A CBR-based bolus recommender system for type 1 diabetes

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Abstract. People with type 1 diabetes mellitus usually need to administer bolus insulin before each meal to keep the blood glucose level in the target glycaemic range. However, the factors involved in the calculation of the appropriate dose can change due to multiple factors and with an unknown relation. This may increase the error in the bolus calculation, and therefore, increase the chances of hypoglycaemia and hyperglycaemia. This paper proposes a bolus recommender system based on case based reasoning developed under project PEPPER, with the objective of recommending personalised and adaptive bolus doses. The system has been tested with *in silico* adults with UVA/PADOVA T1DM simulator. Results show that the use of the proposed bolus recommender system increases the percentage of time in the target glycaemic range.

Keywords: Diabetes, bolus recommender system, case based reasoning, patient empowerment

1 Introduction

Type 1 diabetes mellitus (T1DM) is a chronic disease, which requires people with it to check their blood glucose level and administer insulin to themselves to control and maintain blood glucose in the target range. People with T1DM usually use two types of insulin: bolus insulin, which is a fast acting insulin, and basal insulin, which is a slow acting insulin. However, the calculation of the needed amount of either bolus or basal at each time is not easy and the parameters to calculate it may change due to several factors. Then, T1DM people self-regulate, with the help of clinicians every several weeks or months, the needed doses.

This paper proposes a Case Based Reasoning (CBR) [1] approach to estimate the parameters for bolus calculation and recommend bolus doses. CBR is a lazy learning methodology [5], which consists of using past experiences to solve future problems. CBR traditionally incorporates four main main steps [1]: retrieve, reuse (or adaptation), revise (or evaluation), and maintenance (or storage and management of the case base). These consist of (i) identifying prior similar experiences to the problem to be solved; (ii) adapting the solutions of prior experiences to find a solution to the new problem; (iii) evaluating the outcome of the proposed solution and repair it if necessary; and (iv) storing the current experience (problem and solution) for further problems and manage the case base.

There are various commercial applications that facilitate the calculation of the amount of insulin, usually the bolus dose for a given basal. The author in [2] provides a wide review of the current applications for bolus calculation. However, these applications require the user to estimate the needed parameters to calculate the bolus, such as the insulin to carbohydrates ratio (ICR) besides the amount of carbohydrates. Moreover, these parameters may change due to different factors and without a known relation. This usually makes these applications very ineffective.

Nevertheless the literature presents approaches capable to iteratively adjust some of the parameters for bolus calculation. In this regard, D. Brown presents in [2] a bolus calculator approach based on Case Based Reasoning (CBR) [1], which considers carbohydrate intakes, preprandial blood glucose levels of a few previous meals in order to calculate the appropriate bolus. Conversely, this paper does not consider previous meals and the implementation of the CBR steps are different. Shashaj *et al.* propose in [6] a run-to-run algorithm [9] instead of a CBR, to iteratively adjust bolus calculator parameters. The point of using a CBR is to have different parameters' values for different situations. The authors in [3,4] combine a run-to-run algorithm and a CBR of prototypes to iteratively select and adjust the parameters of a bolus calculator depending on the context (time of day and physical activity). The revise step of CBR approach presented in this paper is based on the one presented in [3]. However, the proposed revise methodology presents some modifications (see Section 2.3). Moreover, the proposed retrieve, reuse and maintenance steps differ from [3], since the proposed approach is not a CBR of prototypes and, therefore, the size of case base can dynamically change according to the attributes of the cases.

Following this line of research, PEPPER (Patient Empowerment through Predictive PERsonalised decision support) project has the objective of providing a personalised adaptive decision support system for bolus dosing that combines multiple data sources. This paper presents a CBR-based bolus recommender system for T1DM and analyses its performance with UVA/PADOVA T1DM simulator [7].

2 CBR-based bolus recommender system

The CBR-based bolus recommender system presented in this paper has the objective of recommending an appropriate bolus dose to people with T1DM before a meal. In order to do so, the CBR considers a set of attributes that describe the situation or case, and the insulin to carbohydrates ratio (ICR) of the user as the solution of the case. Then, this ICR is used to calculate the appropriate bolus dose for a given amount of carbohydrates. The remainder of the section explains the implementation of the CBR steps for bolus recommendation.

2.1 Retrieve

The retrieve step is responsible for selecting similar cases to the query (or new) case. Retrieve methods usually calculate the distance between the query case and those in the case base and, then, select the closest ones.

The proposed CBR methodology considers the ICR of the user as the solution. Therefore, the considered attributes must be variables that can modify the ICR of a user. These variables include time of day (for intra-day variability), physical activity, stress, hours of sleep, alcohol ingestion, ambient temperature, etc. However, there are contextual factors that usually have a great impact on the ICR, e.g. menstruation and digestive illness. As a consequence the proposed retrieve methodology consists of two steps: context reasoning and selection. Context reasoning consists of choosing the appropriate contextual case base and selection consists of choosing the closest cases (in the corresponding contextual case base) to the query case. Note that this retrieve methodology implies that the CBR system manages not one, but several case bases.

2.2 Reuse

The reuse step consists of adapting the solutions of the retrieved cases to the query case. This paper proposes a weighted average of the retrieved ICRs using the distance between the retrieved cases and the query case.

Once the ICR of the query case is derived, the bolus recommendation is calculated as follows:

$$B = \frac{CHO}{ICR} + \frac{G_c - G_{sp}}{ISF} - IOB \tag{1}$$

where CHO is the amount of carbohydrates of the meal, G_c is the blood glucose, G_{sp} is the standard blood glucose level, ISF is the insulin sensitivity factor and IOB is the remaining active insulin (insulin on board). ISF is calculated as stated in [8] using Equation (2), where W is the weight of the user in kg.

$$ISF = \frac{341.94 ICR}{W} \tag{2}$$

2.3 Revise

After the user administers a bolus (e.g. the recommended bolus) and has the meal, the postprandial phase starts. The proposed revise process is based on the idea proposed in [3], which relies on the assumption that an additional bolus is necessary to bring the minimum glucose value, G_{min}, in the glycaemic range. The value G_{min} is calculated as expressed in Equation (3) as the minimum glucose value measured by the continuous glucose monitor $G_{cgm(t)}$ between t_1 time after the meal time t_m and t_2 time after t_m with $t_1 < t_2$, e.g. $t_1 = 2h$ and $t_2 = 6h$.

$$G_{min} = \min_{t \in \{t_m + t_1, t_m + t_2\}} \{G_{cgm}(t)\} \tag{3}$$

Given the minimum postprandial blood glucose, the ICR is corrected if G_{min} is not in the glycaemic range ($[G_l, G_h]$). Then, the corrected ICR (ICR_c) is calculated according to Equation (4), where ICR_a is the previous ICR used in Equation (1) and α is the learning rate (e.g. 0.5). However, conversely to [3], the revise equation incorporates the learning rate α to smooth ICR changes.

$$ICR_c = (1-\alpha)ICR_a + \alpha \frac{CHO + \frac{G_c - G_{sp}}{341.94/W}}{B + IOB + \frac{G_{min} - G_{sp}}{ISF}} \tag{4}$$

2.4 Maintenance

The ICR can change over time. An example is the intra-day variability, which causes some periodicity in the ICR. This is solved by retrieving the appropriate cases of the case base. However, the ICR could change over time without an apparent periodicity because the physiology of the patient changes (age, body weight, etc.). Therefore, the CBR system has to deal with the concept drift problem. This paper proposes to deal with this problem in the maintenance step by replacing old cases with new cases if these are similar enough. Therefore, the proposed retain process is when there is a candidate query case to be stored in a context case base, check if there is another case within a distance lower than a particular threshold. In such a case, delete the old case and store the new one.

3 Results

The proposed CBR-based bolus recommended system has been tested on ten adult *in silico* subjects using the UVA/PADOVA T1DM simulator [7]. However, since the simulator does not incorporate intra-day variability of the insulin sensitivity, this was artificially introduced as proposed in [3].

The performance of the proposed CBR bolus recommender system has been compared in terms of time with blood glucose in target range (70 mg/dl to 180 mg/dl) with the use of a bolus calculator using Equation (1) and default *in silico* subjects' parameters.

Table 1 shows the average and standard deviation over twenty simulations of the percentage of time that subjects had blood glucose level in target range in 90-days simulations. It shows that *in silico* subjects using the CBR-based bolus recommender system increase their time in the glycaemic range and, in average, reduce the standard deviation, meaning that they have a more stable blood glucose level.

Since the simulation used only considers intra-day variability, the case base of the recommender system of each subject was formed by only four cases, the one used to initialise the case base, and another one for each meal (breakfast, lunch and dinner).

Table 1. Percentage time in target of eleven in silico adults using the CBR-based bolus recommender system or a bolus calculator. In bold face those significantly greater according to Wilcoxon tests, p-value = 0.05.

	CBR	Bolus calculator
Subject 1	79.49 ± 2.02	78.33 ± 5.20
Subject 2	$\mathbf{93.43 \pm 2.07}$	91.15 ± 1.26
Subject 3	$\mathbf{74.95 \pm 2.33}$	68.87 ± 4.36
Subject 4	84.76 ± 5.56	79.02 ± 10.08
Subject 5	$\mathbf{88.84 \pm 4.29}$	80.60 ± 7.00
Subject 6	81.91 ± 1.52	81.18 ± 2.02
Subject 7	69.68 ± 6.98	64.10 ± 6.91
Subject 8	$\mathbf{86.87 \pm 1.26}$	82.61 ± 5.82
Subject 9	$\mathbf{90.18 \pm 2.63}$	83.92 ± 3.58
Subject 10	$\mathbf{83.03 \pm 4.04}$	75.24 ± 7.98
Subject 11	$\mathbf{83.26 \pm 4.64}$	77.63 ± 5.39
Average	83.31 ± 3.39	78.51 ± 5.42

4 Conclusions

People with T1DM need to administer a bolus dose, usually before each meal. The calculation of the appropriate bolus is not easy and requires the estimation of a set of parameters, such as the insulin to carbohydrates ratio, that can change over time due to multiple factors. This paper presents a CBR-based bolus recommended system which has been developed under project PEPPER. The objective of the bolus recommender system is to provide personalised and adaptive bolus recommendations to the users (i.e. people with T1DM).

The system has been tested using eleven *in silico* adults with the the UVA/PADOVA T1DM simulator. The results show that the proposed system increases the percentage of time of subjects' blood glucose in the glycaemic target range.

Despite the presented results, there is still research to do, especially in the management of missing data and in the maintenance of the case base.

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References

1. Aamodt, A., Plaza, E.: Case-based reasoning: Foundational issues, methodological variations, and system approaches. AI communications 7(1), 39–59 (1994)

2. Brown, D.: Temporal case-based reasoning for insulin decision support. Ph.D. thesis, Oxford Brookes University (2015)
3. Herrero, P., Pesl, P., Bondia, J., Reddy, M., Oliver, N., Georgiou, P., Toumazou, C.: Method for automatic adjustment of an insulin bolus calculator: In silico robustness evaluation under intra-day variability. Computer Methods and Programs in Biomedicine 119(1), 1–8 (2015)
4. Herrero, P., Pesl, P., Reddy, M., Oliver, N., Georgiou, P., Member, S.: Advanced Insulin Bolus Advisor based on Run-To-Run Control and Case-Based Reasoning. IEEE Journal of Biomedical and Health Informatics 19(3), 1087–1096 (2015)
5. López, B.: Case-Based Reasoning: A Concise Introduction. Synthesis Lectures on Artificial Intelligence and Machine Learning 7(1), 1–103 (2013)
6. Palerm, C.C., Zisser, H., Bevier, W.C., Jovanovic, L., Doyle, F.J.: Prandial Insulin Dosing Using Run-to-Run Control: Application of clinical data and medical expertise to define a suitable performance metric. Diabetes Care 30(5), 1131–1136 (2007)
7. Visentin, R., Dalla Man, C., Kovatchev, B., Cobelli, C.: The University of Virginia/Padova Type 1 Diabetes Simulator Matches the Glucose Traces of a Clinical Trial. Diabetes Technology & Therapeutics 16(7), 428–434 (2014)
8. Walsh, J., Roberts, R., Bailey, T.: Guidelines for Optimal Bolus Calculator Settings in Adults. Journal of Diabetes Science and Technology 5(1), 129–135 (2011)
9. Wang, Y., Gao, F., Doyle, F.J.: Survey on iterative learning control, repetitive control, and run-to-run control. Journal of Process Control 19(10), 1589–1600 (2009)