Robust and Adaptive Control Methods for Patient Response to Anesthesia

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Outline

• **Introduction:** *the anesthesia control problem*

• **Modeling the Patient Response**

• **Robust and Adaptive Control Methods**

• **Control Simulation Results**
Problem Statement
Problem Statement
Anesthesia Control during Surgery

Anesthesiologist:
- Administers sedatives, analgesics, and neuromuscular blockades
- maintains ventilation parameters
- monitors cardiovascular and respiratory functions
- monitors blood chemistry:
  *blood-sugar levels, electrolyte concentrations, gas concentrations, coagulation parameters...*

Goal: automate/optimize delivery and control of anesthesia
Problem Statement
Anesthesia Control during Surgery

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Anesthesia Control during Surgery

Model-based feedback control requirements:
- means of sensing levels of sedation, analgesia, relaxation/neuromuscular blockade
- mathematical models of patient response

Goal: automate/optimize delivery and control of anesthesia
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Anesthesia Control during Surgery

Sensing signals:

- **Neuromuscular block:** Surface electrode or piezoelectric measurements of response to electrical stimuli; typically uncoupled from sedation effects

- **Analgesia:** No standardized or widely accepted means of measuring extent of pain relief; appears to be correlated with sedation

- **Sedation:** Spectral entropies (GE), wavelet analysis methods, **Bispectral Index (BIS)**

Derived from EEG using combination of higher order spectra and other indicators such as spectral edge and median frequencies; reveals synchrony of cortical brain signals characterizing unconsciousness (Covidien)
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Model-based feedback control:

- **Inputs**: inhalational sedative Isoflurane and clinical stimuli

- **Outputs**: vital signs Heart Rate (HR) and Mean Arterial Pressure (MAP); BIS

- **BIS values range from 0 to 100**:
  - 100 – completely alert
  - 60 – moderately sedated
  - 40 – deeply sedated

**Control Goals:**

- *Track BIS reference trajectory signal while maintaining HR and MAP in healthy ranges*

- *Must be adaptive and robust to patient variability*
Patient Response Models
Modeling Patient Response
Compartment Models

- **Pharmacokinetic (PK) models:** Empirically derived linear ODEs
- **Pharmacodynamic (PD) models:** Static nonlinearity (e.g., sigmoidal function) fit to individual patient data
- **Nonlinear SISO Grey-Box Models**
Modeling Patient Response
Clinical trial data

Input Data

Output Data

P. S. Glass, M. J. Bloom, et. al, Anesthesiology, 1997
Modeling Patient Response

Linear Parameter Varying (LPV) Models: Subspace Identification used to construct models for individual patients from clinical data

- **Piecewise-linear models**
  - Awake and Sedated patient states
  - Low-order (3rd to 5th order per patient state)

\[
x_i(k + 1) = A_i x_i(k) + B_i u(k) + w(k) \\
y(k) = C_i x_i(k) + D_i u(k) + v(k) \\
\text{where } i = A \text{ (Alert)}, S \text{ (Sedated)}
\]

- **LPV models**
  - Gain-scheduled with respect to BIS value

\[
A(\delta) = \frac{\delta(\delta-1)}{2} A_A + \frac{\delta+1}{2} A_S \\
B(\delta) = \frac{\delta(\delta-1)}{2} B_A + \frac{\delta+1}{2} B_S \\
C(\delta) = \frac{\delta(\delta-1)}{2} A_A + \frac{\delta+1}{2} A_S \\
G(\delta(t), \lambda) = C(\delta) \left( \lambda I - A(\delta) \right)^{-1} B(\delta)
\]

with \( \delta(t) = 1 - \frac{2}{1+\exp(\frac{\eta*(70-BIS(t))}{\eta})} \)
Modeling Patient Response
LPV model simulation results

Patient 1 data and models:
- Measured data
- Reduced order LPV model
- Compartment model

Modeling Patient Response

- $L_1$-Adaptive output feedback control design method based on standard transfer function models
  - Model structure
    \[ y(s) = G(s) (u(s) + d(s)) \]
  - $G(s)$ is LTI system transfer function; assumed strictly proper
  - $y(t)$ is measured BIS reading
  - $u(t)$ is input anesthesia flow \((\text{percentage concentration of volume})\)
  - $d(t)$ is time-varying disturbance \((\text{may be a function of y(t), assumed Lipshitz with constant L})\)

- State-Space Identification methods used to construct 4th order realizations \(\{A, B, C\}:\)
  \[ G(s) = C(sI - A)^{-1}B \]
LPV and $\mathcal{L}_1$-Adaptive Control
LPV Controller Synthesis

Find R, S, X and Y:

\[
N_R^T \begin{bmatrix}
ARA^T - R & ARC_1^T & B_1 \\
C_1RA^T & C_1RC_1^T - Y & D_{11}^T \\
B_1^T & D_{11}^T - X
\end{bmatrix} N_R < 0
\]

\[
N_S^T \begin{bmatrix}
A^TSB_1 & C_1^T \\
C_1^T & D_{11}^T
\end{bmatrix} N_S < 0
\]

\[
\begin{bmatrix}
R & I \\
I & S
\end{bmatrix} \geq 0 \quad \text{and} \quad \begin{bmatrix}
X & I \\
I & Y
\end{bmatrix} \geq 0
\]

\[
\text{rank}(I - RS) \leq k
\]

**L$_1$-Adaptive Control Methods**

**Overview**

- **Goal:** track a given reference input $r(t)$ under modeling uncertainties

- ** Guarantee:** asymptotic tracking with uniformly bounded system inputs and outputs

- *Prevents high frequency oscillations in control channel, and parameter drifts*
\( \mathcal{L}_1 \)-Adaptive Control Methods

Overview

• Design controller such that output \( y(t) \) tracks reference input \( r(t) \) according to some desired model \( M(s) \): \( y(s) \approx M(s)r(s) \)

• Rewrite original input-output relationship using reference model:

\[
y(s) = M(s) (u(s) + \sigma(s)), \quad \text{where} \]
\[
\sigma(s) = \frac{(G(s) - M(s))u(s) + G(s)d(s)}{M(s)}
\]

• Example: \( M(s) = \frac{m}{s + m} \)
Consider the closed-loop reference system:

\[
\begin{align*}
    y_{ref}(s) &= M(s) \left( u_{ref}(s) + \sigma_{ref}(s) \right) \\
    \sigma_{ref} &= \frac{(G(s) - M(s))u_{ref} + G(s)d(s)}{M(s)} \\
    u_{ref} &= C(s)(r(s) - \sigma_{ref}(s)), \text{ with} \\
    C(s) &= \frac{w}{s+w}
\end{align*}
\]

- \(C(s)\) is low-pass filter used to attenuate high frequency uncertainty in control channel, and \(w\) is a design parameter
- \(r(s)\) is reference input
\(L_1\)-Adaptive Control Methods

Design Architecture

Enforce the following stability condition:

Select \(C(s)\) and \(M(s)\) such that

\[
H(s) = \frac{G(s)M(s)}{(C(s)G(s) + (1-C(s)))M(s)}
\]

is BIBO stable, and

\[
L \cdot \|H(s)(1-C(s))\|_{L_1} < 1
\]

Guarantees BIBO stability of closed-loop reference system
The $\mathcal{L}_1$-Adaptive Controller consists of

- **Output Predictor:**
  \[
  \frac{d\tilde{y}(t)}{dt} = -m\tilde{y}(t) + m(u(t) + \tilde{\sigma}(t)), \quad \tilde{y}(0) = 0
  \]

- **Parameter Adaptation Law:**
  \[
  \frac{d\tilde{\sigma}(t)}{dt} = \Gamma \cdot \Pi(\tilde{\sigma}(t), -mP(\tilde{y} - y)), \quad \tilde{\sigma}(0) = 0
  \]

  where $\Pi(\cdot, \cdot)$ is least-squares type projection operator, $\Gamma$ is adaptation rate, $P > 0$ is arbitrary, and $|\tilde{\sigma}(t)| \leq \Delta$ is projection bound

- **Feedback Control Law:** $u(s) = C(s)(r(s) - \tilde{\sigma}(s))$
It can be shown that for all $t \geq 0$, the $\mathcal{L}_1$-Adaptive Output Feedback Controller guarantees uniform boundedness of the tracking error, i.e.,

$$
\|\tilde{y}(t) - y(t)\|_{\mathcal{L}_\infty} \leq \frac{k}{\sqrt{\Gamma P}}
$$

where $k$ is a (computable) constant
Design and Simulation Results
LPV Design and Simulation Results

BIS reference tracking

Patient 1 LPV controller, patient 1 model:

- Reference signal $r(t)$ constructed to emulate original BIS profiles in clinical data
- BIS signal should track $r(t)$
- MAP within 60-110mmHg
LPV Design and Simulation Results

BIS reference tracking

Patient 1 model: Patient 1 LPV controller and Patient 3 LPV controller

\( \mathcal{L}_1 \)-Adaptive Design and Simulation Results

BIS Tracking – No Disturbances

Patient 1 adaptive output feedback control:

- **design parameters**
  - **initial settings:** \( P = 1, \Delta = 100, \Gamma = 50,000 \)
  - **filters:** \( M(s) = \frac{1}{30s+1}, \quad C(s) = \frac{0.001}{s+0.001} \)
**$\mathcal{L}_1$-Adaptive Design and Simulation Results**

**BIS Tracking – No Disturbances**

Patient 5 adaptive output feedback control:

- **design parameters**
  - *initial settings*: $P = 1$, $\Delta = 100$, $\Gamma = 50,000$
  - *filters*: $M(s) = \frac{1}{30s+1}$, $C(s) = \frac{0.002}{s+0.002}$
$\mathcal{L}_1$-Adaptive Design and Simulation Results

BIS Tracking – Robustness to Patient Variability

Patient 1 controller used on Patient 2, 3, 5, 6 and 7 models
$L_1$-Adaptive Design and Simulation Results

BIS Tracking – Robustness to Patient Variability

Patient 1 controller on Patient 2, 3, 5, 6 and 7 models: *Performance Analysis*

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual Tracking Error</td>
<td>0.0019</td>
<td>0.0062</td>
<td>0.0022</td>
<td>0.0016</td>
<td>0.0036</td>
<td>0.0064</td>
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</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane Use (liters)</td>
<td>2.40</td>
<td>2.86</td>
<td>2.23</td>
<td>2.40</td>
<td>2.29</td>
<td>2.15</td>
</tr>
</tbody>
</table>

Previous control yielded residual tracking errors in the 5-10% range, and average total isoflurane consumption of approximately 3 liters.
$\mathcal{L}_1$-Adaptive Design and Simulation Results

MIMO Control – BIS Tracking and MAP Performance with Disturbances

Patient 1 Multivariable controller – 2 inputs, 2 outputs:

MAP required to be maintained within 60-110 mmHg range

$\mathcal{L}_1$ - Adaptive Controller Designs

Open-loop/Closed-loop mode

$u_a$

Filter mode

$\tau_u$

$\Delta_h$

$C_c(s)c_m^T(sI-A_m)^{-1}$

$C(s)c_m^T(sI-A_m)^{-1}b_m$

$\hat{x} = A_m\hat{x} + b_m u + \hat{\sigma}$

$\hat{y} = c_m^T\hat{x}$

$\mathcal{L}_1$ adaptive controller

$\Phi^{-1}(T_s)\mu(T_s)$

$T_s$

$\tilde{y}$

$r$

$k_gF(s)$

$u\mathcal{L}_1$

$u$

$y$

Patient
Conclusions

- First applications of LPV and $L_1$-Adaptive methods to anesthesia control

- Performance analysis includes intended patient and cross-patient evaluations

- **Implementation issues:**
  - Anesthesiologist controlled induction
  - Enforce bounds on maximum drug concentrations – “Hedging design”
  - Predictor sampling
  - $L_1$/LPV controllers with enable-disable control: “Human-Machine Interface”
  - Multiple synergistic anesthetic agents
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