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

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

Purpose: [information]

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

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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: Ubiquitous 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
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

- Individual in each patient
  - Estimate time variation of BIS considering individual

Fig.1: BIS and anesthetic depth[1]
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

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2.1. PK-PD Model

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

\[
x[k + 1] = A_d x[k] + B_d u[k]
\]

\[
x[k] = [C_1[k], C_2[k], C_3[k], C_e[k]]^T
\]

\[
A_d = e^{A_d T_s} = \mathcal{L}^{-1}[(sI - A)^{-1}],
B_d = \int_0^{T_s} e^{A_d(T_s - \tau)} d\tau B
\]

\[
B_d = \left[ \frac{1}{V_1 T_s}, 0, 0, 0 \right]^T
\]

Fig. 2: PK-PD Model of the Propofol\textsuperscript{®} (Schnider-Minto Model)
2.2. Hill Equation

Hill equation of the BIS value

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

Table 1: Average parameter of the Hill equation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Average value (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( E_0 )</td>
<td>97.3 (0.8)</td>
</tr>
<tr>
<td>( EC_{50} ) [g/L]</td>
<td>3.90 \times 10^{-3} (1.05 \times 10^{-3})</td>
</tr>
<tr>
<td>( \gamma )</td>
<td>1.81 (0.67)</td>
</tr>
</tbody>
</table>

Fig. 3: Numerical example of the Hill equation
2.3. Whole System model

- Predict anesthetic effect using Recurrent Neural Network
- Model Predictive Control using RNN Estimator
- Update RNN Estimator using sensed BIS value

Fig. 4: System model
Agenda

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3.1 Overview of the estimation scheme

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

**Proposal of the anesthetic effect using RNN**

[Problem] Structure 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 $k+1$
  \[ BIS_{k+1} = E_0 \left\{ 1 - \frac{(C_{e,k+1})^\gamma}{(C_{e,k+1})^\gamma + EC_{50}^\gamma} \right\} = E_0 \left\{ 1 - \frac{1}{1 + \left( \frac{C_{e,k+1}}{EC_{50}} \right)^{-\gamma}} \right\} \]

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

- Taylor's series approximation around $C_{e,k+1} = EC_{50}$
  \[ \ln(\frac{C_{e,k}}{EC_{50}}) \approx \frac{1}{EC_{50}} C_{e,k} - 1 \]

- Approximated Hill equation
  \[ BIS_k \approx E_0 (1 - \sigma(w_1 C_{e,k} + w_0)) \]  
  Sigmoid function
  \[ \sigma(x) = \frac{1}{1 + \exp(-x)}, w_0 = -\gamma, w_1 = \frac{\gamma}{EC_{50}} \]
3.2 Theoretical analysis (Cont’d)

- Numerical example: comparison between Hill equation and approximated equation

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

Fig. 5: comparison between Hill equation and approximated equation

Fig. 6: Absolute error between Hill equation and approximated equation
3.2 Theoretical analysis (Cont’d)

- Drug concentration of each compartments (from state equation)

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

- 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.

\[
\begin{bmatrix}
C_{1,k+1} \\
C_{2,k+1} \\
C_{3,k+1} \\
C_{e,k+1}
\end{bmatrix} = A_d \begin{bmatrix}
C_{1,k} \\
C_{2,k} \\
C_{3,k} \\
C_{e,k}
\end{bmatrix} + B_d u_k
\]
3.3. Proposal of Recurrent Neural Network (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
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4.1 Optimization of dosages

➢ Control adaptively based on prediction by our proposed RNN

Objective

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

Constraints:

- Total dosage: $0 \leq \sum_{i=0}^{K} u_{k+i} \leq U_{lim}$
- Single dosage: $0 \leq u_{k+i} \leq u_{lim}$

Diagram:

- BIS levels: 40, 60, 80
- Time intervals: Introduction, Maintenance, Awake
- Desired Range: BIS levels
- Awaken: Transition from desired range

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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

- Case 1: Patient is sensitive to the Propofol
- Case 2: The anesthesia doesn’t work readily to the patient
- Case 3: 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

<table>
<thead>
<tr>
<th>Case</th>
<th>EC_{50} [g/L]</th>
<th>( \gamma )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case1</td>
<td>1.8 \times 10^{-3}</td>
<td>3.15</td>
</tr>
<tr>
<td>Case2</td>
<td>6.0 \times 10^{-3}</td>
<td>3.15</td>
</tr>
<tr>
<td>Case3</td>
<td>2.3 \times 10^{-3}</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Fig. 10: Hill equation in each cases
4.4 Simulation parameters

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

<table>
<thead>
<tr>
<th>Index</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(Proportion) Gain</td>
<td>0.65</td>
</tr>
<tr>
<td>I(Integration) Gain</td>
<td>0.055</td>
</tr>
<tr>
<td>D(Differential) Gain</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Table 4: Simulation parameters**

<table>
<thead>
<tr>
<th>Index</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simulation time [min.]</td>
<td>180</td>
</tr>
<tr>
<td>Surgery period [min.]</td>
<td>120</td>
</tr>
<tr>
<td>Upper limit of the total dosage per hour[g]</td>
<td>0.84</td>
</tr>
<tr>
<td>Upper limit of the single dosage[mg]</td>
<td>0.9</td>
</tr>
<tr>
<td>Sampling interval of the control[sec.]</td>
<td>1.0</td>
</tr>
</tbody>
</table>
4.5 Simulation results

- Conventional: BIS are undershot in the Case1
- Proposed: BIS value are maintained within the desired range
- Confirmed of the Model Predictive Control
Fig. 11: Comparisons of the introduction time

- Case 2,3: Introduction time in the Proposal became shorter than conventional one
- Case 1: 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
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5. Conclusion and future works

Conclusion

Proposed system: An adaptive control system for Anesthesia using Model Predictive Control

- Proposal 1: Estimation scheme of the anesthetic effect using Recurrent Neural Network
- Proposal 2: 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


