Model-Driven Safety Analysis of Closed-Loop Medical Systems

Penn — University of Pennsylvania

PRECISE — Penn Research in Embedded Computing and Integrated Systems Engineering

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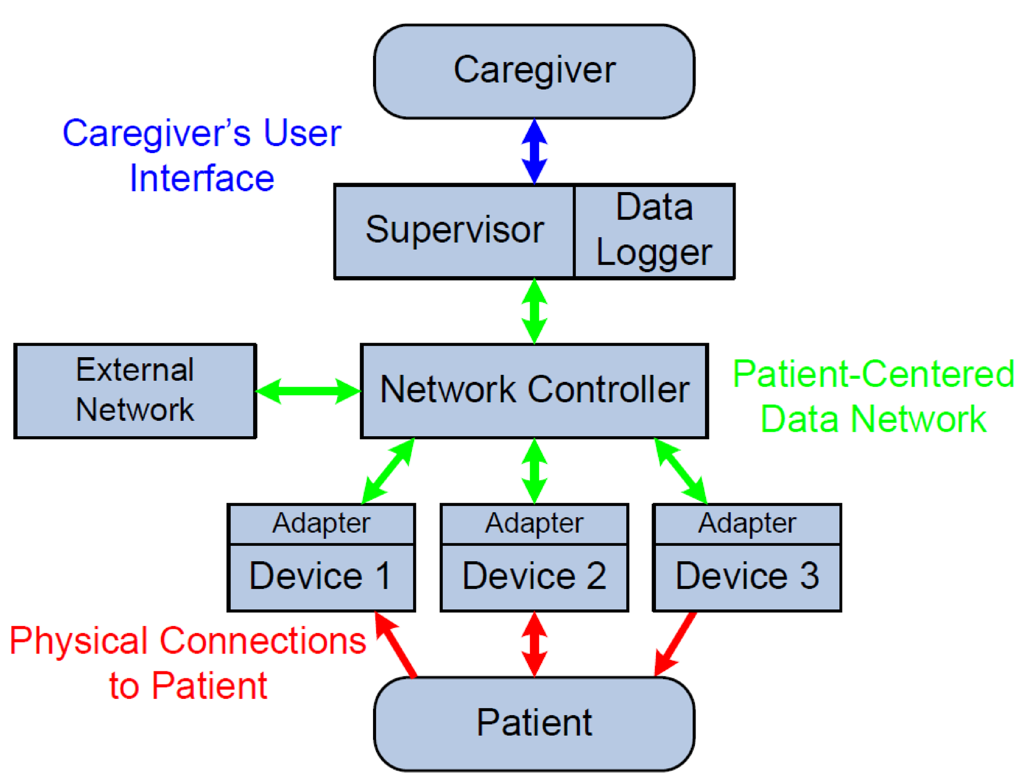
In modern hospitals, patients are treated using a wide array of medical devices that are increasingly interacting with each other over the network. We study the safety of a medical device system for the physiologic closed-loop control of drug infusion. The main contribution is the verification approach for the safety properties of closed-loop medical device systems. The method combines simulation-based analysis of continuous patient dynamics with model checking of a more abstract timed automata model.

For Networked Medical Systems with a Patient-in-loop, how can we guarantee open-loop safety?

1 Interoperability for Patient Safety



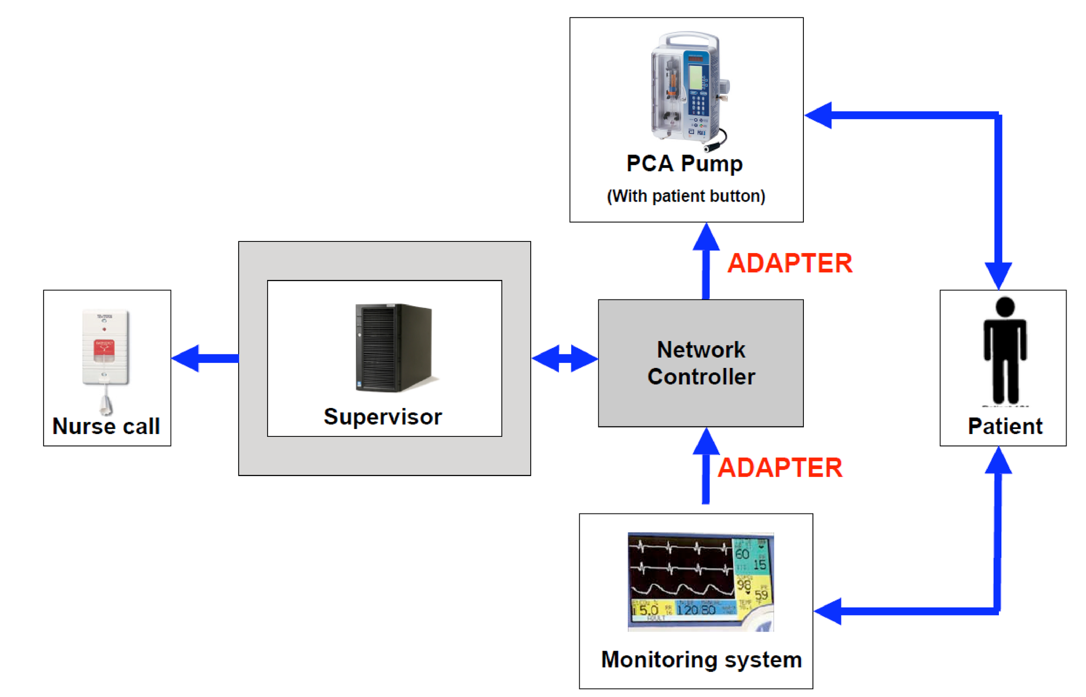
Built according to the Integrated Clinical Environment (ICE) architecture

2 Medical Case Study: Closed-loop PCA pump

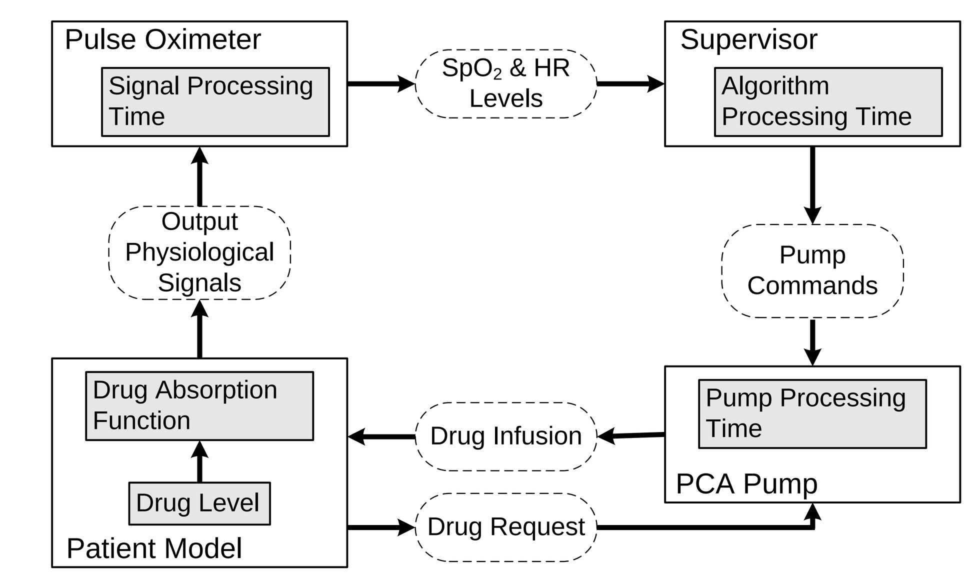
Patient Controlled Analgesia: Common technique for delivering pain medication.

- Patient presses a button to request a dose
- Overdoses result in respiratory distress, ultimately death
- Pumps have safeguards, but overdoses can still happen
- PCA is a significant source of adverse events

3 System Architecture

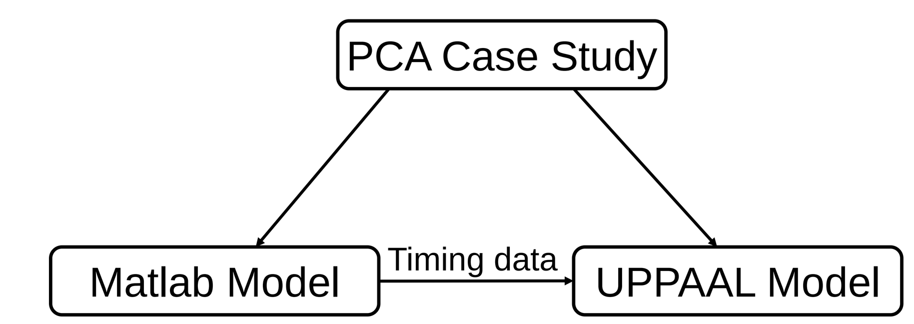


Control Loop



Challenges for system verification:

- Complex interplay between the continuous patient's dynamics and the discrete nature of the controller and communication network.



4 Patient Model

$$\begin{bmatrix}\dot{C}_1\\ \dot{C}_2\\ \dot{C}_3\end{bmatrix} = \underbrace{\begin{bmatrix}-(k_{12}+k_{13}+k_{10}) & k_{21} & k_{31}\\ k_{12} & -k_{12} & 0\\ k_{13} & 0 & -k_{31}\end{bmatrix}}_{A}\begin{bmatrix}C_1\\ C_2\\ C_3\end{bmatrix} + \underbrace{\begin{bmatrix}\frac{1}{V_1}\\ 0\\ 0\end{bmatrix}}_{B} I$$

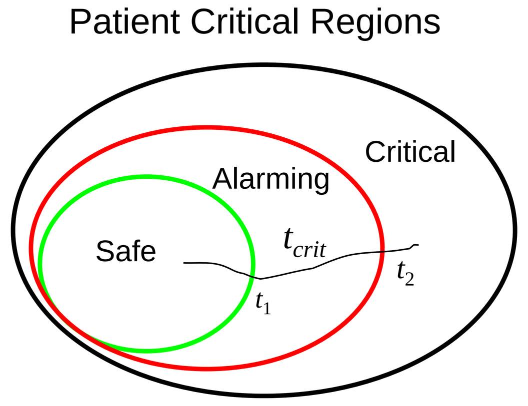
$$dl = \underbrace{\begin{bmatrix}1 & 0 & 0\end{bmatrix}}_{C}\begin{bmatrix}C_1\\ C_2\\ C_3\end{bmatrix}$$

3-compartment model

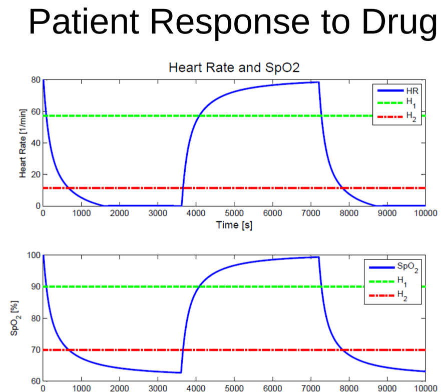
- drug concentration in blood and tissue

Modeling Patient specific behavior: $k_{ij} \in \left[\hat{k}_{ij} - \Delta k_{ij}, \hat{k}_{ij} + \Delta k_{ij}\right]$, $V_1 \in \left[\hat{V}_1 - \Delta V, \hat{V}_1 + \Delta V\right]$

Patient Critical Regions

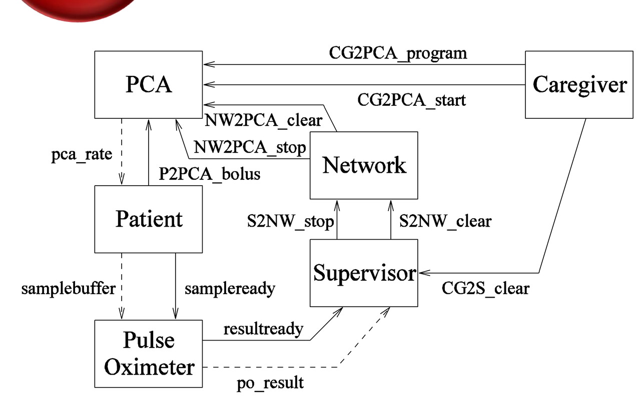


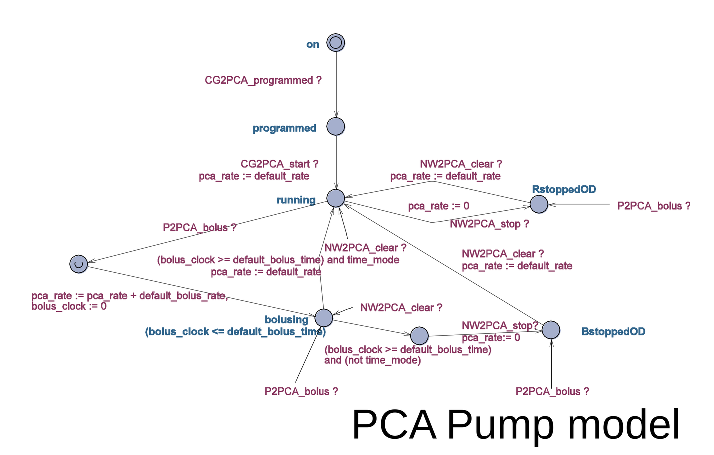
Patient Response to Drug

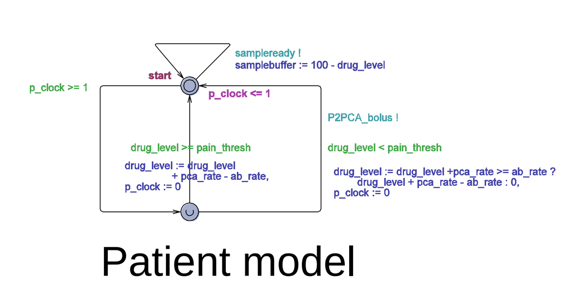


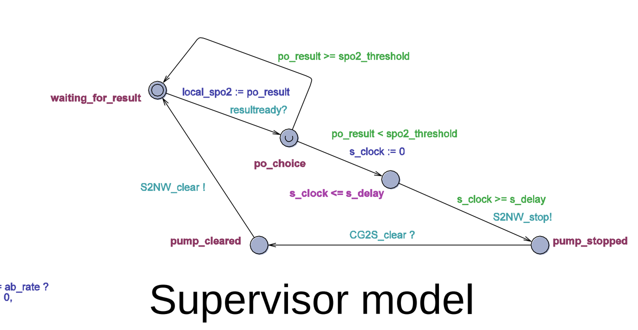
- The model allows estimation of t_{crit}
- For the patient model with fixed parameters tcrit determined analytically

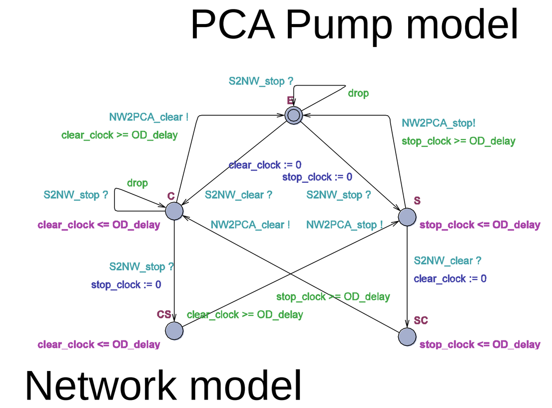
5 UPPAAL Model







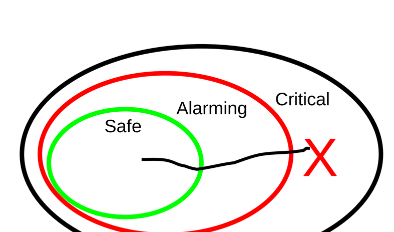


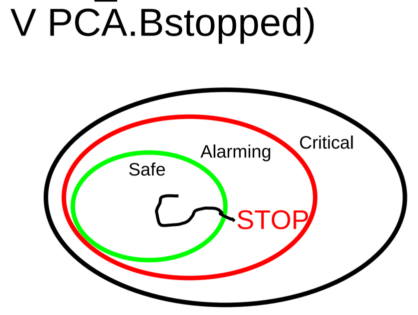


- Effects of unreliable network
- Goal: Guarantee open-loop stability

Properties verified with UPPAAL

- Once SpO_2 drops below pain threshold, it eventually goes back up
  A[] (samplebuffer < pain_thresh -> A <> samplebuffer >= pain_thresh)
- The pump is stopped if patient enters alarming region
  A[] (samplebuffer < alarm_thresh -> A<> (PCA.Rstopped V PCA.Bstopped)
- The patient can not go into the critical region
  A[] (samplebuffer >= critical)





6 Timing analysis

Key Safety Property

- Pump stops in time if total delay ≤ t_{crit}
- For model with uncertain parameters
  - Matrices A, B, C belong to regions

$$\tilde{t}_{crit} = \frac{1}{||\tilde{\mathbf{A}}||}\ln\left(\frac{|\Delta H|/gain}{||\tilde{\mathbf{C}}||\cdot\left(||\tilde{x}_0|| + \frac{||\tilde{\mathbf{B}}u_i||}{||\mathbf{A}_{max}||}\right)} + 1\right)$$

$$\tilde{\mathbf{A}} = \underset{\mathbf{A}\in\Re\{\mathbf{A}\}}{\operatorname{argmax}} ||\mathbf{A}||, \tilde{\mathbf{B}} = \underset{\mathbf{B}\in\Re\{\mathbf{B}\}}{\operatorname{argmax}} ||\mathbf{B}u_i||, \tilde{\mathbf{C}} = \underset{\mathbf{C}\in\Re\{\mathbf{C}\}}{\operatorname{argmax}} ||\mathbf{C}||$$

$$\mathbf{A}_{min} = \underset{\mathbf{A}\in\Re\{\mathbf{A}\}}{\operatorname{argmin}} ||\mathbf{A}||$$

UPPAAL model parameters initialized to guarantee consistency between the UPPAAL model and physical patient model

$$\left[\frac{\Delta H/gain}{PCA\_rateON - ab\_rate}\right] = \left[\tilde{t}_{crit}\right]$$ The pump is ON

$$\left[\frac{\Delta H/gain}{rate\_down}\right] = \left[\frac{1}{||\tilde{\mathbf{A}}||}\ln\left(\frac{|\Delta H|/gain}{||\tilde{\mathbf{C}}||\cdot||\tilde{x}_0||} + 1\right)\right]$$ OFF

7 Demo

The system have been presented at:

- Annual meeting of the American Society of Anesthesiologists in 2007 (first place in the scientific exhibits)
- 2008 HIMMS (Healthcare Information and Management Systems Society) Congress
- 2008 CIMIT Innovation Congress