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# Advanced Insulin Bolus Calculator Using Run To Run Control and Case Based Reasoning Algorithm

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**ABSTRACT:** This paper exhibits a propelled insulin bolus consultant for individuals with diabetes on various day by day infusions or insulin pump treatment. The proposed framework, which keeps running on a cell phone, keeps the straightforwardness of a standard bolus adding machine while upgrading its execution by giving more versatility and adaptability. This is accomplished by method for applying a review enhancement of the insulin bolus treatment utilizing a novel blend of rushed to-run (R2R) that utilizations discontinuous ceaseless glucose observing information, and case-based thinking (CBR). The legitimacy of the proposed approach has been demonstrated by in-silico considers utilizing the FDA-acknowledged UVa-Padova sort 1 diabetes test system. Tests under more reasonable in-silico situations are accomplished by redesigning the test system to copy intrasubject insulin affectability varieties and instability in the capillarity estimations and sugar admission. The CBR(R2R) calculation performed well in reproductions by essentially diminishing the mean blood glucose, expanding the time in euglycemia and totally taking out hypoglycaemia. At last, contrasted with a R2R remain solitary form of the calculation, the CBR(R2R) calculation performed better in both grown-ups and pre-adult populaces, demonstrating the advantage of the use of CBR. Specifically, the mean blood glucose enhanced from 166 ± 39 to 150 ± 16 in the grown-up populaces ($p = 0.03$) andfrom167 ± 25 to 162 ± 23 in the juvenile populace ($p = 0.06$). Furthermore, CBR(R2R) could totally wipe out hypoglycaemia, while the R2R alone was not ready to do it in the immature populace.

**KEYWORDS:** Artificial intelligence, decision support systems, diabetes, iterative learning control, knowledge-based systems, runto-run control.

## I. INTRODUCTION

Sort 1 diabetes mellitus is a ceaseless metabolic infection portrayed by an immune system pulverization of the insulin-emitting β-cells of the endocrine pancreas. The subsequent outright insulin inadequacy results in hyperglycemia [i.e., high blood glucose (BG)]. At present, the greater part of individuals with T1DM control their BG levels through different day by day infusions (before suppers and basally) so as to copy the normal insulin discharge of the pancreatic β-cells and by drawing blood from the fingertips and testing the glucose level with an electronic glucose meter (self-observing of BG). An option treatment to various day by day infusions is given by constant subcutaneous insulin implantation (insulin pump treatment), which permits variable basal rates of insulin and stays away from numerous uncomfortable infusions.

Expansive intercession trials have demonstrated that tight glycaemic control averts long haul smaller scale and macrovascular confusions, to the detriment of an expanded recurrence of hypoglycaemia, highlighting the significance of streamlining insulin measurements for the duration of the day, lessening diabetes intricacies which put an overwhelming weight on wellbeing administrations. Bolus insulin measurements with dinners are computed by assessing sugar admission, separating by an altered starch: insulin proportion and including a remedy dosage got from the people insulin affectability element. To computerize this procedure, a few calculations have been produced. Be that

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as it may, with special case of insulin bolus number crunchers fused in a large portion of the financially accessible insulin pumps and in some glucose meters, none of these calculations have been received economically.

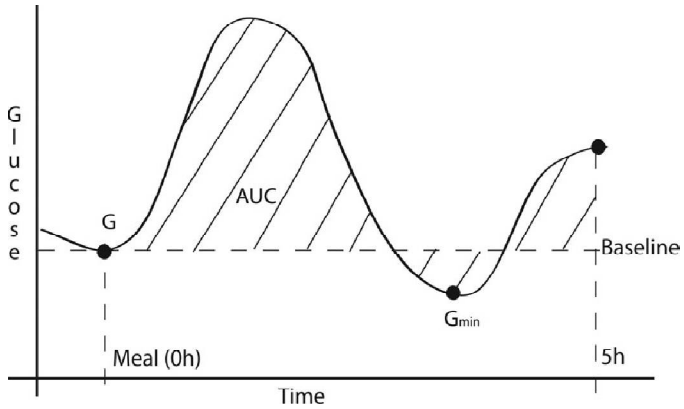


**Fig. 1. Graphical representation of the postprandial glucose area under the curve (AUC) (i.e., striped area). Horizontal dashed line represents the baseline to calculate the AUC. Vertical dashed line represents the meal ingestion time (0 h) and the 5 h postprandial period. G is the BG value at the time of meal ingestion (0 h) andGmin is theminimum glucose values during the postprandial excursion (5 h).**

This absence of commercialization is mostly down to monetary danger, security issues, and inactivity to change, however the principle explanation behind the absence of accessible frameworks is the generally little remedial advantage accomplished by these frameworks contrasted and the huge weight required by the clients. Therefore, extra exertion toward more shrewd self-governing frameworks is required. The clinical advantage of hurried to-run (R2R) control for naturally conforming the insulin-to-sugar proportion (ICR) parameter of a bolus mini-computer has been considered with some underlying promising results. In any case, its appropriateness is restricted by the supposition of strict dreariness in the every day routine of individuals with T1DM. This paper displays an inventive choice bolster calculation for supper insulin dosing that gives improved versatility and adaptability to current bolus number crunchers by utilizing R2R control and case-based thinking (CBR). It is imperative to note that, dissimilar to existing shut circle control calculations for glucose control, which convey an insulin measurements each 5 min in view of a constant enhancement, our proposed calculation is a choice emotionally supportive network giving bolus insulin dosage suggestions taking into account review advancement, which requires endorsement by the client.

The legitimacy of the introduced calculation is shown through an in-silico study utilizing the UVa-Padova T1DM test system, which has been changed to consolidate intrasubject variability, clamor in the slender blood estimations, and instability in the starch admission. This calculation has now been coordinated into an easy to understand cell phone stage for use by subjects with diabetes in a clinical trial.

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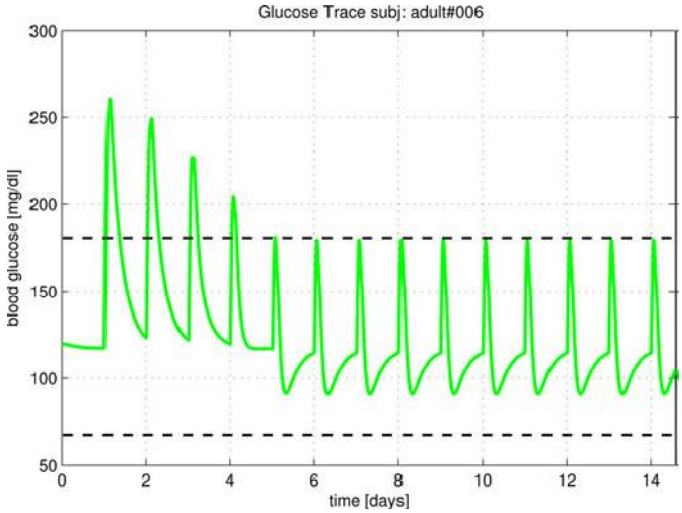


**Fig. 2. Glucose concentration resulting from applying the proposed R2R algorithm over 14 days (single meal) on subject adult 6 of the T1DM simulator with an initial nonoptimal ICR. Upper and lower dashed lines indicate hyper- /hypoglycemia limits (i.e., target zone).**

### A. Insulin Bolus Calculators

Insulin bolus calculators are simple decision support systems incorporated in most of the commercially available insulin pumps and more recently available within capillary BG monitors. These calculators consist of a relatively simple formula that uses subject-specific metabolic parameters to calculate an insulin dose. The standard bolus calculator is described as

$$B = CHO\ ICR + G - GTISF - IOB \quad (1)$$

where B is the recommended dose of insulin (IU) to be taken; CHO is the total amount of carbohydrate in the meal (gram), ICR is the insulin-to-carbohydrate ratio (g/IU), which describes how many grams correspond to one unit fast acting insulin; G is the current capillary BG level (mg/dL); GT is the target BG level (mg/dL); ISF is the insulin sensitivity factor (mg/l/IU), which is a personal relation describing how large a drop in BG one unit of insulin gives rise to; and IOB is the insulinon-board, which describes the amount of insulin still in the body from previous injections. Different formulas are being used by different manufacturers to estimate IOB. It is important to note that parameters ISF and ICR are usually not constant and may vary depending on parameters such as circadian rhythms, physical activity levels, hormone cycles, psychological stress, alcohol consumption, and recurrent illness. Although some of the most recent commercially available bolus calculators allow considering some of these effects (e.g., exercise and stress), this feature is rarely used due to the significant burden that represents. Although the clinical benefit of using bolus calculators has been demonstrated, their performance remains suboptimal and to achieve a significant improvement in glycemic control, a more dynamic, personalized, intelligent system is required. For this purpose, the utilization of iterative learning control and CBR is proposed.

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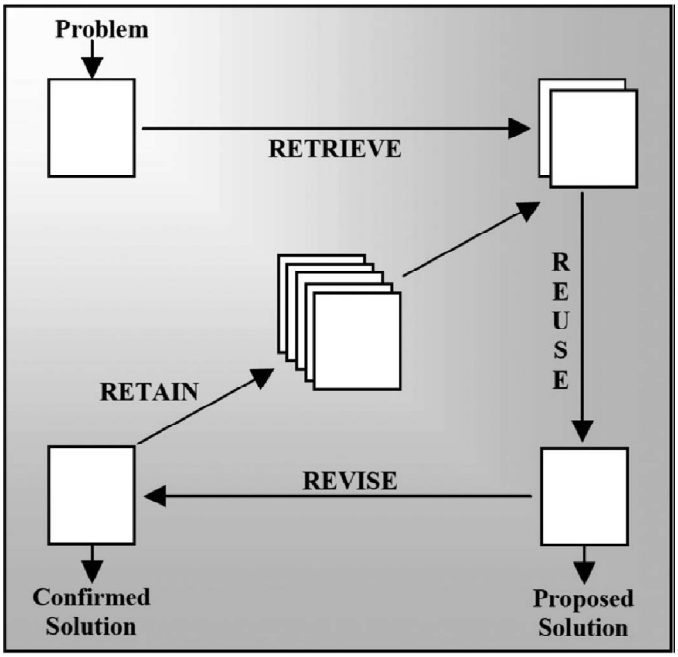


**Fig. 3. CBR cycle proposed by Aamodt and Plaza**

### B. R2R Control

R2R is a control method designed to exploit repetitiveness in the process that is being controlled. Its purpose is to enhance performance, using a mechanism of trial and error. Owens et al. used this idea to exploit the repetitive nature of the insulin therapy regimen of the diabetic patient. This algorithm uses an update law that corrects the ICR of (1) for the next day based on a performance metric used to evaluate the postprandial glucose excursion. A pilot clinical study showed the efficacy of the R2R algorithm in T1DM subjects. However, the R2R algorithm presents some limitations that may restrict its scope of applicability. First of all, the algorithm requires two capillarity BG samples to evaluate the postprandial excursion.

On top of the burden that this represents to the subject, the postprandial excursion of a mixed meal depends on the composition, and these two measurement points may not be valid to evaluate certain meals. Then, R2R assumes that the insulin therapy regimen of the person with T1DM is repetitive, which is somewhat unrealistic in many cases. It is important to note that the original R2R algorithm only distinguishes between three situations (breakfast, lunch, and dinner). Therefore, the utilization of the R2R algorithm may be limited to subjects willing to carry out at least nine capillarity measurements per day and with a very repetitive daily routine.

## II. TUNING AND INITIALIZATION

Reference area under the curve parameter (AUCr) was individually determined using a meal tolerance test functionality provided by the T1DM simulator, which allows obtaining an optimal postprandial glucose excursion. In a real clinical setting, this parameter could be determined by a clinical expert based on retrospective CGM data or a meal tolerance test data. The gain K was tuned to converge toward the solution in a reasonable time frame (e.g., 1 week); the selection of the values for the remaining parameters, which were the same for all subjects, was based on the combination of multiple simulations and clinical knowledge. Note that, in a clinical setting, the gain K could be calculated using linear regression to best match the clinically determined dose adjustment as proposed. Parameter Tol was chosen to cope with the error due to the CGM sensor, and parameters GT , ICRm, ICRM , GL , GH , KT , and KE were selected based on clinical expertize. Finally, parameter TIOB was selected based on the values reported by different pump manufacturers (i.e., 2 h $\leq$ TIOB $\leq$ 7 h). Although this parameter may have a significant intrasubject and intersubject variability, a conservative value of 6 h was selected for all subjects.

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### III. SAFETY AND EFFICACY MEASURES

The following safety and efficacy measures [36] (presented as Mean ± Standard Deviation) were used: The primary outcome was mean BG (mg/dL); secondary outcomes were percentage of time and incidence below range (any BG < 70 mg/dL), percentage of time within the 70–180 mg/dL target range, percentage of time above range in hyperglycemia (BG > 180 mg/dL), and BG risk index and risk zones of the control variability grid analysis (CVGA). CVGA is a method for visualization of the extreme glucose excursions caused by a control algorithm in a group of subjects, with each subject presented by one data point for any given observation period. CVGA is divided into nine zones (A, B, lower-B, upper-B, lower-C, upper-C, lower-D, upper-D, E), being zones A+B (including lower and upper) considered as optimal control and zones D+E considered as suboptimal control.

## IV. RESULTS

In their work, Owen et al. proposed a convergence analysis for their R2R algorithm. However, the same analysis cannot be directly applied to the presented CBR(R2R) algorithm due to the different nature of the algorithms, i.e., addition of a CBR algorithm. Nevertheless, it is important to note that CBR(R2R) is equivalent to multiple incidences of an R2R algorithm. Therefore, by assuming that the information provided to the CBR(R2R) algorithm is within realistic limits of uncertainty, which allow to correctly retrieve the correct case from the case base, the convergence analysis of CBR(R2R) is reduced to the analysis of a single incidence of R2R. Therefore, if the proposed R2R algorithm is proven to converge, the CBR(R2R) algorithm is, by extension, also convergent. To carry out a convergence analysis of the R2R algorithm, a scenario containing one meal with carbohydrate load variability of [40, 60] gram (uniform distribution) was employed. The initial BG was randomly selected within the range [70,140] mg/dl (uniform distribution). The analysis was performed by isolating the parameters CHO, capillary BG and CGM measurements while adding different levels of uncertainty to these parameters. Unlike the convergence analysis proposed, we considered uncertainties within their realistic bounds and the combination of such uncertainties.

The initial ICR0 for the R2R algorithm was randomly selected within a range of [0.25 · ICR, 4 · ICR] (uniform distribution), where ICR is the optimal ICR provided by the T1DM simulator. The past analysis shows the performance of the R2R algorithm for each case study after 20 iterations together with the results for a bolus calculator without adaptation. For this purpose, the ten adult subjects of the T1DM simulator were employed. It can be seen that the algorithm is capable to converge to the target range, i.e., [70, 180] mg/dl, even when significant levels of uncertainty are added. Finally, no significant variability was observed on the number of iterations needed to converge to the glucose target range for the selected levels of uncertainty. The CBR(R2R) algorithmwas evaluated using the one-month scenario presented and four simulation runs. First of all, an initial simulation run (Run 1) was carried out using the bolus calculator formula (1) with nonoptimal parameters (ICR and ISF) and without any adaptation. Run 2 consisted of applying the CBR(R2R) algorithm with a case base containing a unique case with the same solution as the bolus calculator.

Runs 3 and 4 were like Run 2, but starting from the case base generated in the corresponding previous runs. In order to evaluate the benefit of enhancing the R2R algorithm with CBR, the R2R algorithm in a stand-alone mode was executed in the same scenario. For this purpose, the R2R algorithm in a stand-alone mode was configured with three instances of the algorithm corresponding to breakfast, lunch, and dinner show the simulation results corresponding to four runs of the R2R algorithm in a stand-alone mode and the CBR(R2R) algorithm, respectively. Results are presented as mean ± 1 standard deviation.

Improvement on mean BG levels, percentage of time in hyper-/hypoglycaemic range, risk index, as well as percentage in risk zones A + B and D + E of the CVGA, were analyzed using a paired t-test with a significance established at $p < 0.05$. In Table V (i.e., CBR stand-alone mode), a part from the percentage in time below target, all the metrics corresponding to the adult population got worse. Although some improvements were observed in the adolescent population, these ones were not statistically significant. On the other hand, almost all safety and efficacy measures showed statistically significant improvements in both populations when the CBR(R2R) algorithm was employed. When comparing the two versions of the algorithm [i.e., R2R versus CBR(R2R)], the mean BG (i.e.,

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primary outcome improved from 166 ± 39 to 150 ± 16 in the adult populations and from 167 ± 25 to 162 ± 23 in the adolescent population. In addition, CBR(R2R) was able to completely eliminate hypoglycaemia, while the R2R alone was not able to do it in the adolescent population. Fig. 4 shows an example for subject adult#010 comparing the R2R and the CBR(R2R) algorithm during Run 4 of the simulation.

## V. CONCLUSION

We presented a novel decision support algorithm for insulin dosing that enhances current standard bolus calculators through the utilization of an R2R, CBR, and intermittent usage of CGM data. Good in-silico results using an FDA-accepted type 1 diabetes simulator were obtained with the presented CBR(R2R) algorithm. First of all, a convergence analysis for the novel R2R algorithm was successfully carried out. To evaluate the incremental benefit of using R2R and CBR, the full version of the algorithm [i.e., CBR(R2R)] was compared against the R2R control algorithm in a stand-alone mode.

This comparison demonstrated a clear benefit of using CBR in combination with R2R with respect to using R2R alone. The R2R stand-alone version not only underperformed the CBR(R2R) version, but in some cases (i.e., adult population) performed worse than the standard bolus calculator. The reason for the poor performance of the R2R stand-alone version can be explained by its inability to cope with the significant insulin variability introduced in the simulations. It is important to note that R2R is based on the assumption of daily repetitiveness in the process, which is not the case for the employed scenario. The obtained results demonstrate that the propose CBR(R2R) algorithm is able to tackle with intrasubject variability and external perturbations, and robustness in front of uncertain inputs, i.e., carbohydrate intake and noisy CGM measurements.

It is important to remark that, although very useful for designing and testing purposes, simulators have their limitations. In general, simulation environments tend to overestimate the benefits of an intervention, since they do not incorporate all of the uncertainty and perturbations that occur in the real world. For this reason, clinical studies are required in order to fully validate the proposed algorithm. Therefore, modifications in the current version algorithm may be required when tested in a real scenario. Although the proposed algorithm showed robustness against sensor noise in simulation, CGM technology still presents some problems of accuracy and reliability that may affect the performance of the proposed algorithm in a real-life setting. One way to reduce this problem would be the utilization of two sensors.

However, this solution may be too cumbersome for the subject. Another way to improve sensor accuracy would be to ask for a postprandial recalibration (e.g., 2 h), which seems a reasonable measure since it is the recommendation given for the standard therapy. Finally, in order to deal with sensor failures (e.g., sensor drifts and communication problems), a fault detection algorithm could be incorporated to the system. It is important to note that the utilization of a CGM device does not need to be continuous, since the decision support system can still provide advice during the days when no CGM data are available by using the available cases in the case base, even if they are not optimal. Obviously, the R2R control update law can only be executed when these data are available. Therefore, using the CGM sensor periodically, although it may take longer to converge an optimal solution, may be beneficial in some cases because of usability issues.

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