Robust Medical Monitor Design: Part 3 – Implementation of Parameter-Invariant Monitors

James Weimer, Oleg Sokolsky, Insup Lee
Recall Health Monitoring
Recall the Monitor Design Problem

- Design a binary test between:
  - $H_0$ : null hypothesis
  - $H_1$ : event hypothesis

- Performance constraints
  - bound false positive rate
  - maximize true positive rate

- Module 1 covered the fundamentals of parameter invariance:
  - LRT, GLRT, MI, and PAIN

- Module 2 covered the design of parameter invariant monitors:
  - general form: $y = H\theta + \sigma n$

- This module presents the implementation of PAIN monitors
  - real-world applications
Outline

• Meal detection in type I diabetics
  – unknown linear time invariant systems

• Critical pulmonary shunt detection in infants
  – detection in structured linear systems with unknown parameters
Meal Detection in Type I Diabetics
Meal Detection in Type I Diabetics
Meal Monitor Design Problem

- hypothesis testing problem:
  - window of $w$ measurements
  - test meal impulse happening in window $d_1$ or $d_2$
  - use the 2-sided PAIN approach
    - allows for the case where all hypotheses are incorrect

- What is the relationship between events and measurements?
  - i.e. What is the physical model?
Sequential Monitoring/Detection

- Sequential Monitoring of sequential events
Physiological Modeling

- FDA accepted model
  - 12 states, 30 physiological parameters (unknown)
  - non-linear

- Bergman model – 5 states, linear – unknown physiological parameters
  - 5th order model

- test signals – sequential ranges of hypothesized meal times
- disturbances:
  - reported meals = impulse at a time (amount unknown, effect unknown)
  - insulin = impulse at a time (amount known, effect unknown)

- measurements
  - plasma glucose

implement 2-sided PAIN monitor
PAIN monitor for Meal Detection

A Meal Detection Scenario Example

- Glucose Level (mg/dL)
- CGM Data
- Insulin Bolus
- Meal

Statistics (Unitless)

Decision Score (Unitless)

Simulation Time (minutes)

$S(t)$

$S_0$
PAIN Meal Monitor Evaluation

• Generated 10,000 random virtual patients
  • parameters selected from a convex set of FDA-suggested physiological ranges

• Simulated each patient for 20 meals
  • using FDA-accepted T1DM simulator (maximal model, non-linear)

• Compared to prominent approaches in literature
  • Dassau et al. → Kalman, then rate-of-change (RoC) thresholding
  • Lee et al. → a priori specified FIR filter, then RoC thresholding
  • Harvey et al. → multi-stage filter, then RoC thresholding

• Evaluate on the criteria:
  • false positive rate vs. true positive rate
  • time-to-detection (when correct)
  • number of false positives per patient
PAIN Meal Monitor Performance

near-perfect performance
- 99.1% true positive rate
- 0.9% false positive rate

Dassau et al.'s
Lee and Bequette's
Harvey et al.'s
PAIN Meal Monitor Performance

- fast time-to-detection
  - 99.1% detected within 40 minutes
  - mean detection time of 24 minutes

- PAIN-Based
- Dassau et al.'s
- Lee and Bequette's
- Harvey et al.'s
PAIN Meal Monitor Performance

low false alarm variability across patients
- max of 5 false alarms
Summary: Detection with Unknown LTI models

- Sequential detection with sequential inputs is powerful
  - works very well for meal-detection
  - dominates rate-of-change approaches in literature

- Diabetic meal detection is not a new problem (over 15 years old)
  - No classical “machine learning” solution in literature
  - why? ... possibly because of physiological variability between patients

- What if the system has some structure which can be exploited?
Outline

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Detecting Critical Pulmonary Shunts in Infants

Both lungs participating in pulmonary exchange

Shunt

One lung participating in pulmonary exchange
Critical Pulmonary Shunt Detection Problem

• Option A: hypothesize the shunt as an input
  – use the unknown LTI system monitor (as before)

• Option B: build a “structured” model of the dynamics when:
  – a shunt is present
  – a shunt is not present

• Both options require some model information
  – where does this come from?
Compartmental Modeling

• Option A: hypothesize the shunt as an input (use LTI approach)
  - requires little domain expertise

• Qualitative heuristic for option A: add dimension(s) to the LTI model when:
  - physical separation (+1 per degree separation)
  - time-delay (+1 per unit delay)
  - test signal is not “really” an impulse (+ model_order_needed)
  - critical shunt detection: model order = 4
    • diffusion $\rightarrow$ +1, circulation delay $\rightarrow$ +2, sustained event $\rightarrow$ +1

• Concept extends beyond physiology
  - networks (degree of separation)
  - any dynamically coupled linkage
    • e.g. fluid transfer in automotive transmission

Apply 2-sided PAIN monitor as before
Compartmental Modeling

- Option B: build a structured model of the dynamics
  - requires significant domain expertise

\[
\begin{bmatrix}
  x^L(k) \\
  x^R(k)
\end{bmatrix}
= \begin{bmatrix}
  \frac{\alpha}{V(k)} & \frac{\alpha}{V(k)} \\
  \frac{\alpha}{V(k)} & \frac{\alpha}{V(k)}
\end{bmatrix}
\begin{bmatrix}
  x^L(k - \kappa) \\
  x^R(k - \kappa)
\end{bmatrix}
+ \begin{bmatrix}
  \frac{2\alpha}{V(k)} \\
  \frac{2\alpha}{V(k)}
\end{bmatrix}
\begin{bmatrix}
  n^L(k) \\
  n^R(k)
\end{bmatrix}
\begin{bmatrix}
  \mu \\
  \sigma
\end{bmatrix}
\]

\[
y(k) = \begin{bmatrix}
  \frac{1}{2} & \frac{1}{2}
\end{bmatrix}
\begin{bmatrix}
  x^L(k) \\
  x^R(k)
\end{bmatrix}
\]

- pros: potential gains in performance
- cons: difficult to design
PAIN Critical Shunt Monitor Evaluation

• 209 human patients considered (all children)
  • 61 patients experiencing with potential critical shunts
    • annotations are unreliable
  • 148 patients without a shunt

• Compare the following approaches
  • dd-PAIN_{TS} \rightarrow \text{ option A with trained thresholds }
  • PAIN_{PHYS} \rightarrow \text{ option B without trained thresholds }
  • dd-PAIN_{PHYS} \rightarrow \text{ option B with trained thresholds }
  • GLRT_{PHYS} \rightarrow \text{ physiology based GLRT with trained thresholds }

• Evaluate on the criteria:
  • false positive rate variability between patients (false positive rate vs. patient)
    • using patients without a shunt
  • predictive capability of the detector (true positive rate vs. time)
    • using patients with a shunt
Critical Shunt Monitor Performance

- trained option B is the “best”
- trained option A is still good
- GLRT has wide variance in false positive rate across patients
Summary: Detection in Structured Linear Systems

• Improved performance achievable by including physical model knowledge
  – sequential detection of sequential events approach still can be useful

• GLRT can not bound the false positive rate in all applications
  – e.g. critical shunt detection
  – statement generalizes to other classical data-driven approaches
    • e.g. detection/classification via ARMAX features

• Are there any physical model invariances that are easy to exploit?
  – Doesn’t require domain knowledge to build a model.
  – Answer: “Yes, but we haven’t found any in health care ... yet.”
    • Networked dynamical systems have natural invariances
      – e.g. power Grids and buildings
Closing Remarks and Insight

- parameter-invariant monitoring is a structured approach to monitor design that addresses variability in medical monitoring applications.
  - can address some difficulties with classical monitor design

- The general form presented herein is not the only statistic:
  - statistics to deal with missing measurements
  - cases when parts of the model are known
    - e.g. model error is known

- Machine learning + Parameter Invariant statistics
  - use parameter invariant techniques to generate feature
    - invariant to variability
  - learn the best classifier over the parameter invariant features
    - can boost performance

- See all our work at: https://rtg.cis.upenn.edu/parameter-invariant.html