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## Meal and Insulin Effects on Blood Glucose Dynamic Modeling

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## Background

Insulin therapy for tight glycemia regulation in T1DM strongly depends on patients daily decisions about insulin delivery adaptations. Factors to be considered in the decision process include health status, current BG, target BG, insulin sensitivity, diet and foreseen activities. One of the main limiting factors in improving glucose control is the lack of a precise description of meal and insulin intake effects on blood glucose. Knowing magnitude and duration of such effects would be useful not only for patients and physicians but also for the development of a controller targeting glycemia regulation.

## Objective

The purpose of this study was to propose physiological relevant yet parsimonious models for the description of carbohydrate and insulin actions on blood glucose in T1DM patients.

## Data

Under the aegis of the DIAdvisor<sup>TM</sup> project [2], 22 T1DM subjects (17 males and 5 females, age  $42.2 \pm 13.1$  [yr], disease duration  $18.4 \pm 11.5$  [yr], BMI  $24.2 \pm 2.6$  [kg/m<sup>2</sup>], 12 MDI and 10 CSII, HbA1c  $7.4 \pm 1.1$  [%], total daily insulin  $41.5 \pm 11.7$  [IU]) participated in a novel clinical trial. Admitted at the clinical investigation center from 7:00 am to 1:00 pm, fasting from the midnight, equipped with a Dexcom Seven Plus CGMS for interstitial glucose samples and a HemoCue Glucose Analyzer for capillary blood glucose measurements, they were served a standardized breakfast (40 [g] carbohydrate) at 8:00 am. The patients calculated and noted on their personal logbook the amount of insulin needed to cover this meal, based on the outcome of the HemoCue meter at the start of the meal. The insulin bolus was administered 2 hours later. Blood samples were drawn every 10 minutes for the 3 hours following the meal intake and every 20 minutes otherwise to assess glucose concentration by means of a Yellow Spring Instrument (YSI) 2300 STAT Plus blood glucose analyzer. Two weeks later the same meal test was repeated.

## Methods

Second order linear transfer function models with time delays were proposed to approximate the behaviour of glucose in response to meal and insulin intakes. The time delays accounted for food transportation and absorption along the gastro-intestinal tract and insulin transit from the subcutaneous tissues to plasma. The other parameters could be related to glucose tolerance and insulin sensitivity or resistance. Numerical values for the parameters appearing in the models were identified from the first test data by means of system identification techniques.

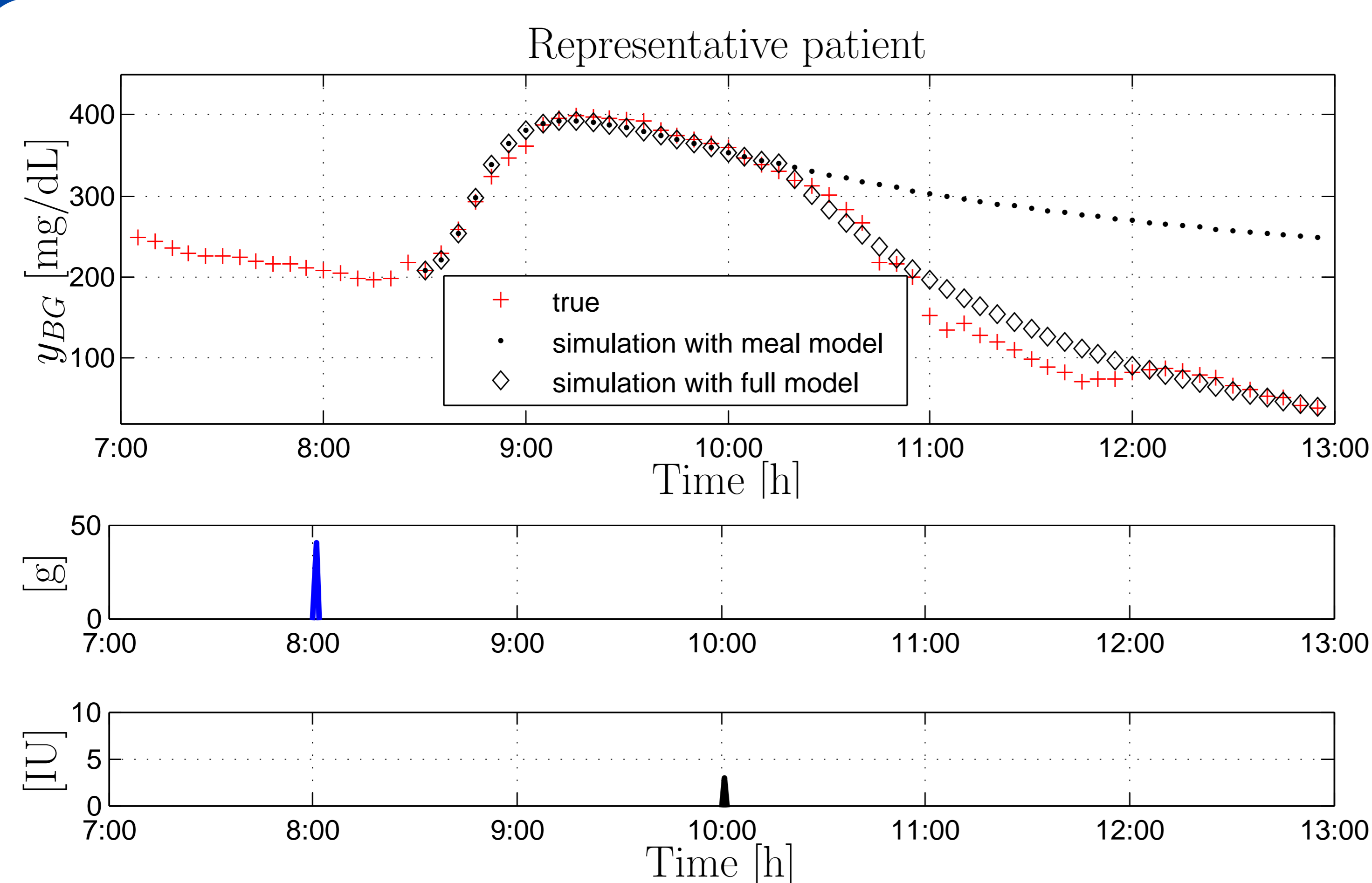


FIGURE 1: Patient UNIPD219. Top Actual CGMS (star) vs. simulated breakfast impact (dot) and simulated joint meal and insulin intakes (diamond) [mg/dL]; Center Carbohydrate intake [g]; Bottom Insulin bolus [IU]. All the measurements vs. time of the day [h]

## Results

Performances were evaluated comparing the actual BG with the model output and resulted in a mean RMSE of 12.44 [mg/dl] on estimation data and 54.45 [mg/dl] on validation data for meal modeling and of 9.88 [mg/dl] on estimation data and 115.78 [mg/dl] on validation data for insulin modeling.

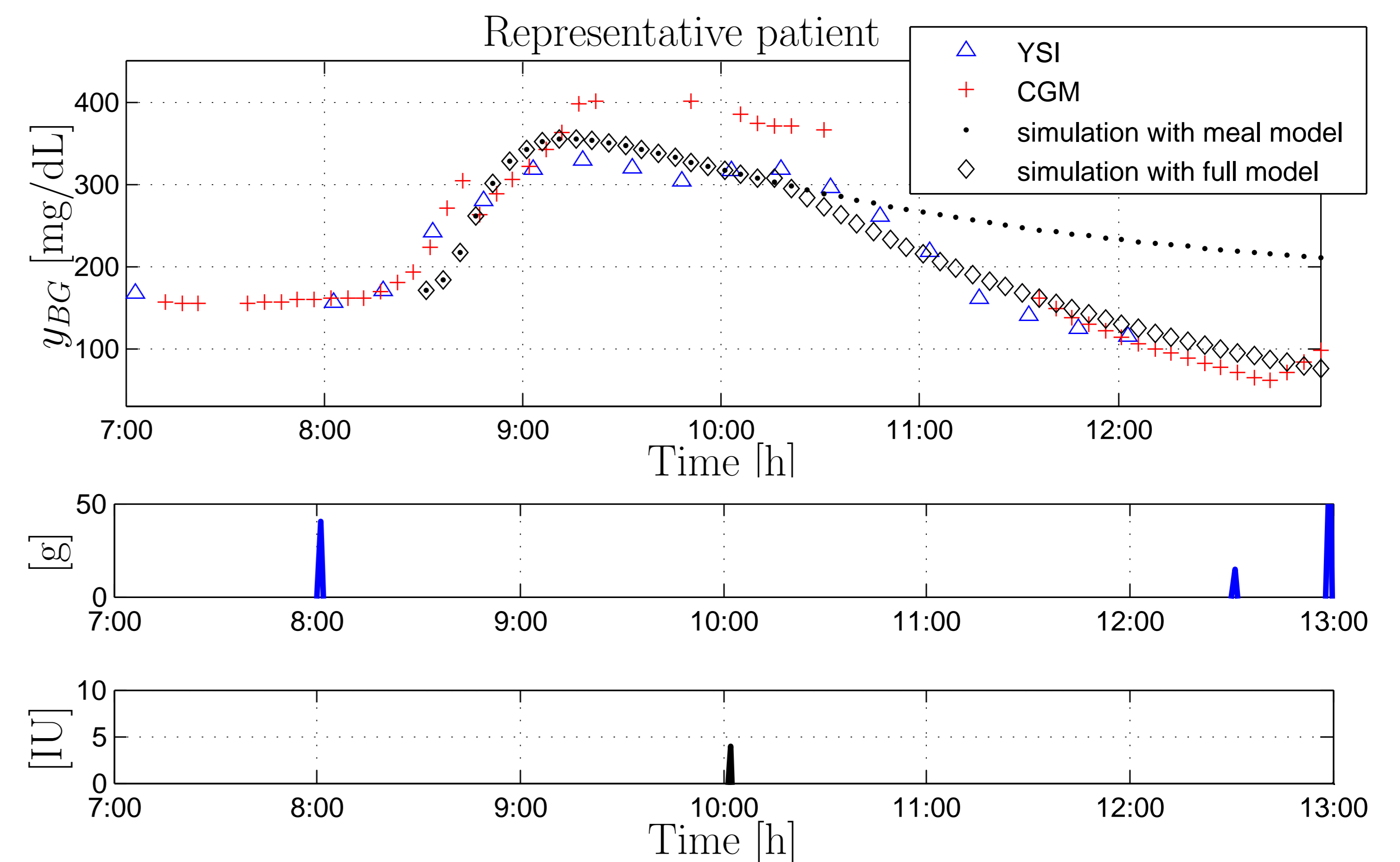


FIGURE 2: Patient UNIPD219. Cross validation. Top Actual CGMS (cross) and actual YSI (triangle) vs. simulated breakfast impact (dot) and simulated joint meal and insulin intakes (diamond) [mg/dL]; Center Carbohydrate intake [g]; Bottom Insulin bolus [IU]. All the measurements vs. time of the day [h]

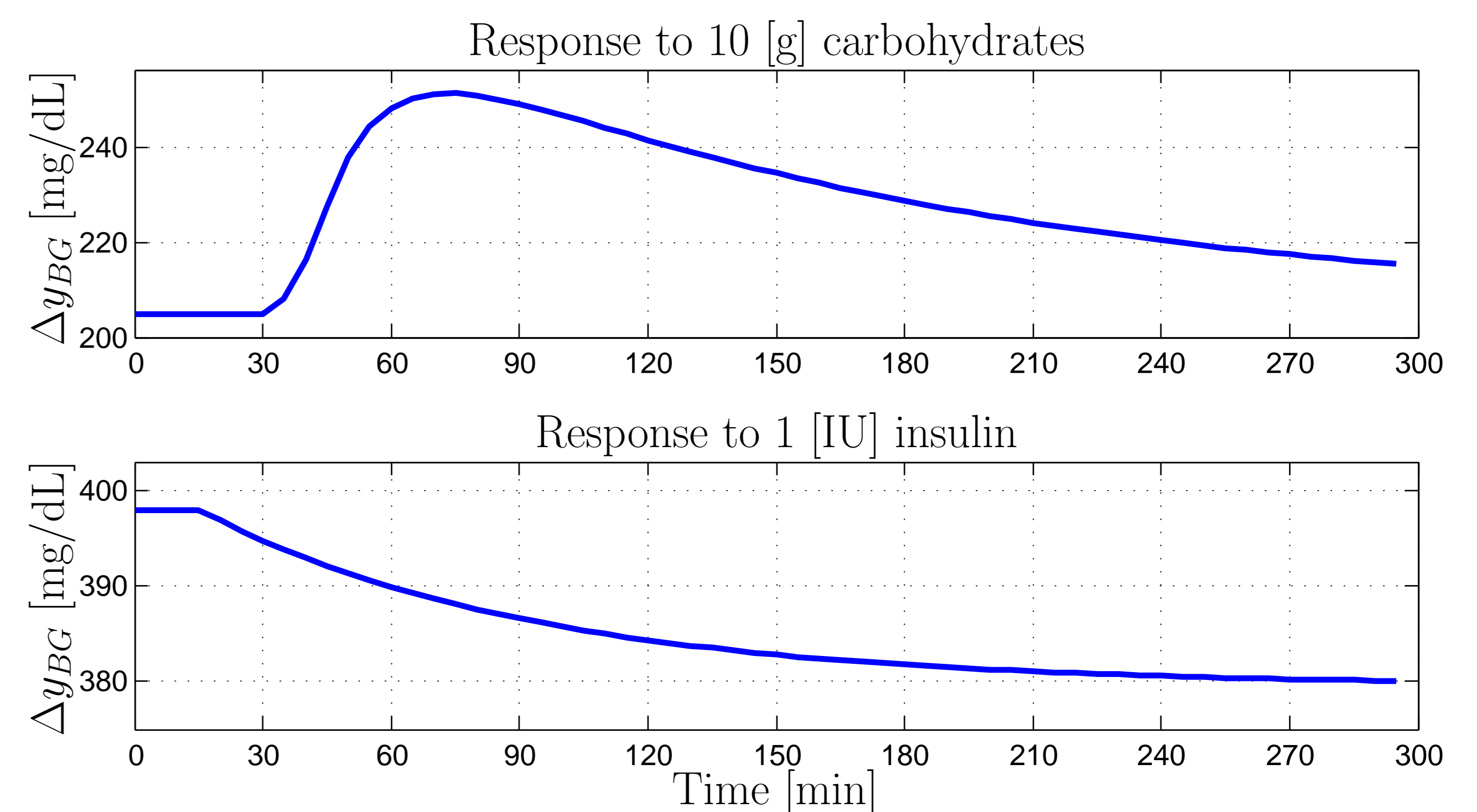


FIGURE 3: Patient UNIPD219. Response to Top 10 [g] of carbohydrate Bottom 1 [IU] of insulin. Blood glucose excursion [mg/dL] vs. time [min]

## Discussion

The choice of the model structure was motivated by inspection of the data series for the available 6 hours test with a physiologically sound interpretation. Despite the simple structure the models are able to sufficiently describe the main dynamics of the gluco-regulatory system. The parameters in the models are linked to clinical variables. Model responses to 10 [g] of carbohydrate and 1 [IU] of insulin were considered physiologically plausible (Fig. 3), resulting compatible with experimental evidence. The inputs were considered impulse-formed, the only information required by the identification method being the size of the meal and of the insulin intakes, retrieved from the patients logbook. Estimation and validation were performed on separate sets of data, collected at least two weeks apart. Intra-patient variability was observed by cross-validation (Fig. 2).

## Conclusions

The impact of a carbohydrate intake and an insulin injection on blood glucose dynamics were quantified by means of system identification techniques.

## Acknowledgments

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## References

- [1] M. Cescon. Modeling and Prediction in Diabetes Physiology. *PhD Thesis*, Department of Automatic Control, Lund University, Sweden.
- [2] www.diadvisor.eu, FP7 IST-216592.