Case-base maintenance of a personalised bolus insulin recommender system for Type 1 Diabetes Mellitus

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Abstract. With the goal of aiding people with Type 1 Diabetes Mellitus (T1DM), some mobile applications are being developed based on artificial intelligence techniques. Some of these applications are based on case-based reasoning methodologies due to the advantage regarding a personal and adapted recommendation. However, the quantity and quality of the cases in the CBR system is crucial for the system outcome. Most of the case-base maintenance methods developed are designed for CBR systems which provide a nominal recommendation. However, recommending a bolus dose involves a numeric recommendation. Therefore, this paper presents a new maintenance approach for an insulin recommender system based on CBR. The resulting insulin recommender system is tested using the UVA/PADOVA T1DM simulator and the results show that the proposed approach is capable of making the case-base more efficient, i.e. the accuracy of the recommendations is maintained or even enhanced while the size of the case-base is reduced.

1 Introduction

The use of systems to continuously monitor blood glucose levels and the increased computation power of mobile devices such as smart-phones has led to the proliferation of applications, based on artificial intelligence, with the aim of aiding people with T1DM. Mobile applications enable the connectivity with sensors to measure and record the glucose level, physical activity, quality of sleep, etc.

In this context, Case-Based Reasoning (CBR) [10] has been proved as a useful methodology to develop adaptive and personalised insulin recommender systems [8, 9, 17, 18] because it is capable of optimising insulin dosage using past experiences.

The performance of a CBR system depends on the experiences or cases stored in the case-base. Moreover, in an insulin recommender system, the contents of the case-base should be maintained in order to capture the persons physiological changes evolution, and provide adapted recommendations over time. All insulin recommender systems based on CBR propose to use a simple technique to maintain the quality of the case-base

and they, mainly, rely on a small set of attributes to keep the case-base small and efficient [13,14,17]. However, the metabolism of carbohydrates, glucose and insulin depends on many factors (e.g. stress, physical activity, time of day, ambient temperature, etc.) and such simplistic approaches may hide. Therefore, applications which consider more attributes are needed, but if the number of attributes grows, so does the combinatorial. In this situation, current maintenance approaches of CBR insulin recommender systems fail in keeping the case-base efficient. Thus, a case-base editing techniques for CBR insulin recommender systems are needed in order to keep the case-base efficient even with a big number of attributes, and to follow possible changes in the users physiology (problem known as concept drift [19]).
This paper proposes a maintenance methodology that extends the methodology of PepperRec, [17], which is a CBR insulin recommender system. The proposed methodology is inspired in the maintenance methodology proposed in [5] which consists of three steps: retain, review and restore. Most case-base editing techniques are proposed for CBR systems which provide a nominal recommendation. Nevertheless, PepperRec provides a numeric recommendation. Thus, this paper presents a new case-base editing methodology for a CBR system which provides a numeric recommendation.
The proposed methodology is finally tested with the UVA/PADOVA T1DM simulator proving that it is capable of achieving a more efficient case-base than PepperRec, and even enhancing the accuracy of the recommendations.

2 Background

This sections briefly explains CBR and the insulin recommender system called PepperRec, which are necessary to follow this paper.

2.1 Case-Based Reasoning

CBR is a lazy learning technique that uses past experiences in order to search a solution for a new problem. The basic CBR methodology was described in [1] using 4 steps. First, given a query problem, situation or case, the retrieve step searches similar past experiences from the case-base. Second, the reuse step adapts the solutions of the retrieved cases to the query case. Third, the revise step analyses the outcome of the proposed solution and corrects it if necessary. Fourth, the retain step decides about to store the query case or not according to some strategy. In so doing, more recent approaches like [5] propose to unfold the CBR methodology into maintenance and application, moving the retain step into the maintenance part, and complementing it with review and restore steps, as depicted in Fig.1. This new approach highlights the importance of the quality and size of the case-base regarding the CBR system performance.
CBR systems can be divided into classification and regression approaches. CBR classifiers aim to provide a nominal solution, e.g. binary. These

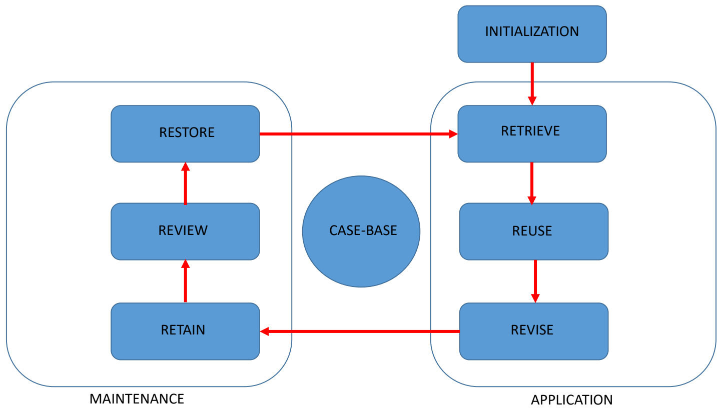

Fig. 1. CBR cycle extended with a maintenance phase.

approaches are the most common ones. On the other hand, regression approaches aim to provide a numeric solution, e.g. a real number. Both types can follow the retrieve-reuse-revise-retain methodology of CBR, but the techniques implementing the steps may be different.

2.2 Pepper insulin recommender

The work presented in this paper is based on the Pepper recommender system proposed in [17], which follows a CBR methodology. The system takes advantage of mobile technology to gather information about different sensors which sends information to the mobile through bluetooth low energy (physical activity band and continuous glucose monitor).
The goal of the system is to provide personalised bolus insulin recommendations for subjects with T1DM. Cases consist of the attributes that characterise and contextualise the ingest (case description) and the solution. Attributes are the following: time of the day, amount of carbohydrates of the meal (g), previous physical activity (quantified in a four-level graded scale) and planned physical activity during the postprandial (in the same scale). The solution consists of the Insulin to Carbohydrates Ratio (ICR) that enables the computation of the insulin dose (bolus).
The CBR system automatically revises the proposed solutions analysing the postprandial blood glucose. In particular, the theoretical optimal bolus is calculated using the minimum postprandial blood glucose. Using this optimal bolus, the ICR is further corrected according to the clinical knowledge as reported in [9, 17].
Finally, the retain step is executed and it consists of storing the new case, but check if there is an equal case (or similar enough) in the case-base independently of the solution. If this is the case, the old case is removed. No other maintenance method was developed. Thus, this paper focuses on the full maintenance procedure of such system, including the review and restore steps.

3 Related work

CBR systems rely on the case-base to provide accurate solutions. Therefore, the case-base is expected to efficiently describe the problem space. Case-base editing techniques are responsible of avoiding case-bases to continuously grow in size and remove cases that may be redundant or not necessary.
However, the problem space can evolve and change throughout time. In such situations, old cases stored in the case-base may become less representative than new cases. This problem is called concept drift and there are some works in the literature that tackle this problem.
The Instance-Based learning Algorithm3 (IB3) [2] was one of the first attempts to handle the concept drift monitoring of the cases accuracy and the retrieval frequency. In [15], the Locally Weighted Forgetting (LWF) algorithm was proposed to reduce the weights of the k-nearest neighbours (k-NN) of a new case, so a case is discarded if its weight falls below a threshold. In [16], Salganicoff achieved suitable results in time-varying and static tasks with a method called Prediction Error Context Switching (PECS). With the aim of controlling in an autonomous manner the size and the composition of the case-base, Beringer and Hllermeier [3] presented an Instance-Based Learning on Data Streams (IBL-DS) algorithm. In [7] Delany et al. Proposed a two-level learning technique with the aim of solving the concept drift issues.
Recently, the authors in [11] proposed a case-base editing methodology to keep the case-base of a CBR binary classifier as small as possible but also capable of following a concept drift. The methodology consists of applying a case-base reduction technique, named Conservative Redundancy Reduction (CRR), but also, monitoring class instances variability to detect changes in the majority class in relevant regions of the solution space. Then, when a change is detected, old instances are removed (forgotten) because it is assumed that there is a concept drift.
Despite this research, there is still need of maintenance algorithms capable of dealing with numerical solutions, in order to dispose of reduced and compact case-bases even with the presence of concept drift.

4 Pepper recommender maintenance

The maintenance approach proposed in this paper consists of the three methods: recent strategy, time analysis and coverage and, finally, reachability analysis, which are applied in the retain, review and restore steps of the CBR methodology as described below. The retain step (recent strategy) uses the same methodology proposed in [17], but the time analysis and coverage and reachability analysis are new. Therefore, this paper extends the methodology proposed in [17] with the time analysis and coverage and reachability analysis.
The methodology proposed in [17] has been proved effective when cases are described with a few attributes. But the aim of this paper is to provide a complete maintenance methodology capable of dealing with cases described by many attributes.

4.1 Retain: Recent strategy

As proposed in [17], the retain step consists of before storing a new case, check if there is an equal case in the case-base regarding the problem description. If an equal case to the new one is found, the old case is removed from the case-base. This approach assumes that a pair of cases with equal attributes but different ICR are due to a concept drift. Therefore, the old case should be removed. On the other hand, if equal cases have equal solutions, they are redundant and there is no need to keep both.

4.2 Review and Restore: Time analysis

If the combinatorial of the attributes is big, and the strategy is limited to the condition of finding identical case description, the capacity of following the concept drift by the proposed retain is low.
Thus, we propose to statistically analyse the ICRs of the cases in the case-base throughout time, and if there are significant differences in the time-line, we assume that there is a concept drift. Specifically, we sort the cases according to their timestamp (time when they were stored), and the mean and standard deviation of the ICR of the cases is calculated using a sliding window. When, significant differences are detected respect the first window, the older cases are removed.

4.3 Review and Restore: Coverage and reachability analysis

Redundancy of cases could happen because cases with equal solutions are closely located in the problem space, i.e. the description of the cases (attributes) and their solutions are equal or very similar. Metrics such as the coverage or the reachability of the cases are then used to evaluate how useful and redundant the cases are. The coverage of a target case is defined as the set of cases that can be accurately solved by the target case. On the other hand, the reachability of a target case is defined as set of cases that can be used to accurately solve the target case.
Review results are then used to restore cases in the case-base, or remove those considered as redundant.
In order to decide if a numeric solution like the ICR is valid to solve another case, this paper proposes to convert the maximum accuracy of insulin infusion (or minimum error) to a maximum allowed difference between ICRs in order to be considered as equal. Thus, if the dose quantification error in the insulin infusion system is half a bolus, then this value is converted to a maximum difference between ICRs. Thus, it is converted to the maximum error in terms of ICR.
Once the maximum difference between ICRs is calculated, reachability and coverage of each case are calculated. Next, given the reachability and the coverage of the cases, restore techniques such as CRR [6] or Iterative Case Filtering (ICF) [4] can be applied.
The CRR algorithm uses the coverage to remove the redundant cases. In particular, it sorts cases by descending order of coverage. Then, it

iteratively adds the cases in the new case-base, but when a case is added, the cases of its coverage are removed from the cases-pending-to-add list. Therefore, these cases are removed from the final case-base.
On the other hand, ICF calculates the reachability and coverage of all cases and then removes those whose reachability is greater the coverage.

5 Results and discussion

Experimentation has been carried out using 11 virtual adults of the UVA/PADOVA simulator [12]. These consist of 180 days and 20 repetitions. The performance of the proposed methodology is evaluated in terms of the portion of time the blood glucose of the subjects is in, below or above the glycaemic target range, which has been set to [70,180] mg/dl for all the virtual subjects. The proposed methodology is also evaluated in terms of size of the case-base.
The performance of the proposed methodology is analysed using CRR or ICF as case-base editing techniques, and it is compared with the methodology proposed in [17] and labelled as *no review-restore*. The attributes of the cases are those specified in [17] (time of day, past and planned activity and quantity of carbohydrates) plus eight random attributes:

- One binary attribute
- Five attributes with three nominal values
- Two attributes with four nominal values

Fig. 2 shows how the proposed method improves the results respect to the absence of a maintenance step in terms of time in the glycaemic target range. In particular, the proposed methodology with CRR significantly outperforms the method without a review-restore approach for all subjects except subject 2 according to t-student tests. Subject 2 has the highest blood glucose stability and this may be the cause for not improving it, i.e. the achieved time in the target range already was very good. On the other hand, the use of ICF instead of CRR achieves slightly worse results, because it outperforms the method without review-restore for subject 1, 3 and 5-8.
Regarding the time below and above the target range, Fig. 3 and 4 show that the proposed methodology achieves similar results than the method without review-restore. T-student test confirm that the proposed methodology using either CRR or ICF achieves significantly better results for some subjects but for other achieves results without significant differences. This means that time below or above the target range is maintained or improved, but never is worsened.
These aforementioned results imply that blood glucose is more stable (has less surges or drops). Therefore, this reduces the risk of hypoglycaemia and its consequent complications (clumsiness, trouble talking, loss of consciousness, seizures, or death), and the risk of hyperglycaemia and its long-term microvascular (retinopathy, nephropathy and neuropathy) and macrovascular (coronary heart disease, stroke and peripheral vascular disease) complications.
The proposed methodology is expected not only to maintain or even improve the quality of the recommendations, but doing it with smaller

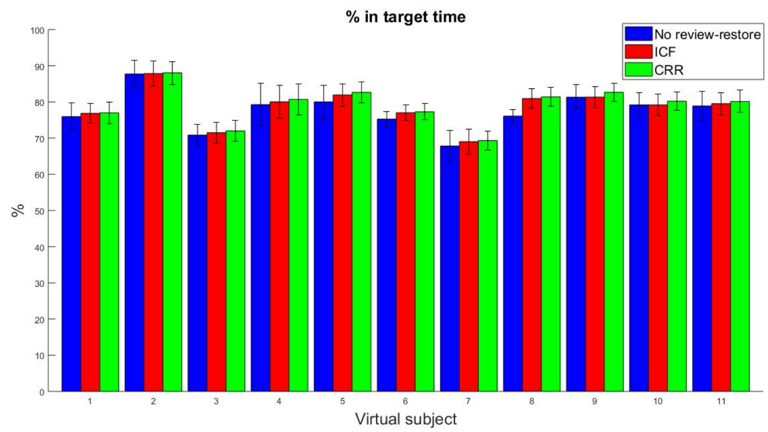

Fig. 2. Time in the glycaemic target range.

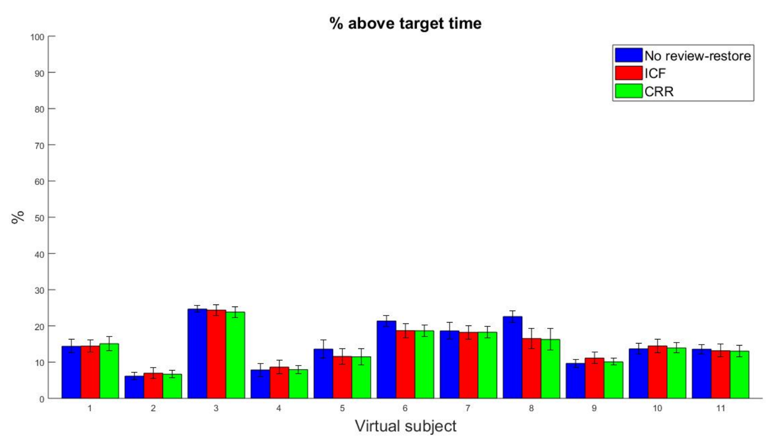

Fig. 3. Time above the glycaemic target range.

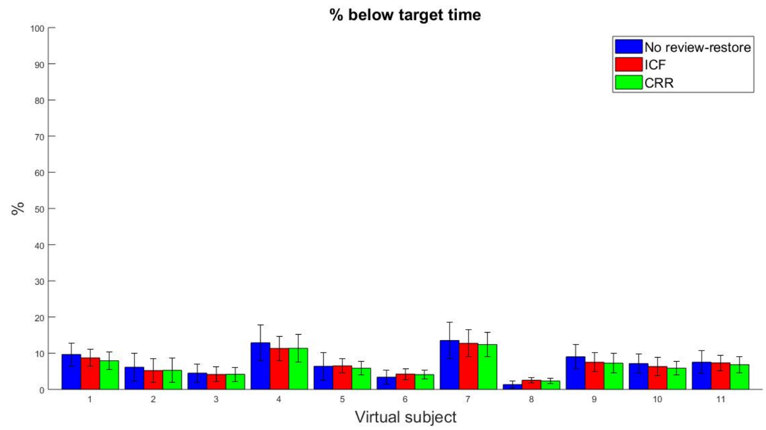

Fig. 4. Time below the glycaemic target range.

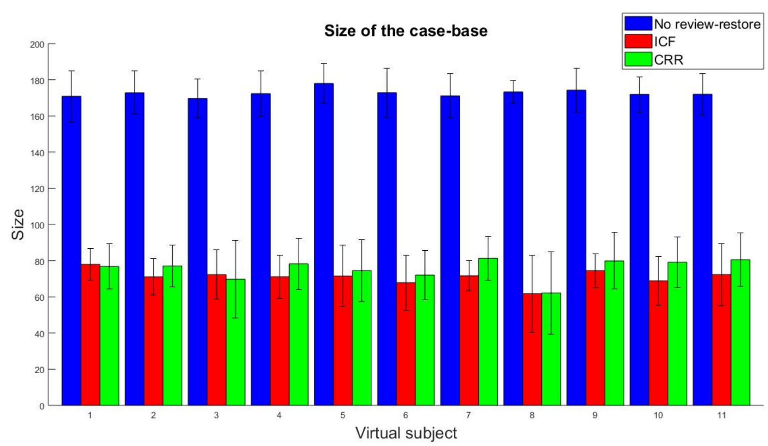

Fig. 5. Size of the case-base.

case-base. Fig. 5 shows the average and standard deviation of the size of the case-bases for all the virtual subjects when using PepperRec (without a review-restore phase) or the proposed methodology with ICR or CRR. The results show that there is a clear reduction in the size of the case-base using the proposed maintenance system.
Thus, the proposed methodology achieves more efficient case-bases, since the CBR system provides slightly better recommendations but using smaller case-bases. This is especially relevant because the system is less computationally demanding.

6 Conclusions

Bolus insulin recommender systems based on case-based reasoning for T1DM have been proven capable of providing accurate recommendations. In order to be useful and accessible to people with diabetes, these systems need to be implemented in mobile devices such as mobile phones. The efficiency of case-based reasoning systems relies on the size and quality of the case-base. As a consequence, this paper presents a methodology for editing the case-base in order to keep it efficient, i.e. small and accurate, and capable of dealing with mid- and long-term changes in the subject's physiology, problem known as concept drift.
The proposed method has been tested with 11 virtual adults using the UVA/PADOVA simulator. The achieved results demonstrate that the proposed method is capable of maintaining the case-base smaller than other methods and the whole system is capable of providing more accurate recommendations. Thus, the case-bases are smaller and the portion of time the blood glucose of the subjects is inside the glycaemic target range is slightly greater, which reduces the probability of hyper- and hypoglycaemia.
This work is still not finished and needs more experimentation to support these encouraging results. Moreover, it would be interesting to study how to complement this work with techniques capable of learning the relevance of the attributes.

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