Data-Driven Robust Control for Type 1 Diabetes Under Meal and Exercise Uncertainties

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CMSB 2017, TU Darmstadt, 27 Sep 2017

Diabetes

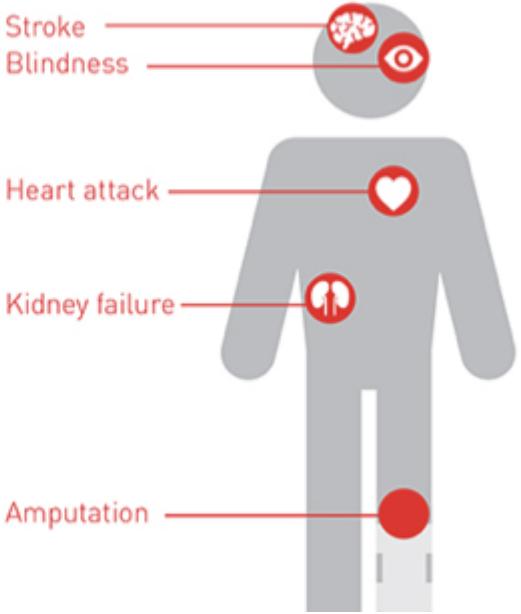
Main types of diabetes

TYPE 1 DIABETES
Body does not produce enough insulin

TYPE 2 DIABETES
Body produces insulin but can't use it well

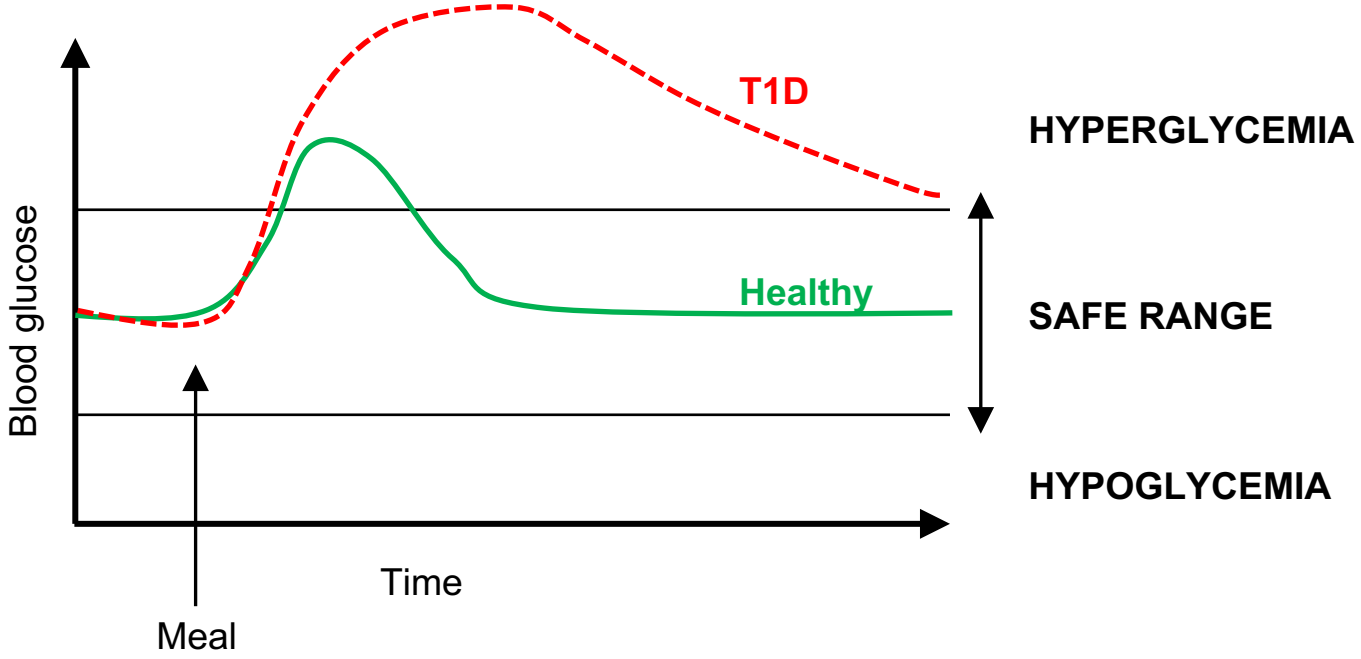
GESTATIONAL DIABETES
A temporary condition in pregnancy

Consequences
Diabetes can lead to complications in many parts of the body and increase the risk of dying prematurely.



WHO Global report on diabetes, 2016

Type 1 Diabetes (T1D)



T1D therapy, devices

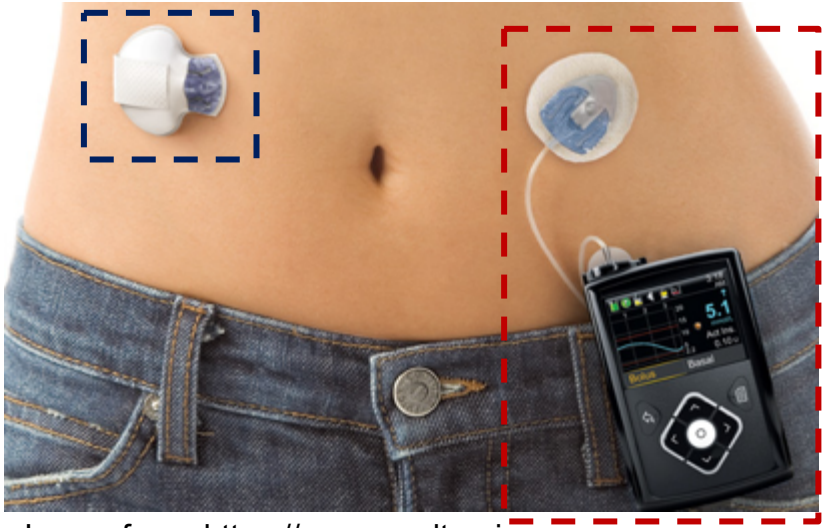


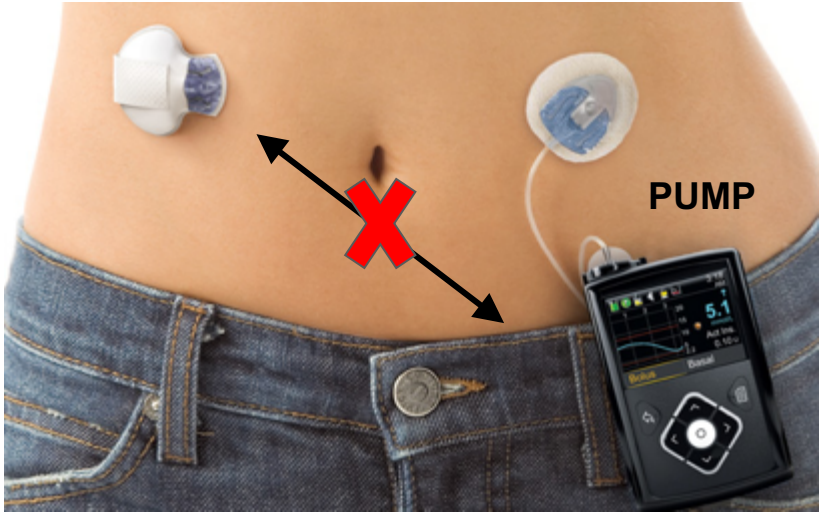
Image from: https://www.medtronic-diabetes.com.au/pump-therapy/what-is-insulin-pump-therapy

Insulin pump delivers two kinds of insulin:

- **Bolus**: high, on-demand dose to cover meals
- **Basal:** to cover demand outside meals

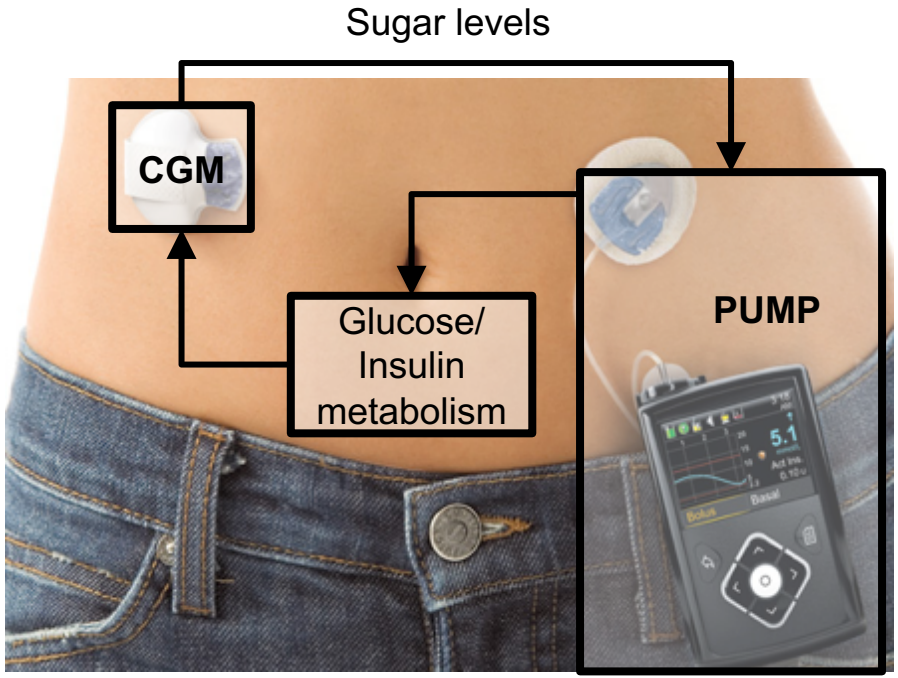
Continuous Glucose Monitor (CGM) detects sugars levels under the skin, a measure of **blood glucose (BG)**

T1D therapy – limitations



- **Pump and CGM don’t communicate with each other**
- Bolus is manually set by the patient → **danger of wrong dosing**

Closed-loop control = Artificial Pancreas (AP)



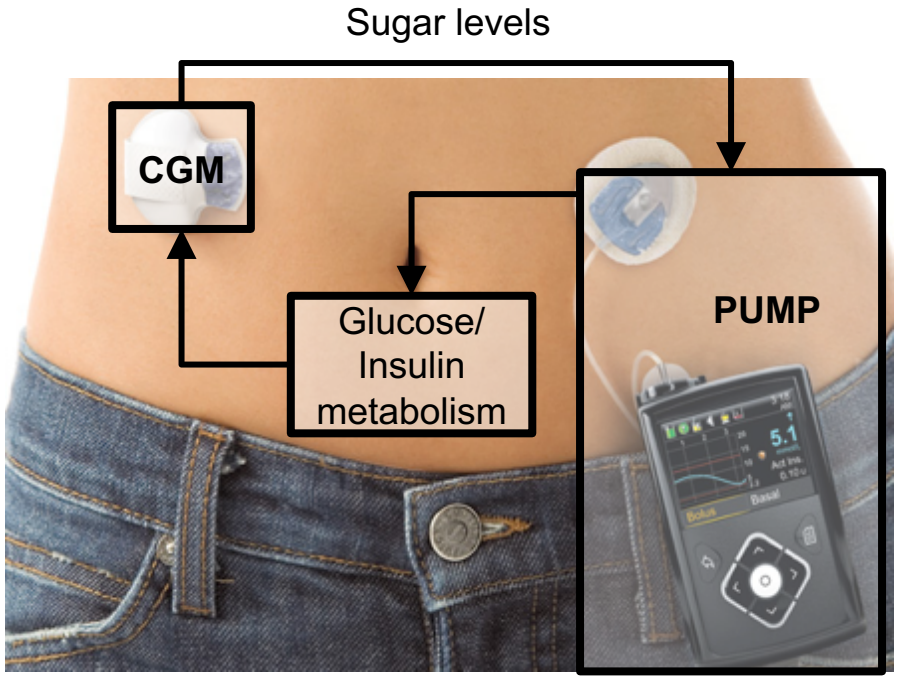
Challenges

→ CGM is a "derived" measure of BG (noisy and delayed)

→ **Disturbances** related to patient behavior (Meals and Exercise)

NOT JUST MEDICAL BUT ALSO AN ENGINEERING CHALLENGE

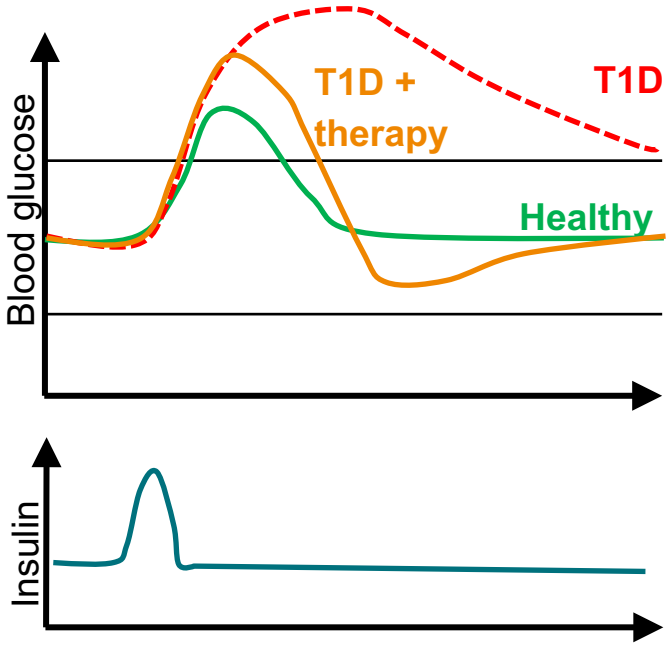
Closed-loop control, aka Artificial Pancreas (AP)



- Only controls basal insulin
- Meals are still announced

NOT JUST MEDICAL BUT ALSO AN ENGINEERING CHALLENGE

Artificial Pancreas, a control problem

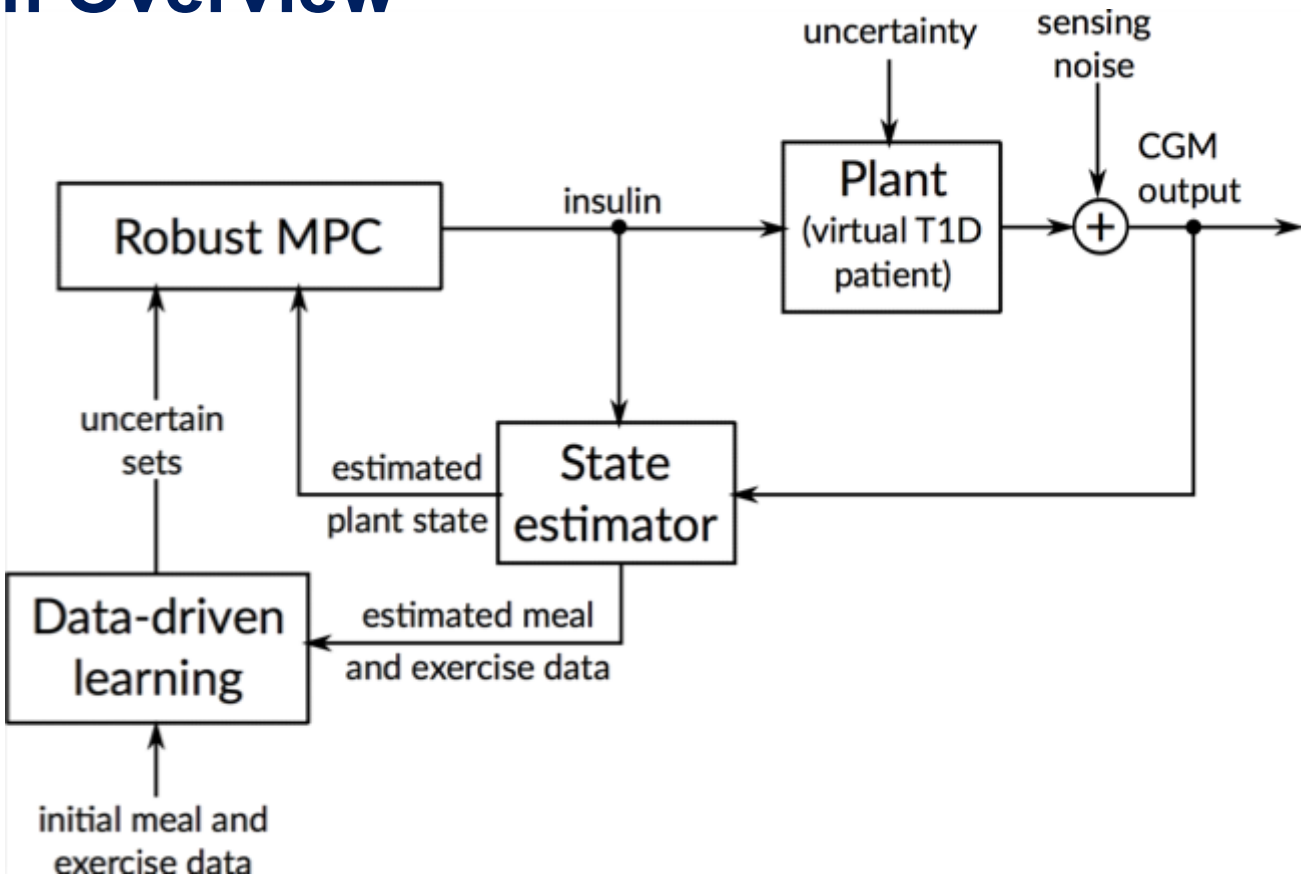


Our solution:

A **data-driven robust model predictive control (MPC)** design for the AP:

- Closed-loop control of **both basal and bolus insulin**
- Handles uncertainty by **learning from data**
- Accurate **state estimation from CGM measurements**

System Overview



Data-driven uncertainty sets

- Learn from data **uncertainty sets** that **capture realizations of uncertainty parameters** (meal and exercise)

- Method that provides **uncertainty sets with probabilistic guarantees** *[Bertsimas et al., Mathematical Programming* (2013): 1-58*]*:

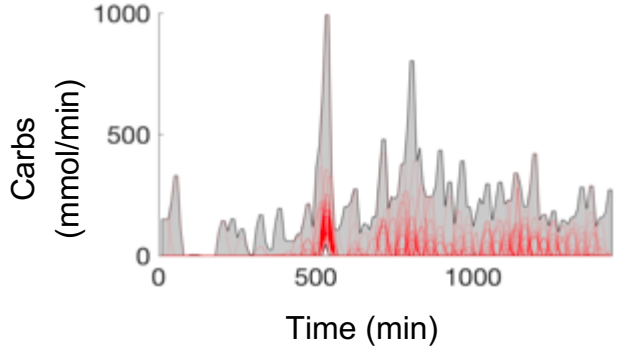
Meal/exercise data

(questionnaires, surveys, sensors, …)

National Health and Nutrition Examination Survey

	Breakfast		
Days	*Start Time*	*Food1*	*Food2*
1st Day	12:49PM	150g Greek Yogurt	3 pieces of toast
2nd Day	9:00AM	1 glass whole milk	150g plain yogurt
3rd Day	9:20AM	1 egg	3 slices of toast

Uncertainty Sets



Robust Model Predictive Control

Find the insulin therapy at time t, t+1,... that minimizes the worst case performance w.r.t. uncertainty parameters

$$\min_{\iota^t,\ldots,\iota^{t+N_c-1}} \max_{\mathbf{u}^t,\ldots,\mathbf{u}^{t+N_p-1}} \sum_{k=1}^{N_p} d(t+k) + \beta \cdot \sum_{k=0}^{N_c-1} (\Delta\iota^{t+k})^2$$

Objective function: combination of distance from target trajectory and step-wise discrepancy of control strategy

State Estimation

We designed a **Moving Horizon Estimator (MHE)**:

- "Estimation *a la* MPC": uses a model to minimize distance between predicted and actual measurements, and between predicted and estimated states over a moving window of length N

- It works also as a **meal estimator:** estimates the most-likely uncertainty parameter values

$$\min_{\mathbf{x}^{t-N},\ldots\mathbf{x}^{t},\boxed{\mathbf{u}^{t-N},\ldots,\mathbf{u}^{t}}} \boxed{\mu \cdot \|\mathbf{x}^{t-N} - \hat{\mathbf{x}}^{t-N}\|^2} + \boxed{\sum_{k=t-N+1}^{t} \frac{\|v^k\|^2}{q^k}}$$

Rao et al., IEEE Trans. Automatic Control 48 (2), 246-258, 2003

Evaluation

Robust controller compared with

- **Perfect controller:** with exact knowledge of uncertainty parameters and full state observability (no state estimation errors)
- **“Hybrid closed-loop” controller:** considers only glucose measurements and not patient behavior

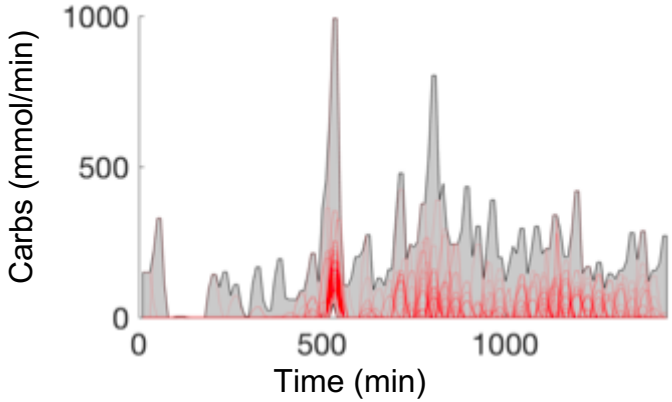
Virtual patient learnt from NHANES database

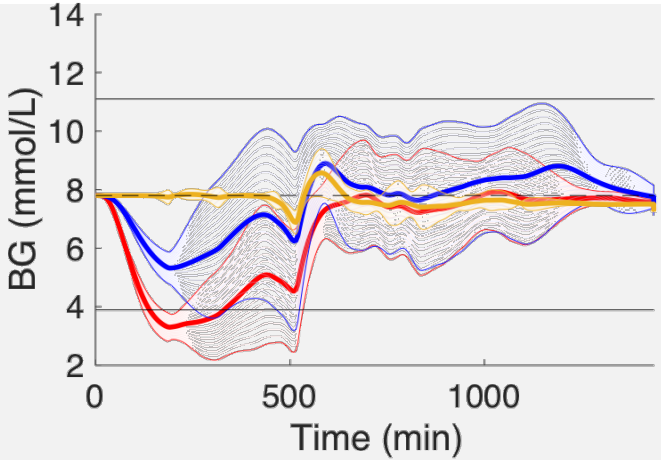
- We learn patient models from CDC's NHANES

National Health and Nutrition Examination Survey

- Meal data from **8,611 participants**
- We cluster data into 10 main groups (finer classification is possible)

GROUP 1: Carbs-rich breakfast

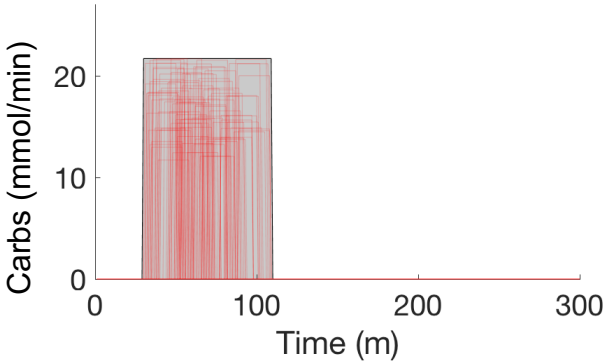


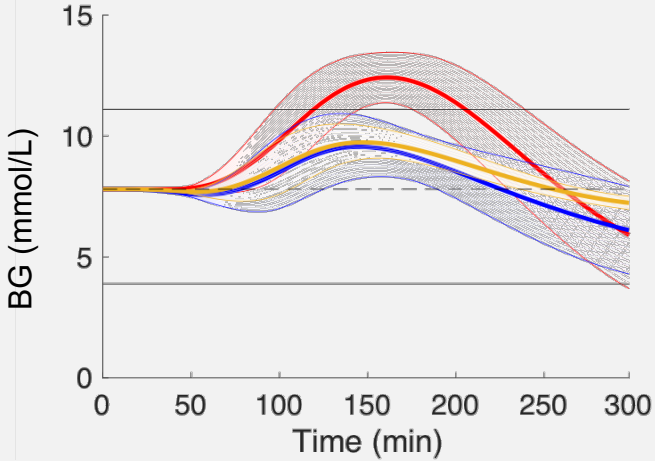


	T hypo	T in range	T hyper
Perfect	0%	100%	0%
Hybrid closed-loop	18.5%	80.97%	0.53%
Robust	**2.02%**	**93.45%**	**4.52%**

Scenario 1 - Meals as expected

Situation where uncertainty set (gray box) is accurate

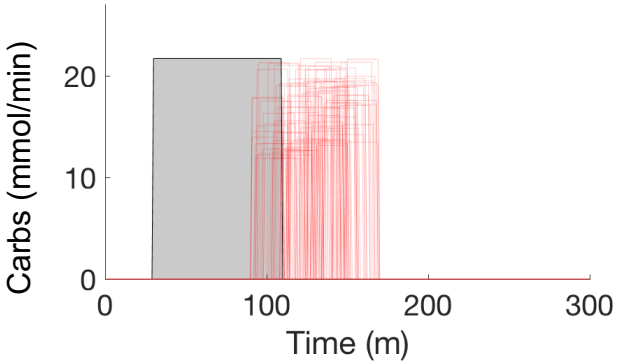


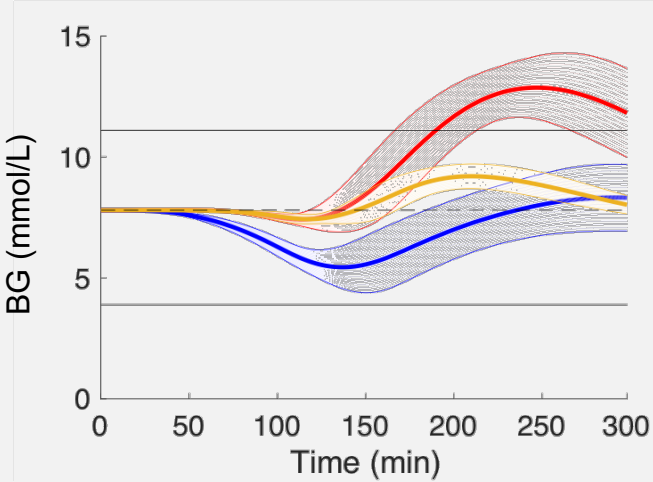


	T hypo	T in range	T hyper
Perfect	0%	99.69%	0.31%
Hybrid closed-loop	1.6%	69.4%	29%
Robust	**0.51%**	**97.7%**	**1.79%**

Scenario 2 - Unexpected delays in meals

Situation where uncertainty set is NOT accurate



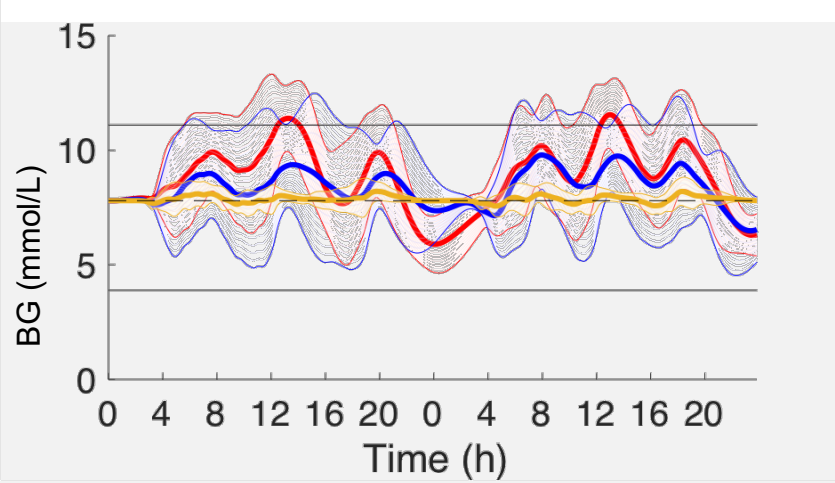


	T hypo	T in range	T hyper
Perfect	0%	100%	0%
Hybrid closed-loop	**0%**	67.25%	32.75%
Robust	0.79%	**99.03%**	**0.18%**

Scenario 3 – High carbs intake, 2 days

Typical settings to test robust AP controllers

	Chance of occurrence	CHO (g)	Time of day (h)
Breakfast	100%	40-60	6:00-10:00
Snack 1	50%	5-25	8:00-11:00
Lunch	100%	70-110	11:00-15:00
Snack 2	50%	5-25	15:00-18:00
Dinner	100%	55-75	18:00-22:00
Snack 3	50%	5-15	22:00-00:00



	T hypo	T in range	T hyper
Perfect	0%	99.52%	0.48%
Hybrid closed-loop	**1.55%**	80.6%	17.85%
Robust	3.11%	**87.56%**	**9.33%**

Summary

- Robust controller design for insulin therapy that well supports meal disturbances.
- Based on deriving uncertainty sets from patient data.
- Evaluated on synthetic scenarios and real data.
- Towards fully closed-loop diabetes therapy and smart medical devices.

Future work

- More advanced patient behavioral model.
- “Human-in-the-loop”: interplay between insulin control and recommendations.