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A New Decision Support System for Type 1 Diabetes Management *

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***Abstract*—Type 1 diabetes (T1D) is a chronic life-threatening metabolic condition which needs to be accurately and continuously managed with care by multiple daily exogenous insulin injections, frequent blood glucose concentration monitoring, ad-hoc diet, and physical activity. In the last decades, new technologies, such as continuous glucose monitoring sensors, eased the burden for T1D patients and opened new therapy perspectives by fostering the development of decision support systems (DSS). A DSS for T1D should be able to provide patients with advice aimed at improving metabolic control and reducing the number of actions related to therapy handling. Major challenges are the vast intra-/inter-subject physiological variability and the many factors that impact glucose metabolism. The present work illustrates a new DSS for T1D management. The algorithmic core includes a module for optimal, personalized, insulin dose calculation and a module that triggers the assumption of rescue carbohydrates to avoid/mitigate impending hypoglycemic events. The algorithms are integrated within a prototype communication platform that comprises a mobile app, a real-time telemonitoring interface, and a cloud server to safely store patients' data. Tests made in silico show that the use of the new algorithms lead to metabolic control indices significantly better than those obtained by the standard care for T1D. The preliminary test of the prototype platform suggests that it is robust, performant, and well-accepted by both patients and clinicians. Future work will focus on the refinement of the communication platform and the design of a clinical trial to assess the system effectiveness in real-life conditions.**

***Clinical Relevance*— The presented DSS is a promising tool to facilitate T1D daily management and improve therapy efficacy.**

I. Introduction

Type 1 diabetes (T1D) is a chronic condition characterized by the autoimmune destruction of the pancreatic beta-cells, which are responsible for endogenous insulin secretion and production [1]. This lack of insulin causes blood glucose (BG) concentration to exceed the safe range thus requiring patients to take numerous daily actions to keep it under control avoiding adverse hypoglycemic (BG < 70 mg/dl) and hyperglycemic (BG > 180 mg/dl) events. Clearly, management of T1D is a particularly delicate and difficult task due to the many factors that impact BG concentration such as diet, physical activity, and patients' habits. For this reason, groundbreaking technologies, such as continuous glucose monitoring (CGM) devices, which allows monitoring BG in real-time [2], and continuous subcutaneous insulin infusion pumps (CSII) [3], have been recently introduced to help people with T1D. These technologies, and the consequent availability of large amounts of data collected by both CGMs and CSIIs, enabled the research community to develop new smart tools able to provide patients with proactive and personalized suggestions and advice to improve BG control [4]. Specifically, one main objective is the development of advanced decision support systems (DSS) [5], i.e., composite automated tools that commonly integrate multiple modules, spanning from insulin bolus calculators to BG forecasting algorithm able to generate smart alarms. However, due to the complex nonlinear relationships which characterize the glucose-insulin regulation system, and the peculiar inter-/intra-subject physiological variability, just to mention a few, the development of a fully operational DSS is still an open challenge.

The aim of the present work is to illustrate a novel DSS, for sake of clarity from now on referred to as Padova Decision Support System (PDSS), based on our recently published algorithms for personalized insulin dosing [6], and hypoglycemic prevention [7]. As summarized in Fig. 1, the PDSS is composed of two main entities: a set of modules implementing the algorithmic core of the system, and a communication platform, named IMPACT [8], where PDSS is integrated into. The PDSS modules are currently two: i) an insulin bolus calculator, based on linear regression, to provide optimal and personalized insulin dosing at mealtime, and ii) an algorithm that targets hypoglycemia by suggesting the assumption of rescue carbohydrates in a preventive manner. The IMPACT platform, totally developed in house, is composed of three elements: a mobile app, which runs the PDSS modules, a cloud server, that safely stores patients' data, and a real-time monitoring interface, that enables clinicians to inspect the status of each patient remotely. These three elements exchange data between each other via custom RESTful APIs.

In Section II, we illustrate the PDSS algorithmic core as well as its in-silico evaluation. Details on the IMPACT platform and its implementation are described in Section III. Section IV draws some conclusions and discuss the next steps to improve and eventually validate PDSS.

II. The PDSS Algorithmic Core

A. The Insulin Bolus Calculator Module

The meal insulin bolus (MIB) calculator module is based on a linear regression model recently proposed by Noaro et al. [6], to which the reader is referred for more methodological

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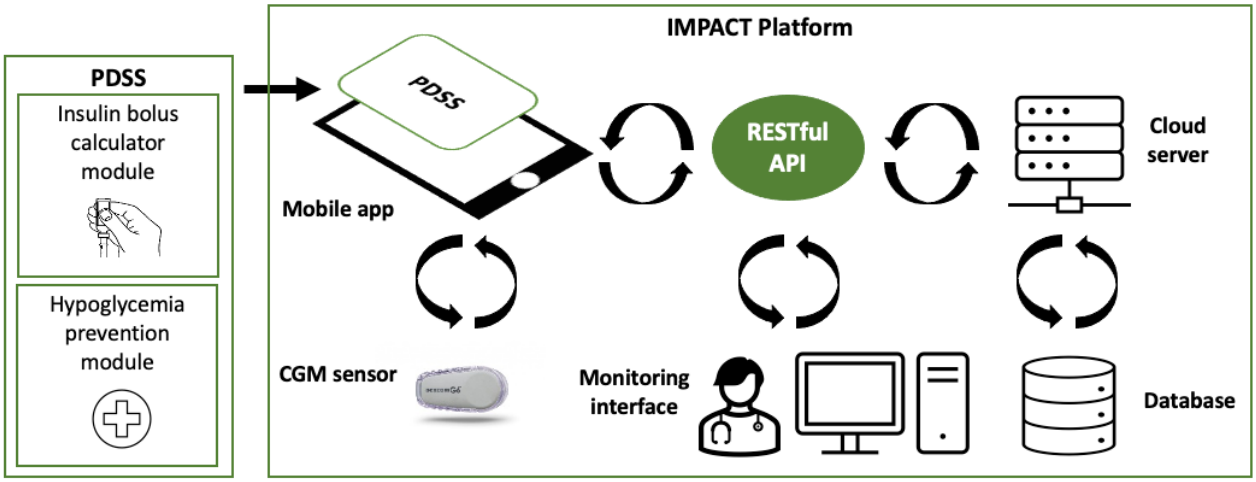

Fig. 1: Overview of PDSS. To the left, the PDSS algorithmic core. To the right the IMPACT platform where the PDSS algorithms are implemented upon.

details and deeper evaluation. The model was developed using a simulated dataset, generated through the UVa/Padova T1D Simulator [9], including multiple single-meal scenarios having different meal conditions in terms of BG concentration (G_C) and BG derivative (G_{der}). Model features include information on the prandial condition, i.e., G_C, G_{der}, the carbohydrate (CHO) intake , and the insulin on board (IOB); the physiology of the subject, i.e., body weight (BW); the therapy parameters, i.e., the correction factor (CF), the insulin-to-carbohydrate ratio (CR), the basal insulin (I_b), and the target BG (G_T); and the baseline insulin dose provided by the standard formula (SF) for MIB dosing commonly used in clinical practice [10], hereafter labeled as MIB_{SF}. Moreover, due to the nonlinear nature of the problem, we extended the feature set by also adding the quadratic value of each feature thus making the model of choice linear in structure but not at the feature level. The generated dataset was properly divided into training and test set, and then normalized. As a linear regression model of choice, we selected a least absolute shrinkage and selection operator (LASSO), since able to naturally perform both automatic feature selection and regularization during the training phase, thus reducing the risk of overfitting. The resulting formula for MIB calculation based on LASSO (MIB_{LASSO}) is:

$$MIB_{LASSO} = 4.603 - 0.198\ CR + 0.789\ G_{der} + 0.234\ CHO + 2.671\ MIB_{SF} - 0.224\ BW^2 + 0.403\ G_T^2 - 0.020\ G_C^2$$

MIB_{LASSO} use was evaluated on the test set scenarios in single meal noise-free simulated experiments, in which the obtained MIB was applied as mealtime insulin amount. A representative example is reported in the upper panel of Fig. 2, where two simulated postprandial BG curves resulting from the usage of SF and LASSO are shown. Compared to MIB_{SF} use, the application of MIB_{LASSO} resulted in tighter glycemic control, and avoided the occurrence of postprandial hypoglycemia. Results in the test set were quantified by computing the percentage of time spent above the target glycemic range (TAR), below the target range (TBR), and within the target range (TIR) over the 6-hour postprandial time window. In the lower panel of Fig. 2, the difference between the metric distributions of MIB_{LASSO} and MIB_{SF} (i.e., ΔTAR, ΔTBR, and ΔTIR) are reported. The proposed model led to a general improvement in terms of ΔTBR and ΔTIR, being the two distributions concentrated below zero (reaching a 25th percentile of about -10%), and above zero (with a median of 20%) respectively, without affecting the ΔTAR.

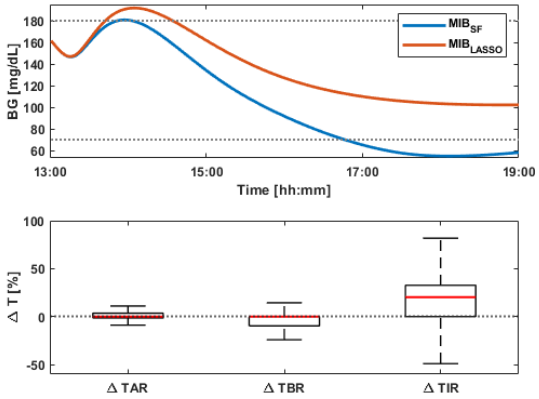

Fig. 2: Upper panel: two representative simulated BG curves during the 6-hour postprandial time window are shown for MIB_{SF} and MIB_{LASSO}. Dashed lines indicate the target glycemic range. Lower panel: distributions of ΔTAR, ΔTBR and ΔTIR between MIB_{LASSO} and MIB_{SF}.

B. Hypoglycemia prevention module

The hypoglycemia prevention module is based on a heuristic approach proposed by Camerlingo et al. [7], to which we refer the reader for details. The approach suggests the assumption of small preventive amounts of fast-acting CHO by leveraging two risk measures: the static risk (SR) [11], and the dynamic risk (DR) [12]. While SR converts every BG reading into a specific penalty score, the DR also considers its derivative, G_{der}, assigning a higher risk to

situations in which BG concentration is low and G_{der} is negative.

Every BG reading, SR and DR are used to distinguish the severity of the forthcoming hypoglycemic event and then to suggest a risk-related CHO amount, according to the following three sequential steps:

1. *Classification of the forthcoming hypoglycemic event:*
   - If DR is 0 and G_{der} is lower than or equal to -1 mg/dL/min, the algorithm foresees a rapid descent in hypoglycemia.
   - If DR is 0 and G_{der} ranges in (0, -1) mg/dL/min, the algorithm foresees a slow descent in hypoglycemia.
2. *Suggestion of hypotreatments:*
   - In case of rapid descent, the algorithm suggests the assumption of a hypotreatment of 20 g.
   - In case of slow descent, the algorithm does not suggest any hypotreatment.
3. *Post-classification actions:*
   - If DR is lower than or equal to the value of SR corresponding to BG equal to 70 mg/dL, it is decreasing, and 15 min are passed since the last hypotreatment, the algorithm suggests the assumption of an additional hypotreatment of 15 g or 20 g in case of slow or rapid descent in hypoglycemia, respectively. The 70 mg/dL threshold and the hypotreatment doses are defined experimentally as described in [7].
   - If the DR is greater than 0, the algorithm restarts from step 1.

The algorithm was assessed using the UVa/Padova T1D Simulator [9] and compared against the American Diabetes Association (ADA) guideline, i.e., the standard strategy for hypoglycemia prevention currently used in clinical practice [13], which suggests the assumption of a hypotreatment of 15 g every 15 minutes while in hypoglycemia. As for the previous module, performances were quantified in terms of ΔTAR, ΔTBR, and ΔTIR. The upper panel of Fig. 3 shows a comparison between the new algorithm and the ADA guideline, for a representative subject. Using the ADA guideline, two hypotreatments occur to mitigate the hypoglycemic event when BG is already below 70, thus not preventing the relative hypoglycemic event. Instead, the proposed algorithm allows avoiding hypoglycemia with only one preventive hypotreatment. The distributions of ΔTAR, ΔTBR, and ΔTIR are reported in the lower panel of Fig. 3. The proposed algorithm greatly reduces ΔTBR (3.52% on average) without any impact on the ΔTAR, thus increasing the ΔTIR (3.75%, on average). As a further note, the proposed algorithm suggests, on average, less hypotreatments than the ADA guidelines (1 vs. 2 per day).

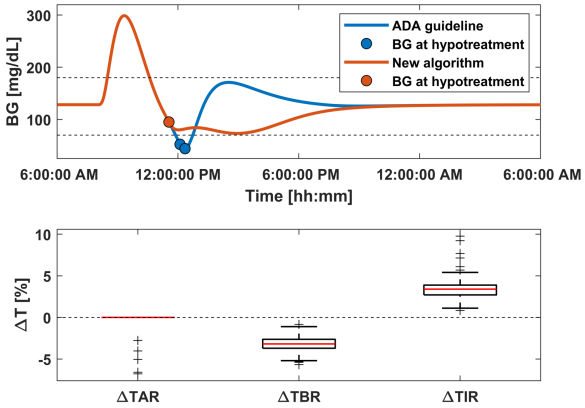

Fig. 3. Upper panel: BG curves of a representative virtual subject with the ADA guideline (blue) and the new algorithm (red). Dots represent the BG value at hypotreatment times. Lower panel: distributions of ΔTAR, ΔTBR and ΔTIR between ADA guideline and the proposed algorithm.

III. The IMPACT Communication Platform

The communication platform of PDSS is based on IMPACT, an integrated platform for data gathering developed by Cappon et al. [8]. The platform consists of three main elements: a mobile app, a cloud server, and a telemonitoring interface. The mobile app has been built in Flutter [14] and records user data by allowing to manually insert meal intakes, insulin administrations events and to record automatically CGM measurements from Dexcom Inc. (San Diego, CA, USA) CGM devices, and health vitals, i.e., step count, sleep, and heart rate, from Apple Watch (Cupertino, CA, USA). The mobile app was designed following user-centered methodologies. This was possible by deeply involving both patients and clinicians throughout the whole process ensuring that their needs and expected outcomes are fully covered in the final solution. The cloud server implements ad-hoc RESTful APIs written in PHP to store patient data collected using the mobile app and to transmit them to the telemonitoring interface. The latter is accessible by clinicians through the web and allows to monitor in real-time each patient using PDSS. Fig 4. shows a representative snapshot of the telemonitoring interface. While, in the upper panel, patient data are shown for a specific day of monitoring, in the lower panel, multiple statistics about patient's glucose control for that day, e.g., number of hypo-/hyperglycemic events, average glucose level, and the glucose variation, are computed to help clinicians in analyzing specific portions of data. Of note, the PDSS platform complies with the General Data Protection Regulations (GDPR) [15] to guarantee data

safety and protect the final users' fundamental rights in this term.

Fig. 4. Upper panel: Example of data collected in a representative subject for a specific day as presented in the telemonitoring interface. Glucose data (dotted trace) coloring depends on value to highlight the different glycemic zones. CHO intakes and insulin boluses are in yellow and blue square dots, respectively. Patient's steps are reported using violet bars. Sleep interval is denoted with a shaded blue area. Physical activity is highlighted with a shaded red area. Lower panel: glucose control statistics of the specific portion of data.

The platform functionalities has been tested within our facilities in a small beta session of 20 days involving one patient with T1D. This short testing session allowed to prove the usability of the platform and solve bugs that would come out during long-term use of the application. The general self-reported feedback received by both patient and clinicians is positive. The usability appeared good, and all shown statistics allowed the users to improve data readability. The mobile app has been reported to be intuitive and user-friendly.

IV. Conclusion and Future Steps

A DSS can be of great help for T1D patients in managing the disease. In this work, we presented a new system, the PDSS, which, to date, comprises two state-of-the-art algorithms that have been proven to outperform, in silico, the current T1D standard of care. The algorithms have been integrated into a novel communication platform that allows to safely store data and to monitor patients in real-time.

Even if PDSS is potentially ready to be tested in a dedicated clinical trial, further work is still necessary in order to refine the system. This will start by implementing multiple constraints, specifically targeting the insulin bolus calculator module, in order to avoid potentially dangerous insulin overdosing, thus guaranteeing patient safety. In addition, the hypotreatment dose could be adjusted to the subjects' physiologic features, in order to optimize its effect. Once refined, PDSS will require an additional in silico assessment on more challenging scenarios, e.g. multiple meal experiments to quantify its impact in the medium-/long-term. Moreover, PDSS will be evaluated using real data, by leveraging the ReplayBG framework [16], i.e., a recently proposed in-silico tool to assess new therapy guidelines for T1D management on retrospective data. In parallel, the validation will focus on an extensive comparison of PDSS against other state-of-the-art DSS [5] to identify possible margins of improvement.

Finally, we will investigate the expansion of PDSS features. In this context, work currently undergoing in our group focuses on the possibility of integrating into PDSS a new module able to target hyperglycemia by recommending the administration of corrective insulin boluses [17].

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