A Predictive Algorithm for the Administration of Corrective Insulin Bolus for Decision Support Systems in Type 1 Diabetes

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1. INTRODUCTION

Type 1 diabetes (T1D) is a chronic **autoimmune disease** characterized by the lack of insulin production and the inability to keep blood glucose (BG) level in a safe range ([70-180 mg/dL]). **Continuous glucose monitoring** (CGM) devices, **portable pumps** for insulin infusion (CSII) and **mobile applications** enable the development of **decision support systems** (DSSs) that can **support patients** in their decision-making process, considerably improving T1D management.

2. AIM

To propose a **novel algorithm for the preventive administration of corrective insulin boluses (CIBs)** to be used in T1D DSSs.

3. THE NEW PREDICTIVE ALGORITHM (pCIB)

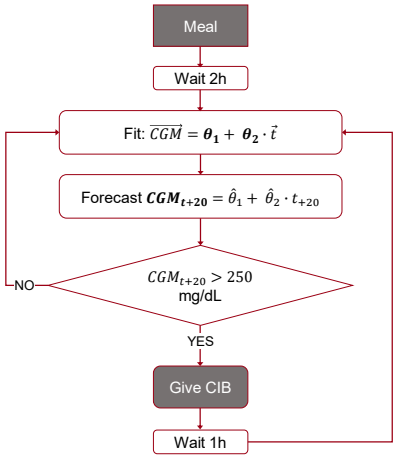

Fig.1 New predictive algorithm's flow-chart.

The flow-chart of the pCIB algorithm is reported in Fig.1. In details:

1. wait 2 hours after the meal
2. every time a new CGM sample is available
   a) a first-order polynomial is fitted on the CGM samples available in the last 15 minutes

$$\overrightarrow{CGM} = \theta_1 + \theta_2 \cdot \vec{t}$$

   parameters θ_1 and θ_2 are estimated through the least square method.
   b) the fitted model is used to forecast the future CGM value 20-minute ahead in time

$$CGM_{t+20} = \hat{\theta}_1 + \hat{\theta}_2 \cdot t_{+20}$$

   c) IF the predicted CGM_{t+20} is above the severe hyperglycemic threshold (i.e., 250 mg/dL) a preventive CIB is administered according to the standard formula (SF):

$$CIB = \frac{CGM - BG_{target}}{CF} - IOB$$

   where
   - CGM is the current BG measured via CGM sensor
   - BG_{target} is the patient target BG level
   - CF is the patient correction factor
   - IOB is the insulin on board, calculated from insulin inputs of the previous 12 hours

   and wait at least 1 hour before eventually computing another CIB.
   OTHERWISE, return to point a) with the next CGM sample.

As a comparator, we implemented the heuristic-based methodology proposed by Aleppo et al. [1], which suggest insulin correction starting from SF and according to BG and its rate of change (ROC) after at least 2 hours from meal.

4. DATASET & ASSESSMENT PROCEDURE

The assessment was performed using ReplayBG [2], a novel tool that retrospectively assesses the outcome of alternative therapy regimes on real-world T1D data. It works in two steps: i) a physiological model of glucose-insulin dynamics is identified from CHO, insulin and CGM data already collected by the individual; ii) the identified model is used to simulate the glucose concentration that should have been obtained, in the same individual and in the same time window, by adopting an alternative insulin therapy.

The pCIB and Aleppo et al. have been tested using ReplayBG on the OhioT1DM dataset [3]: a total of 15 days (considering form 1 hour before breakfast until 6 hours after dinner) has been extracted.

For each individual and for each algorithm, we calculated: Time In Range (TIR, i.e., 70 < BG < 180), Time Above Range (TAR) and Time Below Range (TBR).

5. RESULTS

Result on a representative subject

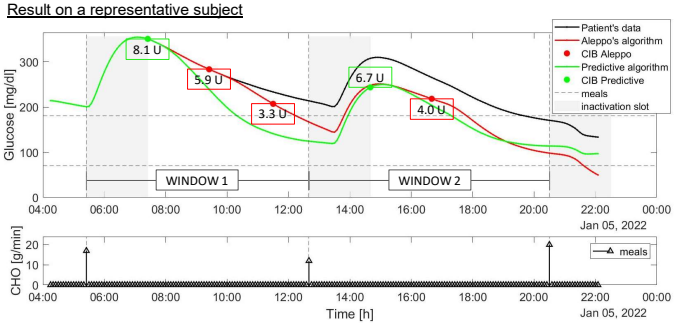

Fig.2 Comparison between patient's data (black), simulated CGM with Aleppo's methodology (red) and pCIB algorithm (green) in subplot 1; ingested meals in subplot 2

The predictive algorithm pCIB (green) **acts proactively** then Aleppo (red) after the 2h waiting window (grey area)

- Window 1 – from breakfast (05:25) to lunch (12:40): pCIB gives **1 bolus only** of 8.1 at time 07:25, vs 2 boluses (5.9 U, 3.3 U at time 09:25, 11:30, respectively) of Aleppo, driving more rapidly BG into target (70 – 180 mg/dL) and **avoiding unnecessary CIBs** when glycemia is already lowering.
- Window 2 – from lunch (12:40) to dinner (20:30): both algorithms generate 1 CIB, but pCIB trigger it earlier, driving BG into target and avoiding hypoglycemia

Results on the whole dataset

Tab.1 Distributions of TIR, TAR and TBR in terms of median and [IQR] ranges for Aleppo and pCIB.

Algorithms	*Temporal metrics*		
	TIR [%]	TAR [%]	TBR [%]
Aleppo's	41.86 [27.55, 52.96]	50.23 [38.67, 56.62]	0.00 [0.00, 18.17]
New Predictive Algorithm (pCIB)	**49.77 [41.47, 58.01]**	**48.23 [38.61, 58.29]**	**0.00 [0.00, 0.35]**

Through pCIB algorithm, median values of TIR and TAR have been **significantly** increased and decreased (respectively) compared to Aleppo's approach, without leading to any increase to TBR due to the additional insulin delivered.

6. CONCLUSIONS

We proposed a new predictive algorithm (pCIB) for the generation of preventive CIBs, which proved to be effective in decreasing hyperglycemia duration without increasing the time in hypoglycemia. Future works will further validate the proposed methodology on a larger dataset.

REFERENCES:
[1] Aleppo, Grazia, et al. "A practical approach to using trend arrows on the Dexcom G5 CGM system for the management of adults with diabetes." Journal of the Endocrine Society 1.12 (2017): 1445-1460.
[2] Cappon, Giacomo, et al. "ReplayBG: a Simulation Methodology to Retrospectively Assess Therapies on Type 1 Diabetes Data." submitted to IEEE Transactions on Biomedical Engineering, 2021.
[3] Marling, Cindy, and Razvan Bunescu. "The OhioT1DM dataset for blood glucose level prediction: Update 2020." CEUR workshop proceedings. Vol. 2675. NIH Public Access, 2020.

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