Closed-loop Medical Cyber-Physical Systems: Networked Glucose Control System

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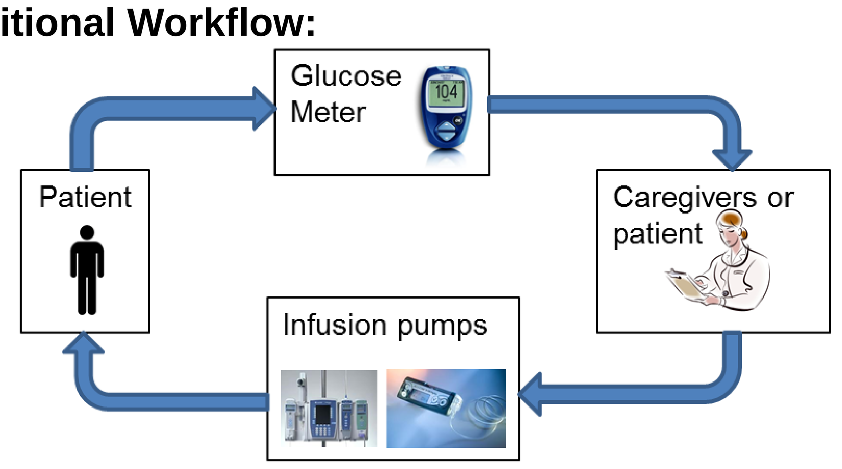
PRECISE — PENN RESEARCH IN EMBEDDED COMPUTING AND INTEGRATED SYSTEMS ENGINEERING

Introduction

- Diabetes: a growing problem
  - 26 million (8.3% of the population) in US have diabetes
  - 7-th leading cause of death
  - Costs $174 billion annually
  - Complications: heart attacks, strokes, high blood pressure, kidney failure, blindness
- Two types:
  - Type 1 (T1D, 5-10%): loss of the insulin-producing beta cells in the pancreas, leading to insulin deficiency
  - Type 2 (T2D): insulin resistance which may be combined with relatively reduced insulin secretion
- Improved blood glucose regulation benefits
  - maintain glucose level within certain ranges
- Traditional Workflow:



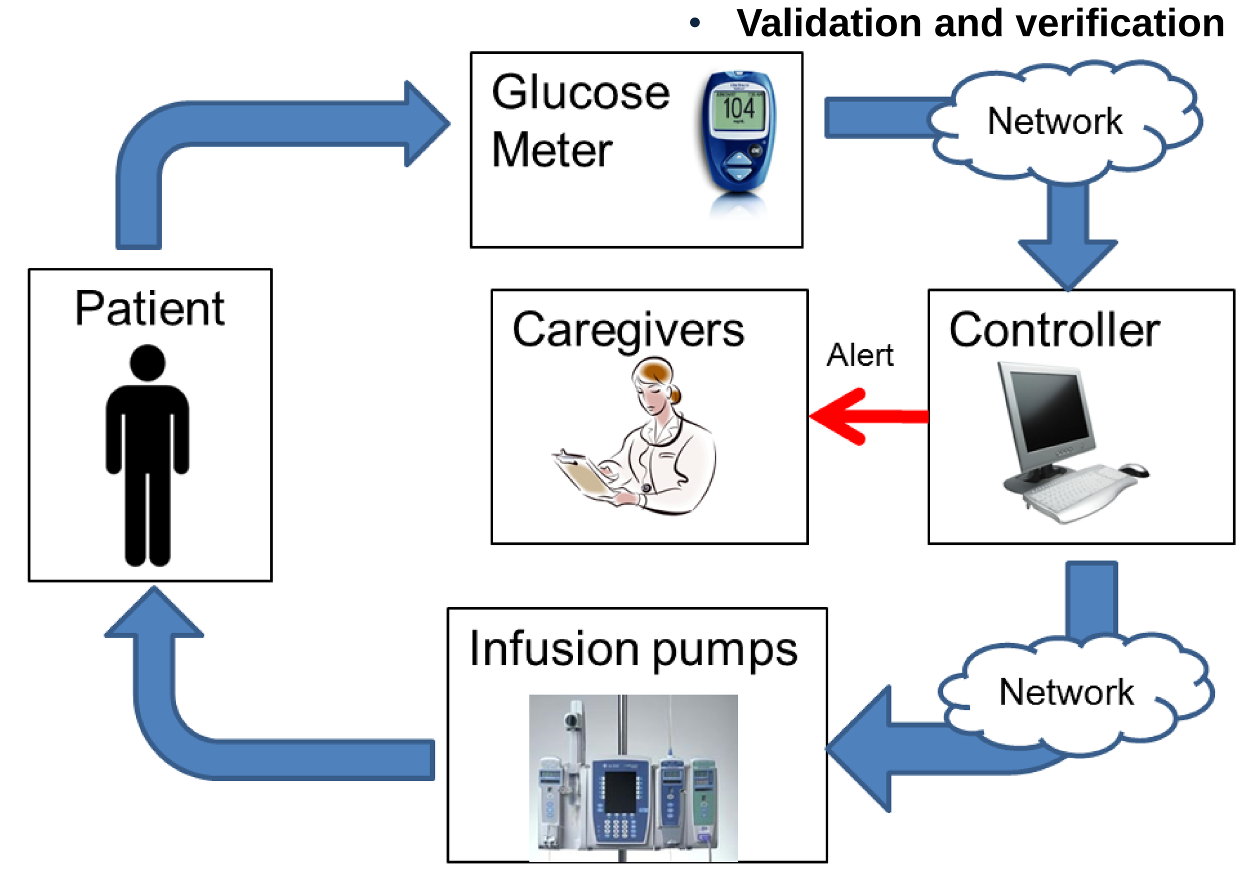
Our Vision

General Vision

- A networked glucose control system
  - promote the quality of glucose regulation
  - reduce caregivers' workload
  - improve patient safety
- Only alert caregivers to adverse events

Research Issues

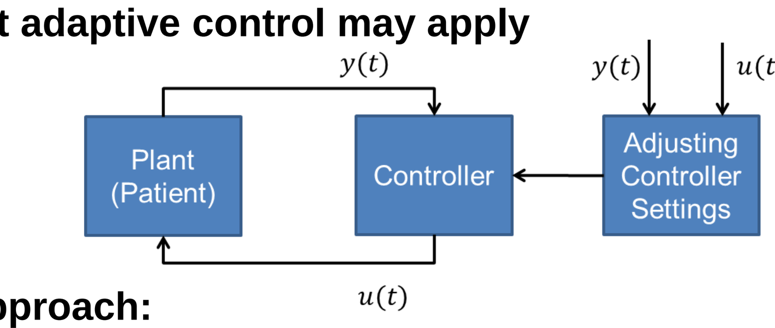
- Safe and effective networked glucose control system
  - Hazards: *communication* and *components* may fail
  - How to guarantee safety under failure conditions
- Validation and verification



Approach

Model-based safe adaptive/robust control

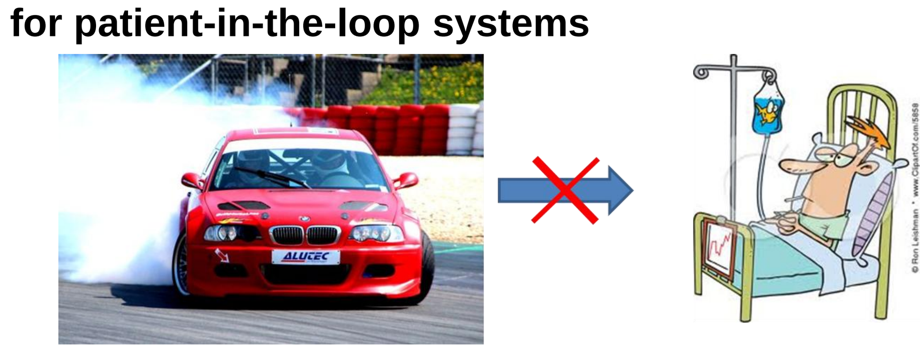
- Manage physiological parameter uncertainties
  - Adaptive approach:
    - Adjusting controller settings at run-time
    - Explicit adaptive control: learn model parameters at run-time
      - Difficult for a ~20-D non-linear model with ~30 parameters
    - Implicit adaptive control may apply



  - Robust approach:
    - stabilize the plant with bounded parameter uncertainties
- Challenges: verification of adaptive/robust controller

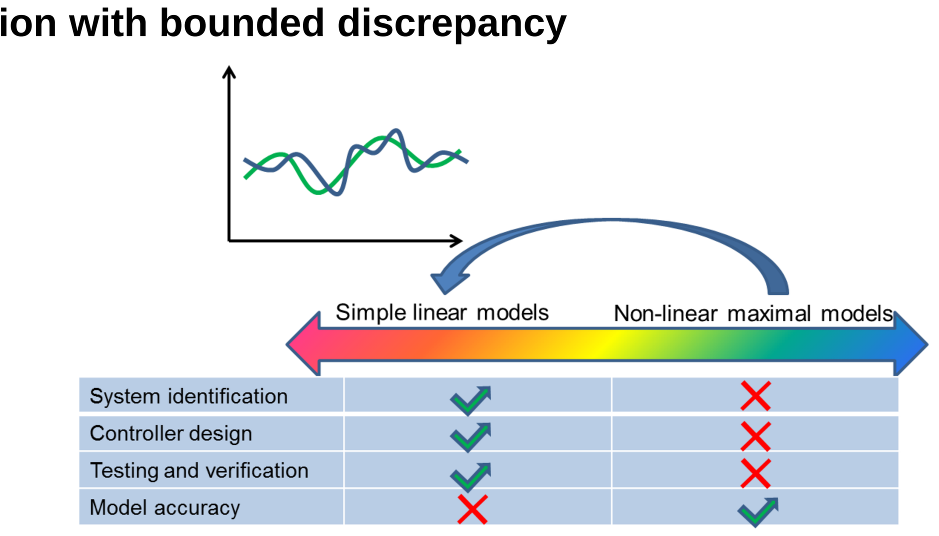
Safe Adaptive Exploration

- Adaptive control often involves learning the parameters by feeding in extreme inputs
  - Example: aggressively turning a car
- Not safe for patient-in-the-loop systems



Safe Non-linear Model Reduction

- Model complexity trade-off
- Reduction with bounded discrepancy



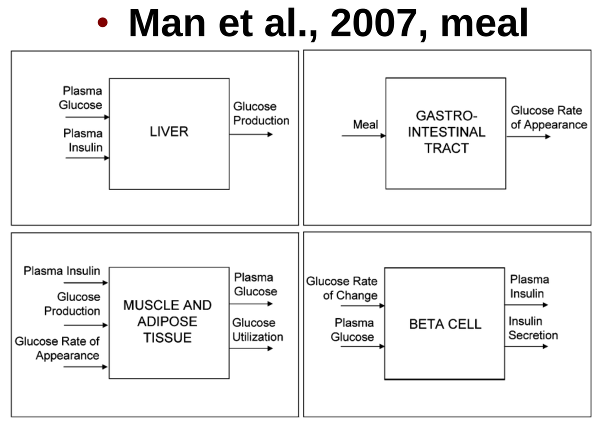
Safety Analysis

- Identify platform hazards in the networked control setting
  - Develop mitigation strategies
    - Unlike the closed-loop PCA system, where only overdosing is undesirable, in the BG system, both hypo- and hyper- glycaemia must be avoided
    - No trivial fail-safe mode for closed-loop BG control
  - Perform system-level safety verification and validation

Background

Patient Model

- Modeling the human glucose-insulin dynamics
  - 60's: simplest linear model by Bolie
  - 70's – 80's: minimal (coarse-grain) modeling strategy
  - 90's – now: maximal (fine-grain) models
    - High-order nonlinear model with many unknown parameters
    - Not easily identifiable
    - Man et al., 2007, meal



Glucose Controller

- Clinical guidelines
  - Fixed rule tables
  - Unlike classical controllers
  - Developed at individual departments
  - Implemented by nurses
- Automatic glucose controllers
  - 70's: proportional-derivative (PI) control
    - Clemens, 1979
  - 80's: classical pole-placement approach, adaptive control
    - Fischer et al., 1987
  - 90's: optimal control
    - Parrish and Ridgely, 1997
  - Late 90's – now: model predictive control (MPC)
    - Parker et al., 1999, Hovorka et al., 2004, Magni et al., 2007

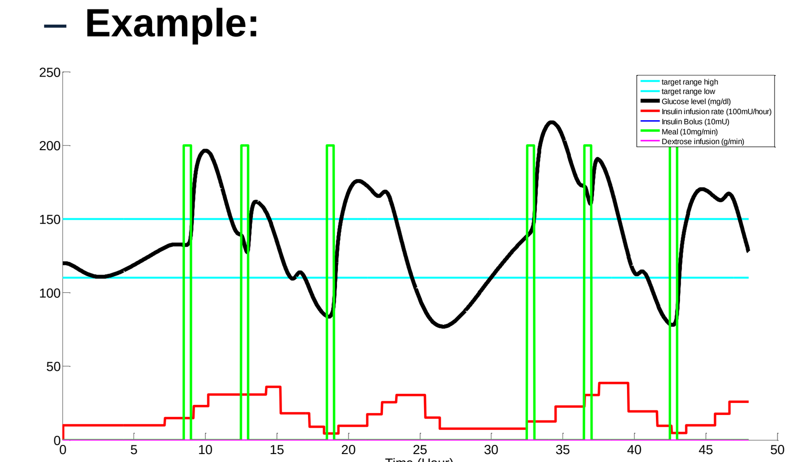
In Silico Guideline Evaluation

Simulation-based Evaluation

- Controller: clinical guidelines
  - 5 ICU insulin infusion guidelines from a hospital
  - programmed as rule-based controllers
- Patient model: UVa/Padova T1DM Metabolic Simulator © 2011, The Epsilon Group
  - Based on a maximal model (Man et al., 2007)
  - 30 "virtual" subjects settings
- Model-based evaluation of clinical guidelines

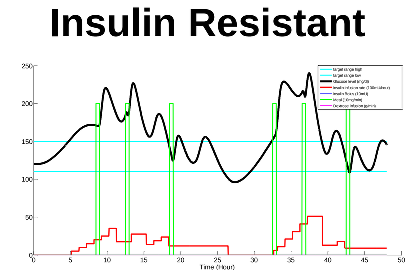
Key Observations

- Guideline controls are not always effective
- Hypoglycemia (low glucose) and serious oscillations in glucose level observed on some virtual subjects
  - Example:

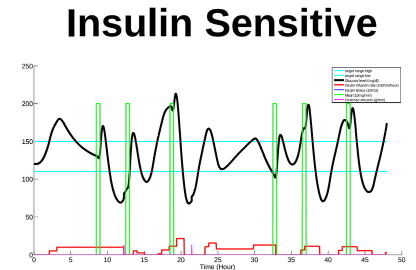


- Individual insulin sensitivity varies:

Insulin Resistant



Insulin Sensitive



- Clinical guidelines use fixed rule tables
  - Not adaptive to inter-subject variability within the same patient population
- Need more effective controllers for the networked control system