Effect of Carbohydrate Counting Errors on Glycemic Control – A Hybrid In Silico Study

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Introduction

Most patients with type 1 diabetes mellitus (T1DM) use methods from Advanced Carbohydrate Counting (ACC) to determine their bolus insulin requirements. They calculate their bolus insulin needs using the following simple formula:

$$BI = \frac{CHO}{CIR} + \frac{BG - BG_{target}}{ISF} - IOB \tag{1}$$

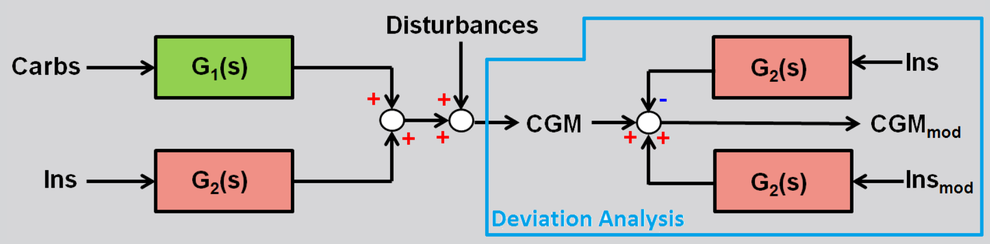
with BI, the required bolus insulin amount in IU, CHO, meal carbohydrates in g, BG, the measured preprandial blodd glucose (BG) value in mg/dl, BG_{target}, the target postprandial BG in mg/dl and IOB, the insulin-on-board in IU.
The quality of the BG control with ACC is directly linked to the ability of a patient to correctly estimate the carbohydrate amount of meals. It is well known that many T1DM patients have difficulties to correctly estimate meal carbohydrates. However, there is a scarcity of data on how exactly these estimation errors affect glycemic control.

Methodology

The effect of carb counting errors on glycemic control during basal-bolus-therapy is studied by means of so-called Deviation Analysis calculations [1]. Furthermore, it is analyzed how inaccuracies in the carbohydrate estimates affect the insulin therapy settings. This is done using the previously published Adaptive Bolus Calculator (ABC) algorithm [2,3] which can retrospectively identify estimates for CIR and ISF from recorded data.

- **Deviation Analysis**

  The basic workflow for performing Deviation Analyses is displayed in the figure below. The rough idea is to assume a model of insulin action, a transfer function model $G_2(s)$ in the case of the figure below, and then subtract the effect of the measured insulin (Ins) and add the effect of the proposed insulin dosing (Ins_{mod}) to measured continuous glucose monitoring (CGM) traces.



  For this work the nonlinear Deviation Analysis approach presented in [1] is used.

- **Adaptive Bolus Calculator (ABC)**

  In [2,3] the ABC method is proposed to identify diurnal profiles of insulin action from standard diabetes data, *i.e.* CGM data and recordings about meal carbohydrates and bolus insulin injections. In order to do so, a simple, control oriented model is used to describe the effect of carbohydrates and bolus insulin on the glucose concentration:

$$\text{IG}(s) = \frac{K_1}{(1+s\cdot T_1)^2\cdot s}\cdot\text{Carbs}(s) + \frac{K_2}{(1+s\cdot T_2)^2\cdot s}\cdot\text{Ins}(s) \tag{2}$$

  where parameters K_1 and K_2 are assumed to be daytime-dependent.

  Estimates for (patient and mealtime specific) CIR and ISF can be computed from the identified model parameters:

  – the identified K_2/K_1 values correspond to CIR
  – K_2 has the same meaning as ISF

Hybrid In Silico Evaluation

- **Description of the dataset**

  For the current work data from a recent clinical trial performed at the Institute for Diabetes Technology, Germany is used [4]. In this clinical trial 37 subjects with T1DM on basal bolus therapy spent seven days hospitalized. During this time the following data were collected:

  – CGM signals
  – Injected/infused insulin amounts and estimated carbohydrate amount of meals

  Additionally, meals have been analyzed by a dietitian who retrospectively calculated the carbohydrate content of the meals. These values are used for the Deviation Analyses.

- **Description of the simulation setup**

  The effect of carb counting errors has been simulated in Deviation Analyses. The "estimated" carbs to be used in (1) have been computed from the calculated carbs according to:

$$\text{carbs}_{\text{est.,i}} = \text{carbs}_{\text{calc.,i}} \cdot (1 + \text{bias} + e_i) \tag{3}$$

  with

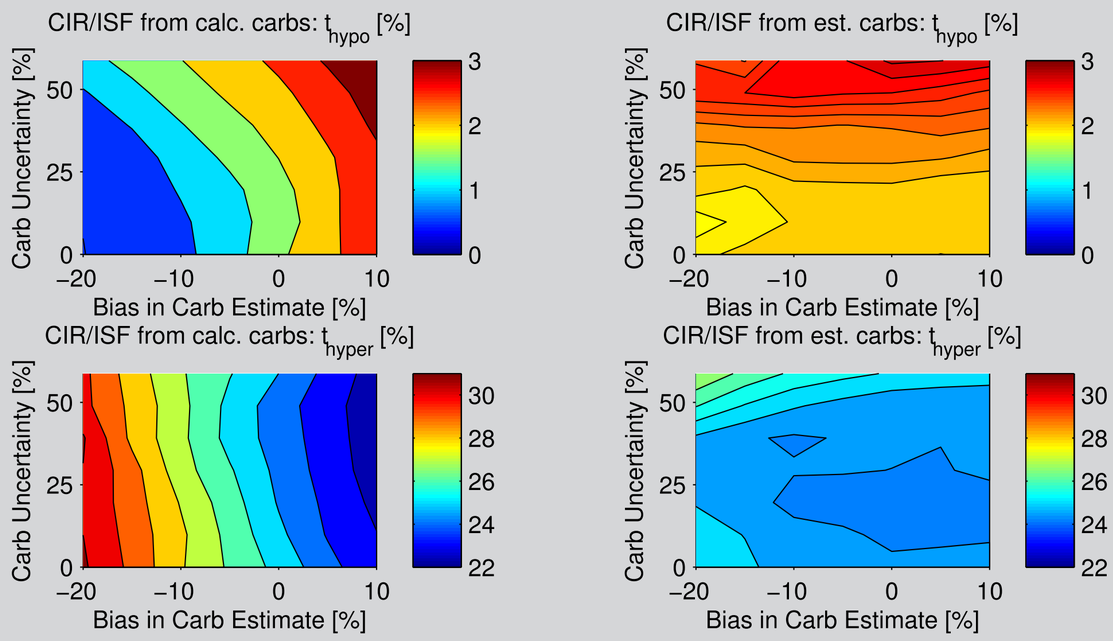
$$e_i \sim \mathcal{N}(0, (\text{uncertainty}/1.96)^2) \tag{4}$$

  In the Deviation analyses different values for bias (between -20 % and +10 %) and uncertainty (between 0 % and 60 %) in the carb estimates have been simulated. The CIR and ISF values used for calculating the bolus insulin have been estimated with the ABC approach. Two cases have been considered:

  – Using the calculated carbs for estimating CIR and ISF with the ABC approach, but the estimated carbs for calculating the bolus insulin in the Deviation Analyses.
  – Using the estimated carbs for both, identifying the CIR and ISF settings with the ABC approach and calculating the bolus needs in the Deviation Analyses.

Results

In the figure below average results (average over all 37 patients) are shown for time in hypoglycemia (t_{hypo}, upper panels) and time in hyperglycemia (t_{hyper}, lower panels) for both analyzed cases (left panels vs right panels).



Conclusion

Systematic estimation biases in carbohydrate counting hardly affect the results if those biases are implicitly accounted for in the CIR and ISF settings (as can be expected to be usually the case for T1DM patients; corresponds to the second analyzed case in the Deviation Analyses). Otherwise they can lead to a strong increase for time in hypoglycemia/hyperglycemia. Random carb counting inaccuracies on the other hand always lead to a certain deterioration of glycemic control, but ACC is relatively robust towards this type of inaccuracies.

References

[1] Reiterer, F., Reiter, M., del Re, L. (2017) *Nonlinear approach to virtual clinical trials for insulin dosing systems*. In: Proceedings of the 2017 American Control Conference: 586-591.
[2] Reiterer, F., Kirchsteiger, H., Freckmann, G., del Re, L. (2015) *Identification of diurnal patterns in insulin action from measured CGM data for patients with T1DM*. In: Proceedings of the 2015 European Control Conference, 1-6.
[3] Reiterer, F., Kirchsteiger, H., Assalone, A., Freckmann, G., del Re, L. (2015) *Performance assessment of estimation methods for CIR/ISF in bolus calculators*. In: Proceedings of the 9th IFAC Symposium on Biological and Medical Systems: 231-236.
[4] Zschornack et al. *Evaluation of the performance of a novel system for continuous glucose monitoring*. Journal of Diabetes Science and Technology, 7(4): 815-823.