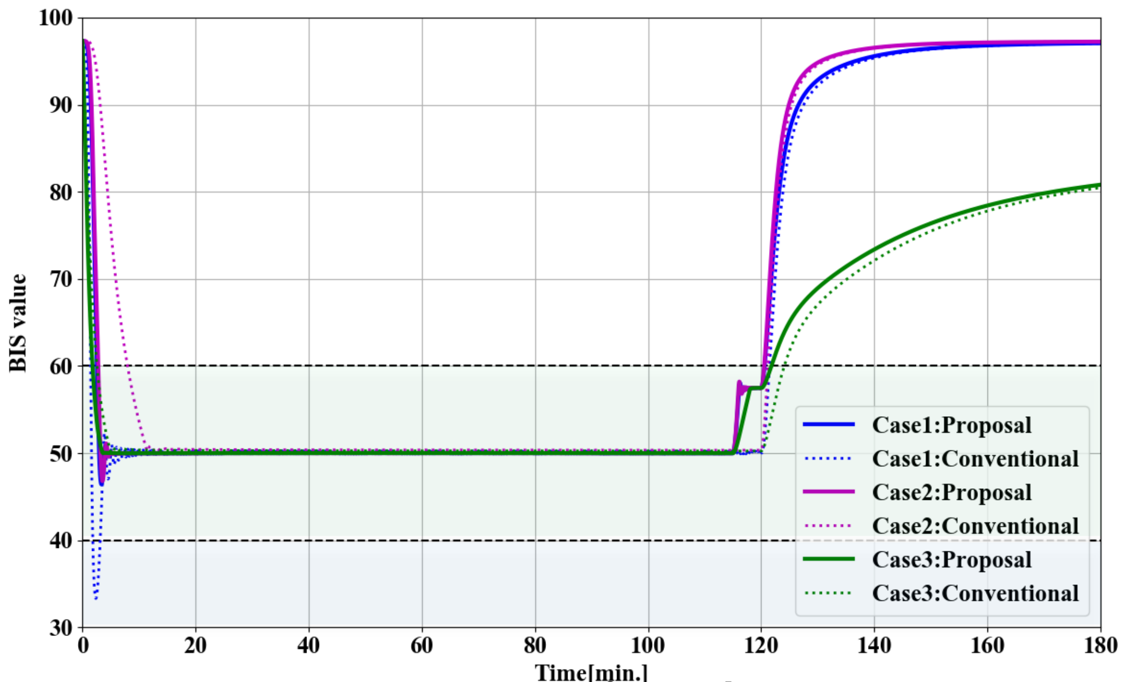


Fig.10: Time transition of BIS value

- **Conventional: BIS are undershot in the Case1**
- **Proposed: BIS value are maintained within the desired range**
- **Confirmed of the Model Predictive Control**

Yoshitomo Sakuma(YNU),
Ryuji Kohno(YNU/CWC-Nippon)

4.5 Simulation results(Cont'd)

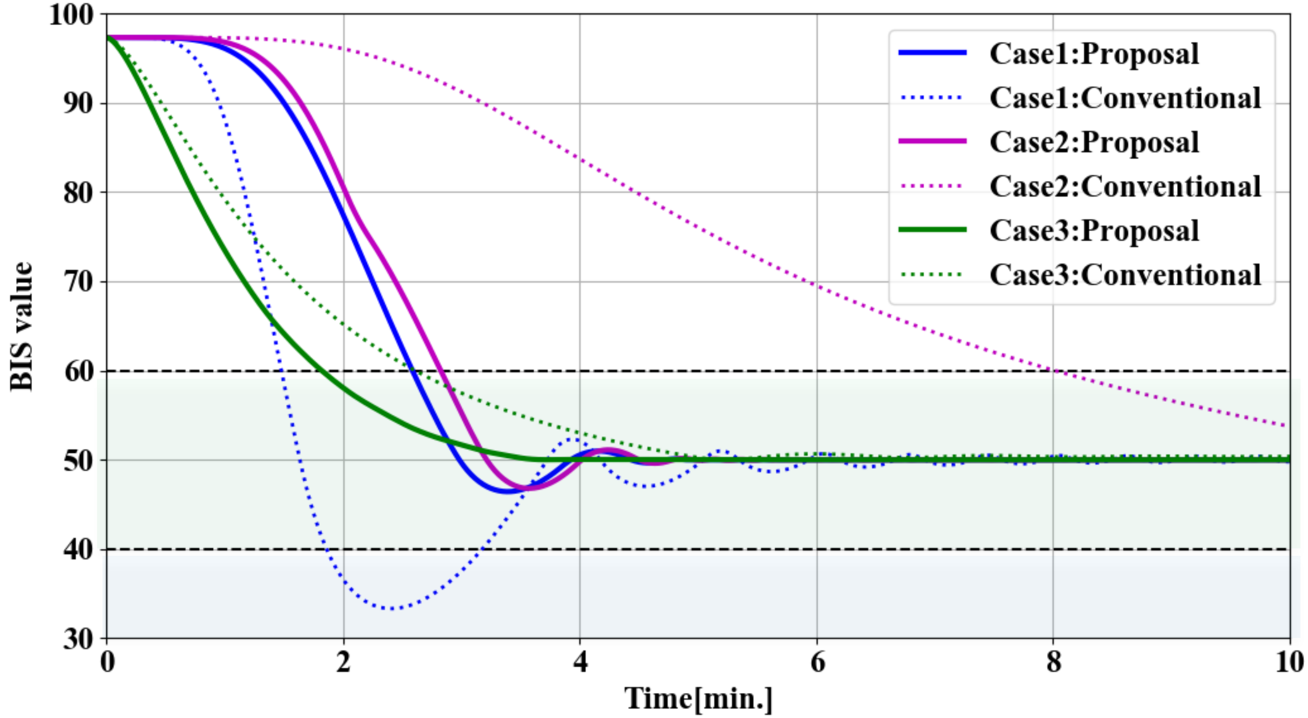


Fig. 11: Comparisons of the introduction time

- **Case2,3: Introduction time in the Proposal became shorter than conventional one**
- **Case1: BIS value in the conventional are overshoot**

4.5 Simulation results(Cont'd)

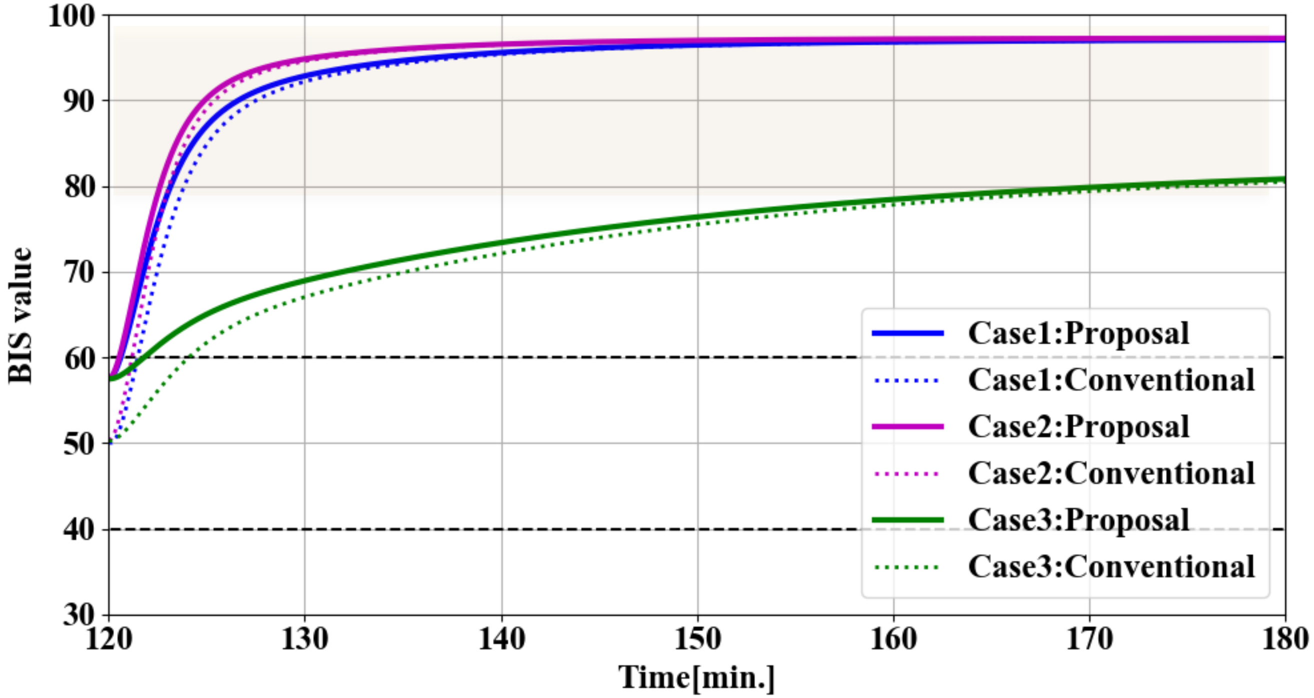


Fig. 12: Comparisons of the required time to awake

- **Required time to awake in the proposal are faster than those of conventional**

Agenda

1. Background
2. System Model
3. Estimation scheme of the anesthetic effect using Recurrent Neural Network
4. An adaptive control scheme for anesthesia using Model Predictive Control
5. Conclusion and future works

5. Conclusion and future works

- Conclusion

- **Proposed system: An adaptive control system for Anesthesia using Model Predictive Control**
- ✓ Proposal1: Estimation scheme of the anesthetic effect using Recurrent Neural Network
- ✓ Proposal2:An adaptive control scheme for anesthesia using Model Predictive Control

- Future Works

1. Performance evaluation considering error and delay of the sensing and control data
2. Proposal of the communication protocol to manage multiple surgery room by one system
3. Study about control scheme using multiple vital sensor and multiple drugs
4. Application proposal to the similar case: control insulin pump for diabetic

References

[1] DIPRIVAN(R) (Propofol) INJECTABLE EMULSION, USP, (http://www.accessdata.fda.gov/drugsatfda docs/label/2014/019627s062lbl.pdf).

[2] Bispectral Index Monitor An Evidence-Based Analysis, Ontario Health Technology Assessment Series 2004, Vol. 4, No. 9, 2004.

[3] J. A. Mendez et al. ”Adaptive computer control of anesthesia in humans” ,Computer Methods in Biomechanics and Biomedical Engineering, Vol. 12, No. 6, December 2009, pp. 727-734

[4] M.M.R.F.Struys, T.D.Smet, J.B.Glen, H.E.M.Vereecke, A.R. Absalom, T.W.Schnider, The History of Target-Controlled Infusion, Anesthesia & Analgesia, Vol.122, Issue 1, pp.56-69, 2016.

[5] Y.Sawaguchi,E.Furutani,G.Shirakami,M.Araki,and K.Fukuda, A Model-Predictive Hypnosis Control System Under Total Intravenous Anesthesita, IEEE TRANSACTIONS on Biomedical Enginieering, Vol.55, No.3, pp-874-887, 2008.

[6] I.N.Nascu, A.Krieger, C.M Ionescu, and E.N.Pistikopoulos, Advanced Model-Based Control Studies for the Induction and Maintenance of Intravenous Anaesthesia, IEEE TRANSACTIONS on Biomedical Engineering, Vol.62, No.3, 2015.

[7] T.W.Schnider,C.F.Minto,P.L.Gambus,C.Andersen,D.B.Goodale,and S.L.Shafer, The Influence of Method of Administration and Covariates on the Pharmacokinetics of Propofol in Adult Volunteers, Anesthesiology, Ver.88, No.5 , pp.1170-1182, 1998