Designing a robust artificial pancreas using patient data: a computational study

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Diabetes

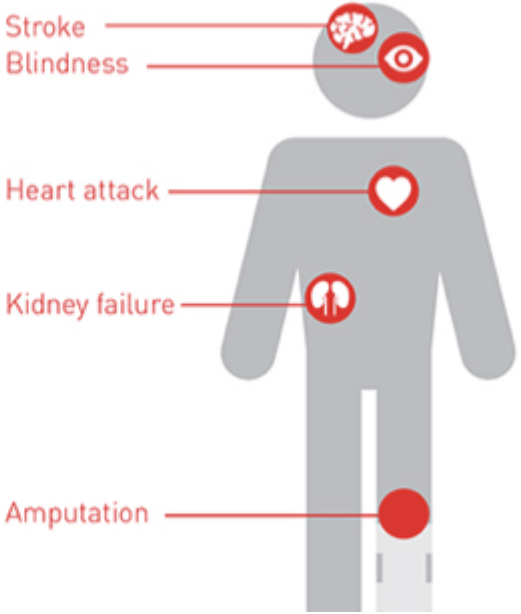
Main types of diabetes

TYPE 1 DIABETES
Body does not produce enough insulin

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

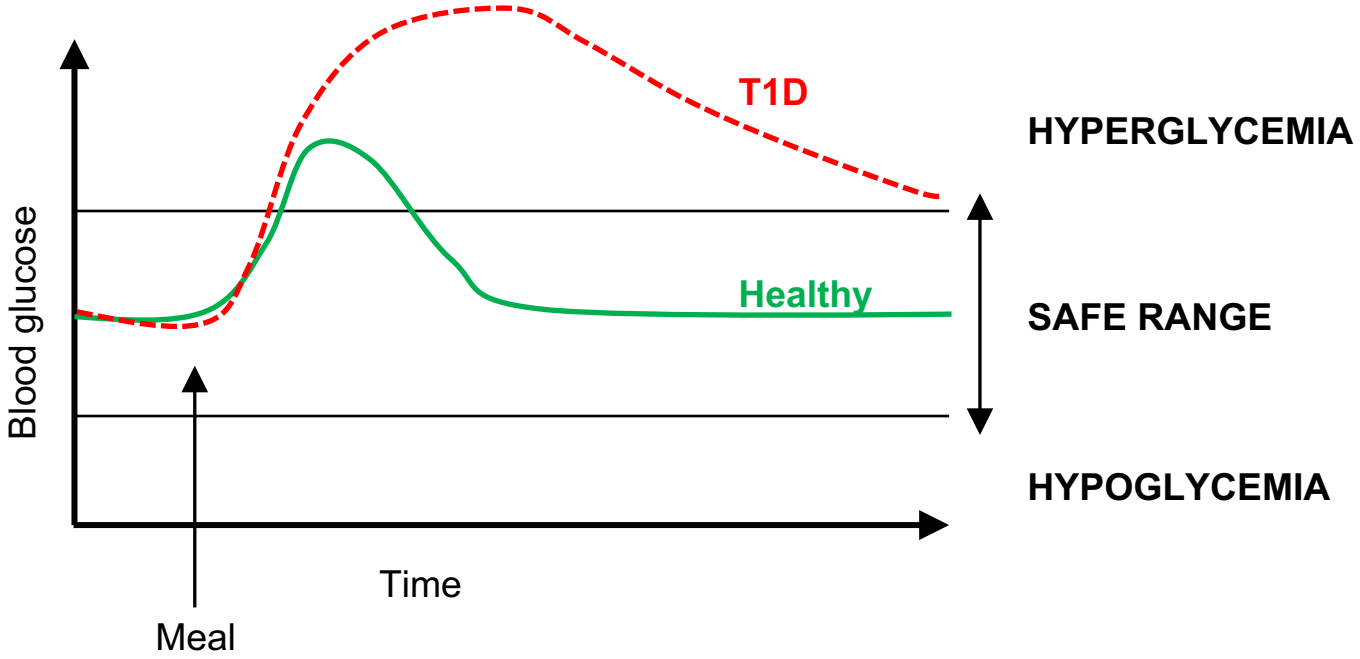
GESTATIONAL DIABETES
A temporary condition in pregnancy

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)



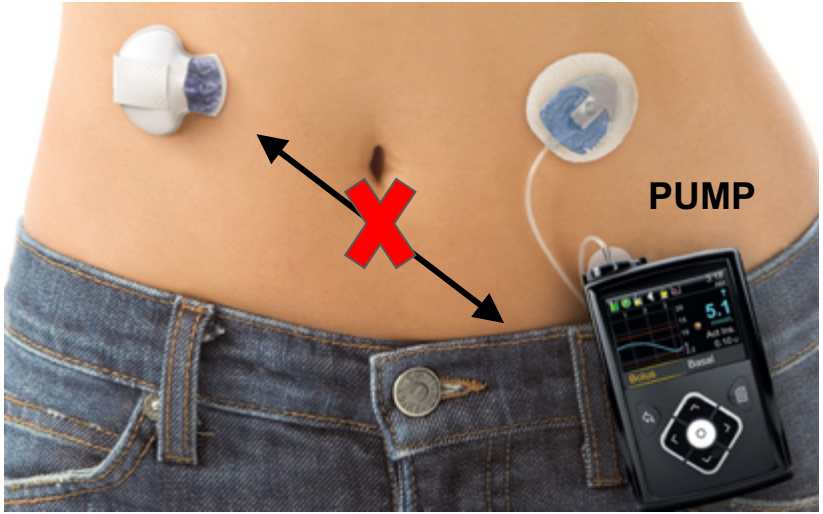
Type 1 Diabetes (T1D) therapy – Insulin pumps

- Devices for continuous insulin infusion, with 1M T1D users estimated worldwide (source: American Diabetes Association)
- More accurate therapy → better glucose profile than injections
- It delivers two kinds of insulin:
  - **Bolus**: high, on-demand dose to cover meals
  - **Basal:** to cover demand outside meals

T1D therapy – Continuous Glucose Monitor

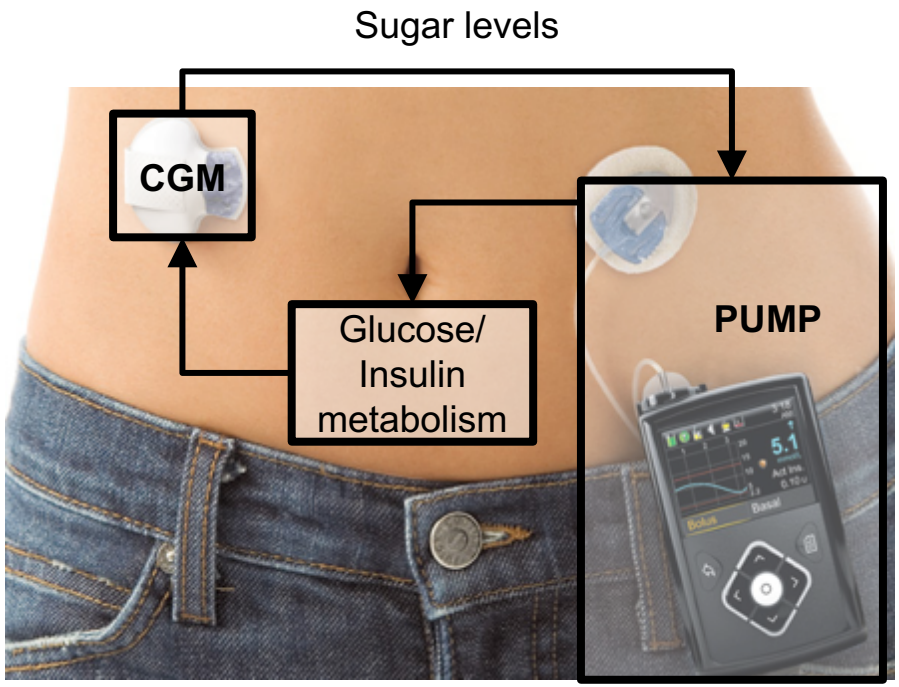
- **Continuous Glucose Monitor (CGM)** detects sugars levels under the skin, a measure of **blood glucose (BG)**
- It reads glucose levels every 5 minutes and sends them wirelessly to display devices
- Fingerstick measurements no longer needed (only for calibration)

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, aka Artificial Pancreas (AP)



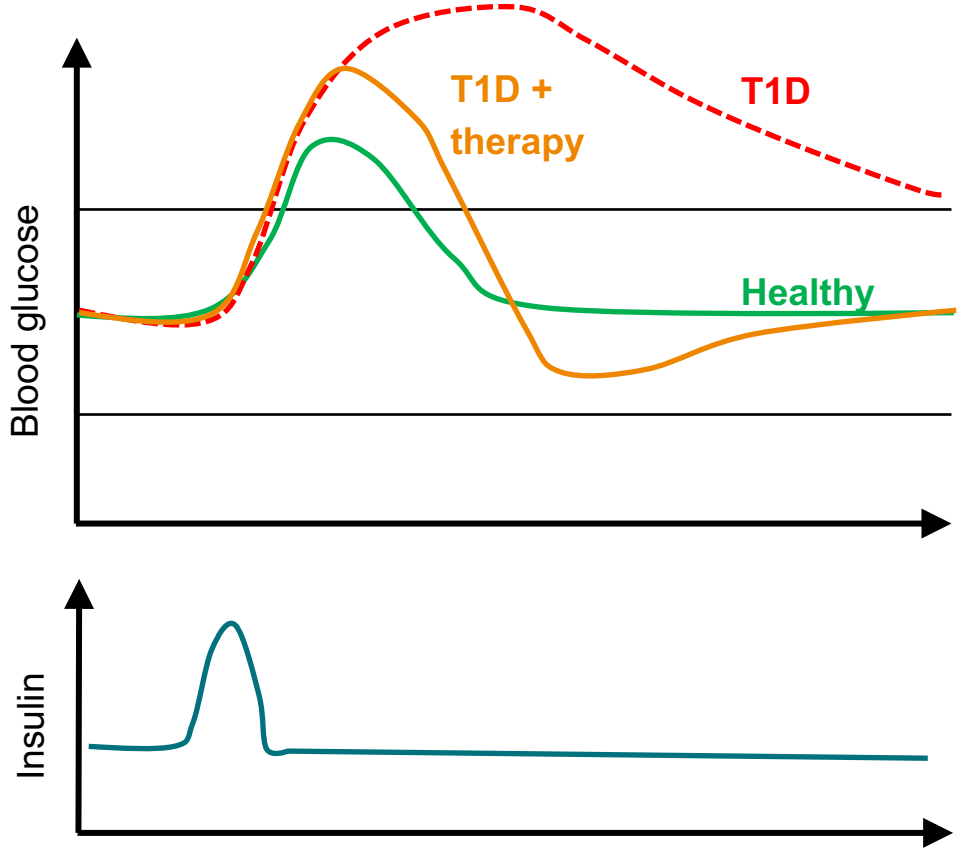
Challenges

→ CGM is a “derived” measure of BG (and noisy)

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

NOT JUST MEDICAL BUT ALSO AN ENGINEERING CHALLENGE

Artificial Pancreas, a control problem



Problem:

Automatically find the insulin therapy (amount and timings) that best keeps blood glucose (BG) “in range”

Our idea

- Use data to get an overall picture of the patient → **learn data-driven models of meal and exercise behavior**
- Such models **make the controller robust to uncertainties** due to patient's daily activities

Meal/exercise data

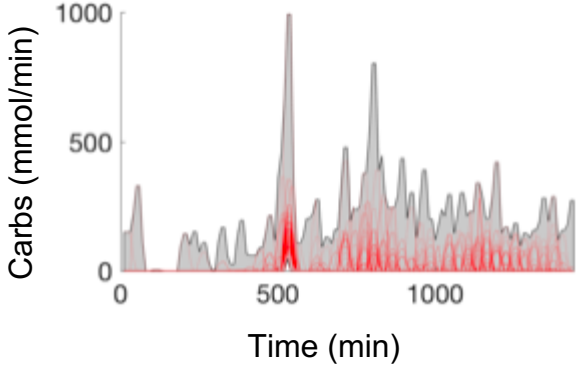
(questionnaires, surveys, sensors, …)

National Health and Nutrition Examination Survey

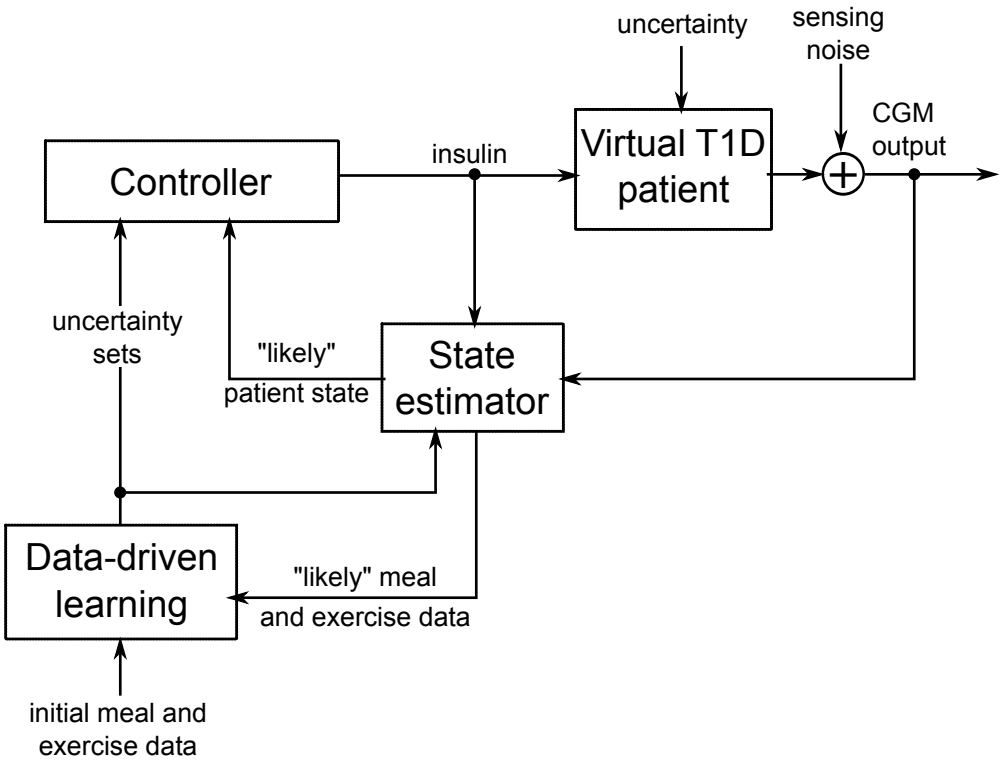
	Breakfast		
Days	*Start Time*	*Food1*	*Food2*
1st Day	12:49PM	150g Greek Yogurt	3 pieces of toast
2nd Day	9:00AM	1 glass whole milk	150g plain yogurt
3rd Day	9:20AM	1 egg	3 slices of toast
4th Day	8:20AM	Tangyuan*5	2 pieces of toast
5th Day	7:30AM	2 slices of toast	50g turkey bacon

Mathematical abstraction

(captures all input data with statistical guarantees)



In-silico Artificial Pancreas: overview



- **Controller** computes “optimal” insulin based on an internal predictive model of the system.
- **T1D patient model** is a “high-fidelity” mathematical model of glucose/insulin metabolism
- **State estimator** derives from CGM measurements the internal state of the patient model, detecting meals and exercise. It uses a predictive model too
- **Data-driven learning** computes mathematical abstractions of patient behavior for controller and estimator

Evaluation

Our robust controller compared with

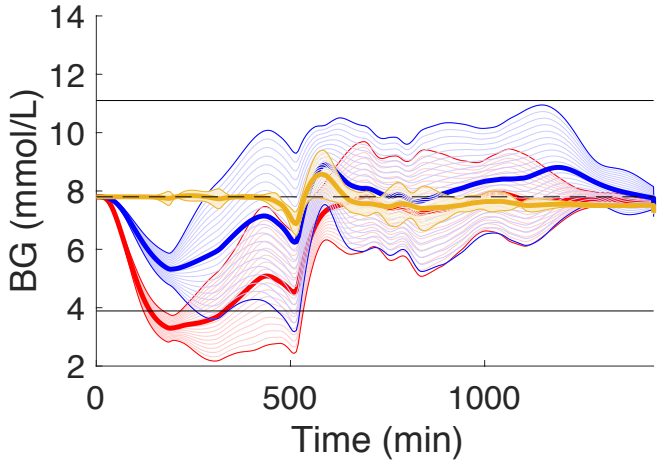
- **Perfect controller:** with exact knowledge of meal and exercise behavior, and full state observability (no state estimation errors)
- **“Hybrid closed-loop” controller:** considers only glucose measurements and not patient behavior

Virtual patient learnt from NHANES database

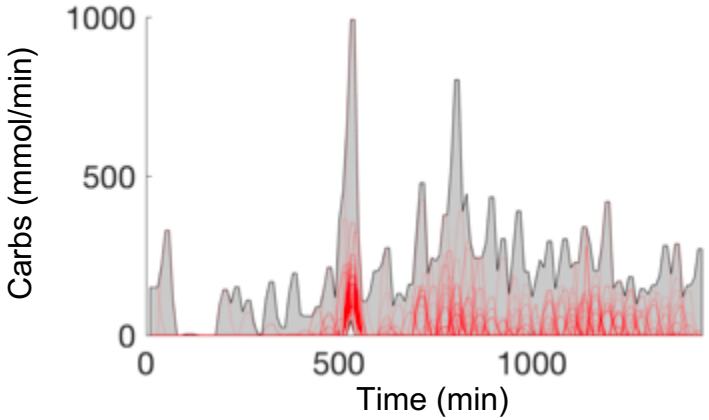
- We learn patient models from CDC's NHANES

National Health and Nutrition Examination Survey

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



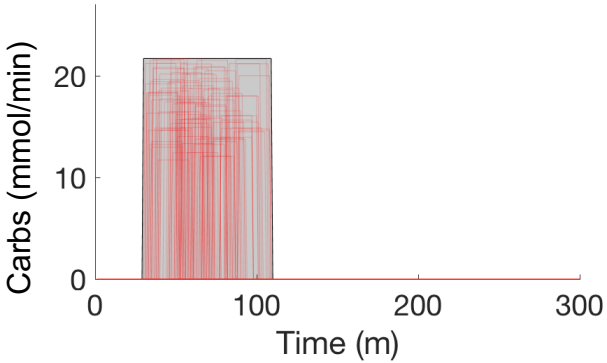
GROUP 1: Carbs-rich breakfast

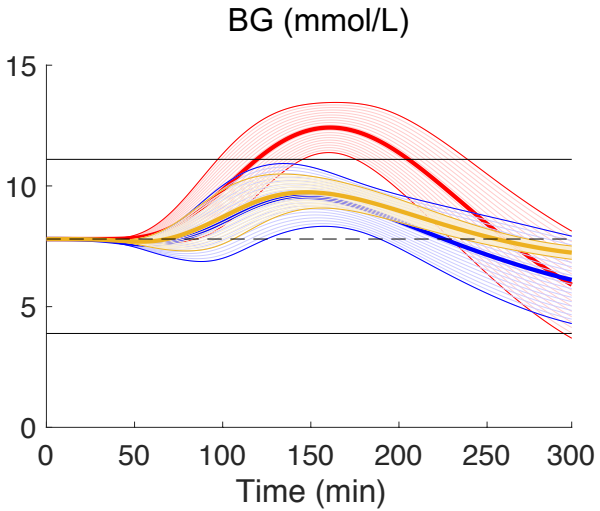


	T hypo	T in range	T hyper
Perfect	0%	100%	0%
Hybrid closed-loop	18.5%	80.97%	0.53%
Robust	**2.02%**	**93.45%**	**4.52%**

Scenario 1 - Meals as expected

Situation where uncertainty set (gray box) is accurate

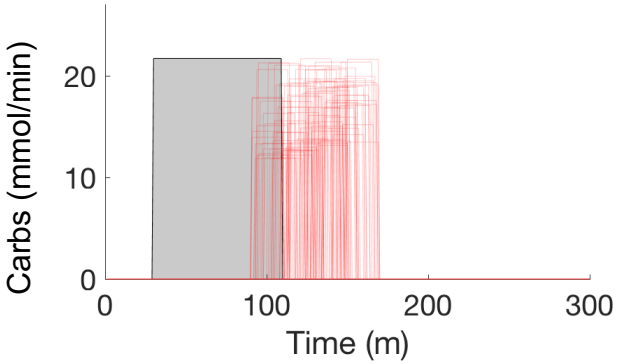


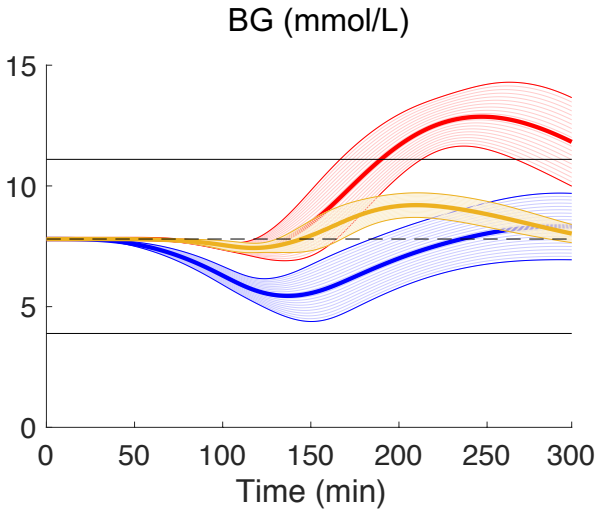


	T hypo	T in range	T hyper
Perfect	0%	99.69%	0.31%
Hybrid closed-loop	1.6%	69.4%	29%
Robust	**0.51%**	**97.7%**	**1.79%**

Scenario 2 - Unexpected delays in meals

Situation where uncertainty set is NOT accurate

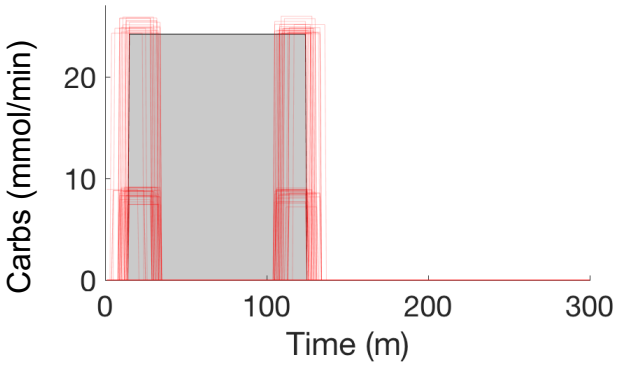


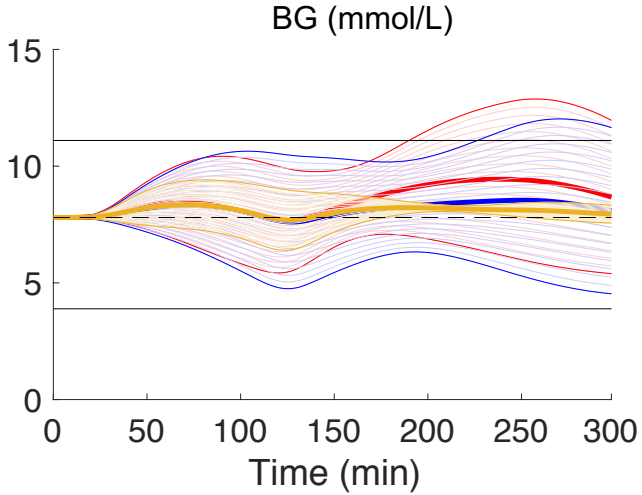


	T hypo	T in range	T hyper
Perfect	0%	100%	0%
Hybrid closed-loop	**0%**	67.25%	32.75%
Robust	0.79%	**99.03%**	**0.18%**

Scenario 3 - Outliers

Situation where the virtual patient behaves far from the average case (both meal size and timing)



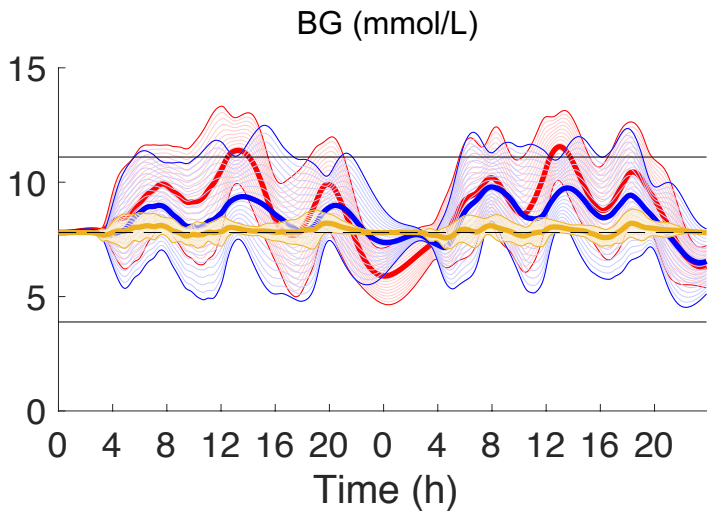


	T hypo	T in range	T hyper
Perfect	0%	100%	0%
Hybrid closed-loop	1.03%	81.51%	17.45%
Robust	**0.28%**	**84.19%**	**15.53%**

Scenario 4 – 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 learning mathematical representation of patient data
- Evaluated on “synthetic” scenarios and real data
- A step towards exploiting data deluge from sensors and smart devices for medical applications

Ongoing and future work

- More advanced patient behavioral model
- Interplay between insulin control and recommendations