

Post-prandial Plasma Glucose Prediction in Type I Diabetes Based on Impulse Response Models

F. Ståhl, R. Johansson and Eric Renard

Abstract—In this paper the impact of different meals and rapid insulin were estimated as Finite Impulse Response Models from a data set of 18 patients. Based on these models short-term individualized predictors were tested for 20 and 60 minute prediction. The predictors were evaluated using Clarke Grid Analysis and had on average more than 94 % and 75 % in the A zone and less than 1 % and 3 % in the errorous C/D/E zones, which in comparison to other published results is competitive.

I. INTRODUCTION

Type I Diabetes Mellitus is a chronic metabolic disease characterized by impaired plasma glucose regulation normally treated with intense insulin therapy. To determine the quantity and timing of the insulin injections various approaches are used. Currently, mostly qualitative and semi-quantitative models and reasoning are used to design such a therapy. The closed-loop regime is evolving as a powerful alternative using a Continuous Glucose Monitor (CGM) sensor together with an insulin pump [1]. Whichever approach is considered a model of the impact of the main control variables is of outmost importance. To this purpose, this paper addresses the identification of the impact of different meals and rapid insulin on plasma glucose dynamics from patient data. Such models could be used for the design and implementation in a closed-loop context [2], or as a predictive tool per se to facilitate for patients and clinicians to understand the consequences of different actions [3], [4], [5], [6], [7]. In the European DIAdvisor project such a predictive advisory tool is pursued [8].

II. DATA ACQUISITION

The data were collected within the European FP7 project DIAdvisor at the Montpellier University Hospital [8]. The study was conducted in-hospital during a three-day visit. Standard meals were served for breakfast (08:00), lunch (13:00) and dinner (19:00), the amount of carbohydrates included being about 45, 70 and 70 grams, respectively. No specific intervention on the usual diabetes treatment was scheduled during the study since a trueful picture of normal blood glucose fluctuation and insulin-glucose interaction was pursued. The patients, thus, adapted their insulin therapy according to meter-provided glucose measurements as they used to do. In total 30 patients participated. Out of these one patient withdrew, and of the remaining, 18 patients could be selected

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for identification according to the outlined approach, based on data quality aspects.

A. Signals

Data collection consisted of CGMS measurements obtained with the Abbott FreeStyle Navigator™[9], fingerstick measurements with a personal glucose meter (HemoCue™[10], average 38 measurements/day), and carbohydrate intake and insulin administration reported in a personal patient logbook. The HemoCue measurements were interpolated using a shape preserving interpolation method (pchip in Matlab [11]) to retrieve an equidistant sampled signal.

In Fig. 1, an example of a patient data set can be seen.

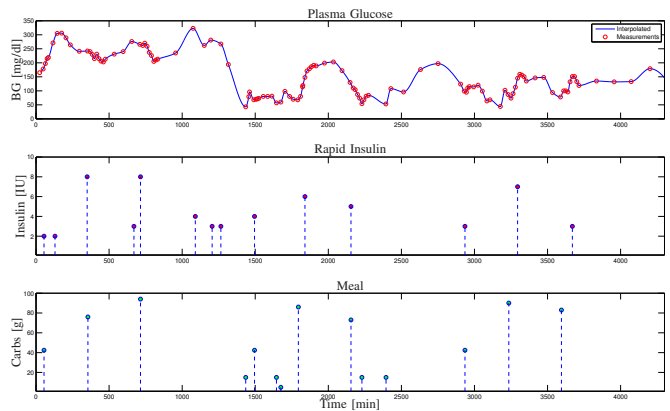


Fig. 1. Example of data set (patient 0103). Upper plot: Interpolated HemoCue measurements, Middle plot: Injections of Rapid Insulin, Lower plot: Ingested Carbohydrates.

III. MODELS AND IDENTIFICATION METHOD

Due to the lack of data and the opposing effects of meal and insulin, empirical identification of each module is difficult, often resulting in merged models or that assumptions have to be made on intermediate model levels. Previous attempts at meal and insulin impact modeling and identification often rely on structured models, where compartment models dominate. A nice summary of PK models for insulin diffusion following a subcutaneous injection is found in [12]. Modeling the digestion process and the flux of glucose from the gut from a meal has been initiated in [13]. In this paper no such models are imposed. Instead, black-box Finite Impulse Response (FIR) models were considered for each input.

$$\Delta y_k = \sum_{i=k-N_1}^{k-1} H_i^1 \cdot u_i^1 + \sum_{j=k-N_2}^{k-1} H_j^2 \cdot u_j^2 \quad (1)$$

where Δy_k is the difference in plasma glucose between sample k and $k-1$, u_k^1 and u_k^2 are the insulin and meal intakes at sample k , and H_i^1, H_j^2 are the impulse response terms for each inputs.

To guarantee qualitatively correct responses, i.e., negative response to insulin infusion and positive for meals, the identification was constrained giving the following least-squares optimization problem over the time set $[T_1, T_N]$.

$$\hat{p} = \underset{p}{\operatorname{argmin}} p^T Q p \quad (2)$$

$$Q = [-\Delta Y \ U_1 \ U_2]^T \cdot [-\Delta Y \ U_1 \ U_2] \quad (3)$$

$$A p \leq 0 \quad (4)$$

where $\hat{p} = [1 \ H_1^1 \dots H_{N_1}^1 \ H_2^1 \dots H_{N_2}^2]$, $\Delta Y = [y_1 - y_0 \dots y_N - y_{N-1}]^T$, $U_1 = [u_1^1 \dots u_N^1]^T$, $U_2 = [u_1^2 \dots u_N^2]^T$ and A is a diagonal matrix of 1:s and -1 :s in relevant positions.

A. Insulin and Meal Impulse Estimation

The estimation for each patient was divided into two parts; identification of the insulin response and thereafter the impulse response of each meal. To estimate the insulin response the entire data set was considered. This yields an average insulin and meal impulse response. The average meal response was discarded as a dummy parameter set, whereas the average insulin response was considered as the estimate of the insulin impact.

Thereafter each meal was considered separately. Using the estimated insulin impulse response model, the residuals in glucose change corresponding to the meal impact were used to estimate each meal impulse response. For each type of meal (breakfast, lunch, dinner), the average impulse response was thereafter retrieved.

IV. EVALUATION CRITERIA

To evaluate the predictive performance of the models 20 and 60 minute predictions were considered. The correspondence to the reference HemoCue measurements were assessed using the Clarke Pointwise Error Grid Analysis (pCGA) [14], standard deviation and maximum absolute error.

V. RESULTS

A. Impulse Responses

In Fig. 2 the average impulse responses to the different kinds of inputs can be seen for each patient as well as over the entire population.

B. Prediction

The predictive capacity of the model was evaluated for all patients using a 20 minute and a 60 minute predictor. In Table I the different metrics are summarized. As reference a zero-order hold (ZOH) predictor with the same prediction horizons was given. An example of the 20 and 60 min predictions for each meal using the patient specific average meal input models can be found in Fig. 3.

An example of a Clarke Grid plot is found in Fig. 4.

TABLE I
PERFORMANCE EVALUATION FOR THE 20 AND 60 MINUTE PREDICTOR USING AVERAGE MEAL MODELS COMPARED TO CORRESPONDING ZERO ORDER HOLD PREDICTIONS (ZOH).

	pCGA[%]			STD	max e
	A	B	CDE	[mg/dl]	[mg/dl]
Model 20					
mean	94.2	5.0	0.8	11.8	48
std	8.2	7.1	2.3	12.0	49.2
ZOH 20					
mean	86.2	12.5	1.3	19.0	75.7
std	13.4	11.6	2.9	19.4	77.6
Model 60					
mean	75.7	21.7	2.6	22.1	86.2
std	23.9	20.8	8.0	22.8	91.2
ZOH 60					
mean	51.3	41.3	7.4	41.4	141
std	23.8	20.3	9.7	43.0	147

VI. DISCUSSION

A. Impulse Estimates

The insulin impulse responses differ, especially in terms of magnitude, among different patients, and this difference is expected due to patient specific insulin kinetics and dynamics, including insulin sensitivity. Apart from a few outliers, the dynamic response in temporal aspect seems to be more similar though. Looking at the meal impulse responses the breakfast seems to be a somewhat homogeneous meal and could maybe serve as a meal classifier. It is also significantly different from the other meals, and this is probably due to a combination of factors, such as the so called dawn phenomena [15], to the high content of carbohydrates of low complexity typically digested for breakfast, and probably to the fact that many people tend to have the same breakfast routines every day. The lunch and dinner meals seem to be more heterogenous, with a slightly faster response to the lunch meal. It seems that other meal markers than just the attributes *lunch* and *dinner* need to be used to classify these meals. As the prediction results indicate, however, some information, at least on a patient-specific basis, could be retrieved from this classification.

B. Prediction

The predictors are generally doing well, clearly outperforming the ZOH predictor, and the 20-minute predictor keeps up with with rapid glucose changes in all regions of glucose levels with a CGA-value of 94.2 % in zone A and less than 1 % in the deviating zones. The relatively large standard deviations of both the C/D/E score as well as the maximum absolute error may indicate that the general performance is good but that these average metric values are heavily influenced by a few poorer predictors. Further analysis is thus required to evaluate the overall population performance. In comparison to earlier published results on prediction based on neural networks [7], AR-models [16] and sub-space identification [5] the prediction is competitive. Short-term predictors will be utilized in the DIAdvisor project for advisory purposes [8].

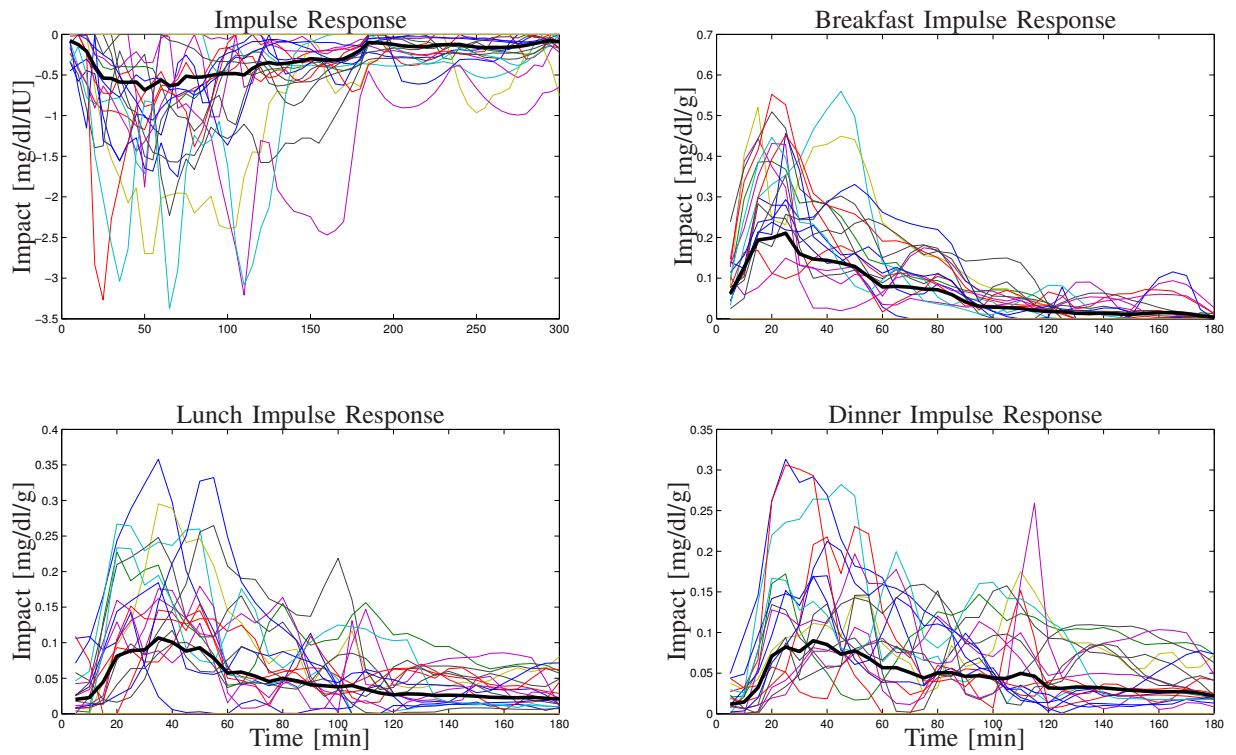


Fig. 2. Thick Solid line: Average over all patients. Upper Left: Average Impulse Response to 1 IU of rapid insulin. Upper Right: Average Impulse Response to 1 gram of Breakfast Carbohydrate. Lower Left: Average Impulse Response to 1 gram of Lunch Carbohydrate. Lower Right: Average Impulse Response to 1 gram of Dinner Carbohydrate.

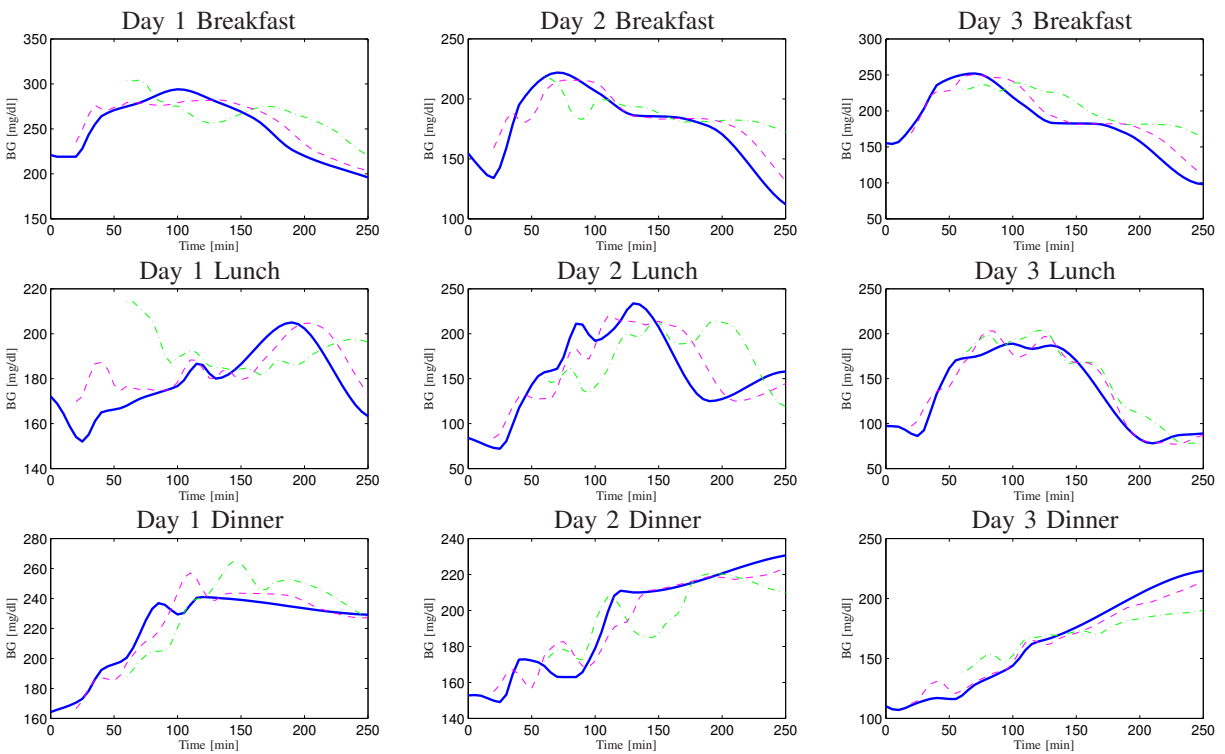


Fig. 3. Solid line: Interpolated Plasma Glucose Measurements (BG), Magenta dashed: 20 minutes prediction, Green dash-dotted: 60 minute prediction. (Patient 0125).

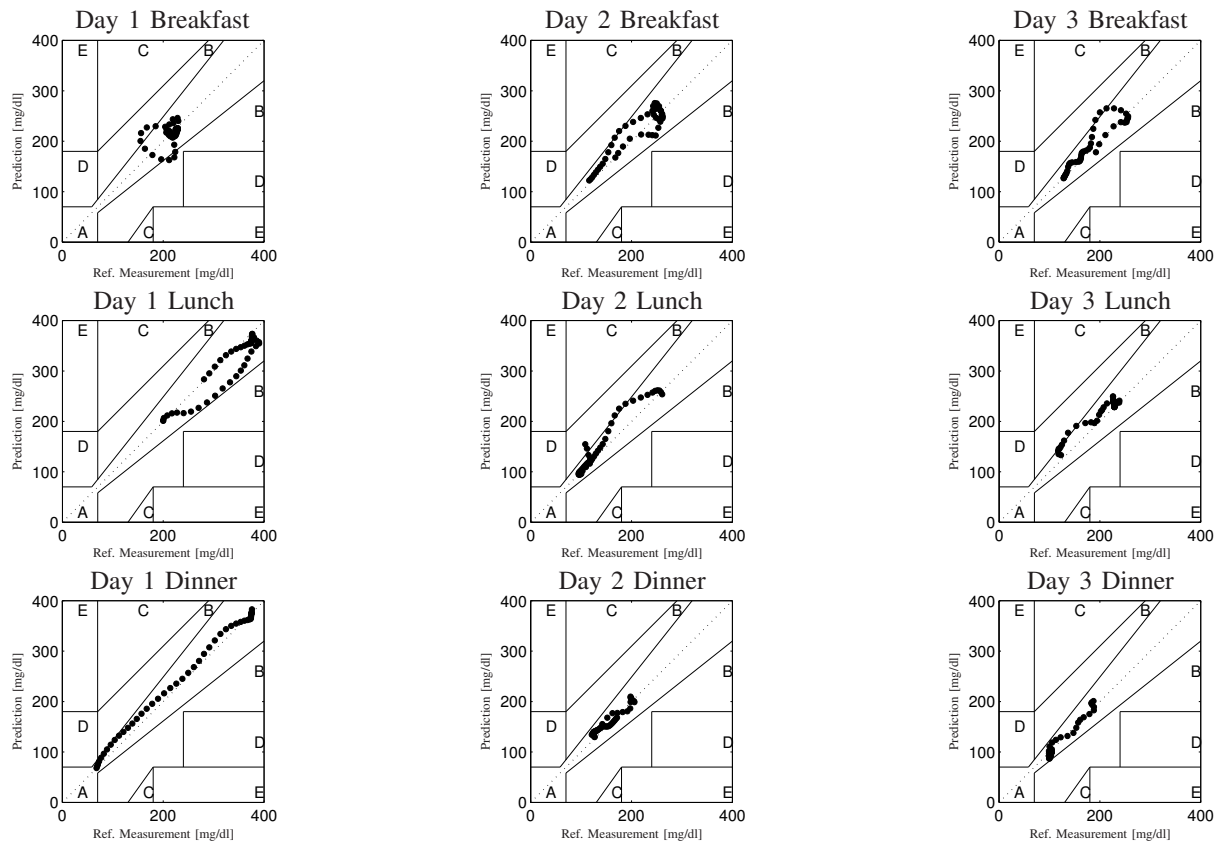


Fig. 4. Clarke Grid Error Plot for a 20-minute prediction (patient 0114). Notice especially the width of excitation for dinner day 1.

VII. CONCLUSIONS

This paper addressed the estimation of meal and insulin impact on plasma glucose dynamics in type I diabetic patients. The results indicate that the outlined methodology could be used to estimate patient-specific FIR models of different meals and insulin response. Implementing these models in a predictor enables reliable short-term predictions of post-prandial glucose excursions following different kinds of meals. Further work on glucose prediction and control will be pursued in the European FP7 IST-216592 DIAdvisorTM project [8].

VIII. ACKNOWLEDGMENT

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