Article

Active Labeling Correction of Mealtimes and the Appearance of Types of Carbohydrates in Type 1 Diabetes Information Records

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Abstract: People with type 1 diabetes are required to adhere to their treatment rigorously to ensure maximum benefits. Diabetes tracking tools have played an important role in this regard. Type 1 diabetes monitoring has evolved and matured with the advent of blood glucose monitor sensors, insulin pens, and insulin pump automation. However, carbohydrate monitoring has seen little progress despite carbohydrates representing a major potential disruption. Relying on the modeling of carbohydrate intake using the rate of exogenous glucose appearance, we first present a methodology capable of identifying the type of carbohydrates ingested by classifying them into fast and non-fast carbohydrates. Second, we test the ability of the methodology to identify the correct synchrony between the actual mealtime and the time labeled as such in diabetes records. A deep neural network is trained with processed input data that consist of different values to estimate the parameters in a series of experiments in which, firstly, we vary the response of ingested carbohydrates for subsequent identification and, secondly, we shift the learned carbohydrate absorption curves in time to estimate when the meals were administered to virtual patients. This study validates that the identification of different carbohydrate classes in the meal records of people with type 1 diabetes could become a valuable source of information, as it demonstrates the potential to identify inaccuracies in the recorded meal records of these patients, suggesting the potential abilities of the next generation of type 1 diabetes management tools.

Keywords: classification; carbohydrates; machine learning; type 1 diabetes; meal identification

MSC: 68T07

1. Introduction

Type 1 diabetes (T1D) is a metabolic disorder characterized by elevated blood glucose (BG) levels and insufficient insulin production [1]. T1D, most commonly diagnosed in young adults under 30 years of age, requires external insulin doses and strict adherence to treatment. The management of T1D is complex and depends on a large number of factors, such as the quantity of administered insulin, exercise, menstruation, seasons, and dietary alterations. Regardless of this variability, the goal is to control BG levels throughout the day within a safe range of 70–180 mg/dL [2]. A drop in BG levels below 70 mg/dL is referred to as hypoglycemia, whereas an increase above 180 mg/dL is known as hyperglycemia. Long-term complications of untreated hyperglycemia include cardiovascular disease, nerve damage (neuropathy), ketoacidosis, diabetic retinopathy, and poor blood flow, which can result in serious skin infections, ulcerations, and, in severe cases, amputations [3]. Similarly,

hypoglycemia is one of the most dangerous conditions for diabetics; in severe cases, it can result in unconsciousness, confusion, muscle spasms, and even death [4].

T1D management is challenging, and people with this disease are expected to tightly control their BG levels as well as maintain a strong adherence to their treatments for them to be fully effective. Monitoring BG levels has always played an important role in effectively managing diabetes. In the last few decades, diabetes tracking has been aided by the advent of continuous glucose monitors (CGMs) and flash glucose monitors (FGMs), which are technologies that use quantifying sensors to continuously measure BG levels. Tracking BG levels, either with a BG monitor, a CGM, or an FGM, is extremely valuable, as it helps patients and professionals track how effectively they are controlling their diabetes and it enables real-time informed decisions about any insulin dosage adjustments. In addition, data collected over a period of time also allow patients and healthcare professionals to assess trends and triggers, as well as allowing for a rigorous assessment of the extent of time in which patients actually remain within their glycemic targets. Likewise, insulin administration needs to be closely monitored and is thus another target of automated data collection systems that have been spearheaded by new technologies for automated insulin recording using insulin pumps or smart pens. In addition to glucose and insulin, an accurate estimation of the carbohydrates ingested during meals is another of the most important factors in adjusting insulin doses properly, being crucial to proper glycemic control [5]. In the latter case, although the literature has proposed applications with automatic support for carbohydrate counting [6], mainly through carbohydrate estimation with photo-based recognition and estimation approaches, apps integrating these tools are not being put on the market, and few people with T1D are currently using them.

Despite the aforementioned advances, most people with diabetes still have to manually record essential data for the complete assessment and monitoring of their treatment, which may include standard BG measurements, insulin boluses for multi-day injection (MDI) treatments, or carbohydrate estimations. The burden of manually performing this task, as well as the complexity of related estimates, leads to quantity errors, annotation errors, missing values, or directly the deliberate decision not to register some of the information. This results in inaccurate or incomplete information that hampers the medical team in making further assessments or even undermines the ability of the data-driven tools to deliver satisfactory results. Machine learning (ML) algorithms have already positioned themselves among the tools with the greatest impact that have future potential in general healthcare management to provide specific support for people suffering from this disease [7]. This study presents a collection of controlled experiments in which we map the potential of ML algorithms to ameliorate errors in patient data entries regarding meal intake times and the types of carbohydrates consumed. The goal is to investigate the capabilities of ML algorithms to identify different types of errors through the retrospective analysis of patient-recorded data. In the first batch of experiments, we tested whether the distinct patterns of the rate of exogenous glucose appearance (RA) in the blood, determined by the carbohydrate composition itself, can be identified by an ML algorithm. In the second round of experiments, the focus was on identifying labeling errors and filling in mealtime information, thus testing the ability of the ML algorithms to detect shifts in the actual timing of meal consumption. The contributions of this study are the following:

- The presentation of a machine learning methodology able to identify meals using distinct response profiles of the RA.
- Proving that the proposed methodology is also useful for the identification of the time of food intake.

The remaining sections of this paper focus on describing the methodology, reporting the results to support the proposed hypothesis, and discussing the limitations and possibilities of this study. Section 2 is devoted to the methodological approach adopted. Section 3 summarizes the experiments performed, while Section 4 analyses the results in light of their potential application in T1D treatments and closes the article with possible future directions and suggestions based on this study's findings.

2. Methodology

2.1. Patient Cohort Scenario and Preprocessing

This study analyzed a cohort of virtual T1D patients that was generated and simulated using a modified version of a recently published realistic simulator [8]. The software application is based on the Hovorka model [9] and allows for the generation of challenging scenarios; in this study, it was used to generate models of circadian variability in insulin sensitivity and exercise, as well as a library of mixed meals.

A cohort of 40 virtual patients was generated over a 42-day scenario. Three meals were scheduled each day: breakfast, lunch, and dinner. Breakfast was at 08:00 $\pm$ 50 min, and the amount of carbohydrates was 41 grams. Lunch was scheduled at 13:00 $\pm$ 50 min, and the carbohydrate content was 85 grams. Finally, dinner was at 20:00 $\pm$ 50 min, and the corresponding quantity of carbohydrates was 75 grams. All of the above-mentioned carbohydrate values were subject to a random variability of 5 percentage points. Treatment decisions were made based on the simulation of MDI therapy combined with CGM sensors. The CGM samples measured BG levels in intervals of 5 min, resulting in 288 values recorded per day.

The experiments in this study relied on the mixed-meal library presented in [8,10]. The mixed-meal library is based on real meals, providing the possibility of experimenting under realistic conditions and parameters. The dataset presents data from the RA profiles of a total of 54 meals that are categorized according to their composition and size (large, medium, fast, and small meals) according to the Kolmogorov–Smirnov distance metric. In addition, information on meal composition (fat, protein, fiber, and energy) is provided. The library has been included as a supplementary data source, as it can be a useful resource for testing a large number of applications, such as closed-loop insulin delivery systems, insulin bolus calculators, algorithms for predicting adverse glycemic events, or fault detection systems.

Different data processing steps were performed to prepare the data feed for the ML algorithms. From the raw datasets, data related to timestamps, CGM values, meal intake details, RA values, and insulin doses administered were collected.

2.2. Machine Learning Modeling for Time-Series Prediction

Based on the hypothesis that the amount, timing, and composition of carbohydrate intake are elements with a significant impact on future blood glucose (BG) levels, it was proposed that the performance of data-based prediction models should be analyzed when the carbohydrate information is manipulated. This hypothesis was partially tested in [11], in which different digestion curves were used to feed a machine learning model to assess the accuracy when predicting upcoming values of BG levels. In this study, an ML predictive model (described at the end of this subsection) was also applied to the problem of predicting BG in people with T1D using the simulated dataset described in the previous subsection, in which the absorption curves and the meal information are known. The current study's focus was on proving that the results of BG predictions, and hence the performance of ML techniques, is strongly tied to the accuracy and veracity of the available meal information, such as the type and amount of food, and meal timing information.

The prediction methodology was applied by making two-hour time-series predictions (24 output values) using CGM, insulin, and CHO historical time series corresponding to the two hours before the instant at which the prediction was made. Figure 1 shows a graphical representation summary of the predictions and related datasets used in a daily period. A total of 16 prediction windows per day were analyzed. As the main focus is on carbohydrates and their effects on BG, the daily period in which the predictions were performed was set from 08.00 to 24.00 h to avoid most of the sleeping period, which is when carbohydrates already have a reduced impact on BG levels.
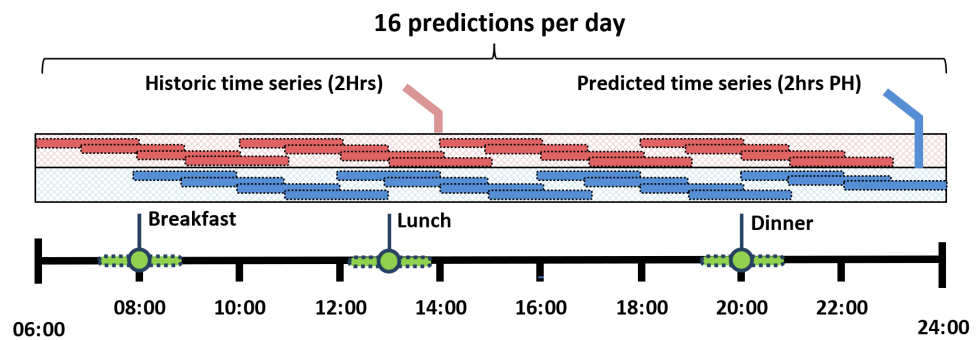
Figure 1. Graphical representation of prediction periods and mealtimes within ±50 min of variability (green). A total of 16 prediction windows per day comprising 2 h of historical time series (red) and 2 h of time series for validation and training (blue).

In previous related studies, a variety of ML techniques have been applied to the task of generating diabetes prediction models [7], where the most common techniques are based on artificial neural networks (ANNs). ANN models are trained to extract features from the input values based on their hidden parameters and generate outputs that minimize a loss function concerning the observed outputs. Once trained, ANNs can estimate the expected output for new unobserved data. These networks have demonstrated a great ability to self-learn from data, and as a result, they have become some of the most effective and widely used methodologies in studies based on ML methods. Different variants of ANNs have been applied for BG predictions or for the classification of adverse glycemic events (see [12–19], among others). In this study, a time-series prediction approach based on a Recurrent Neural Network (RNN) with a long short-term memory (LSTM) [20] architecture is proposed. The LSTM architecture is based on the previously validated model in [21], in which carbohydrate, insulin, and BG sequences of recent values were used to estimate upcoming values for BG levels. The main architecture implemented is shown in Figure 2. A four-layer architecture consisting of two LSTM layers of 48 units, an intermediate 20% drop-out layer, and an output dense layer was defined. The model was fed with the values from the time series for the last two hours of the BG, insulin, and carbohydrate sequences. A stochastic optimizer based on an adaptive moment estimation algorithm [22], together with a loss function implementing a root mean square deviation, was applied to guide the algorithm through the training process and, finally, to assess the goodness of the final BG predictions. The LSTM networks were trained for 60 epochs using a batch size of 8 and a validation/training ratio of 20/80.
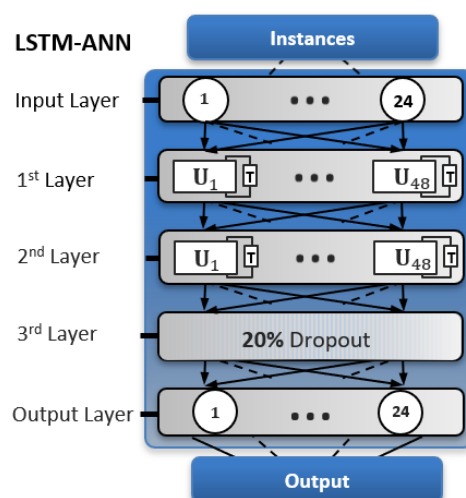

Figure 2. Graphical representation of the architecture of the long short-term memory neural network employed in the experiments.

The LSTM-based model in Figure 2 was used in two application scenarios. The first one replaces the historical carbohydrate amounts for each meal in the dataset (capturing the total amount of carbohydrates taken at the particular time in which the meal was administered) with candidate meal absorption curves. Each candidate curve is used as an input to the LSTM ML model (together with BG levels and insulin data). The ML model is trained for each candidate meal absorption curve shape in order to predict the subsequent BG levels. The ML model is trained to extract the information in input signals in order to provide estimations that are as accurate as possible. In this first application scenario, candidate absorption curves that better fit the real ones are expected to achieve better predictive accuracy values. Different meal absorption curves are generated based on the different physiological RA models used in the configurations representing variations in carbohydrate response in the dataset. For this purpose, synthetic RA curves are generated and combined with the total carbohydrates ingested during the time series by the virtual patients. Thus, the LSTM networks are fed with synthetically generated RAs and historical CGM and insulin series. The types of carbohydrates originally administered to patients are identified based on the performance of the prediction algorithm and the analysis of the original meal data, which are specified and classified in the mixed-meal library and for which we know the values of the RA time series. Figure 3 shows a graphical representation of the methodological scheme applied. In the second scenario, the ability of the presented methodology to detect the erroneous labeling of mealtimes in diabetes records, either due to database errors or the misalignment of patient entries, is evaluated by examining the forecasting accuracy of the LSTM networks when modifying the mealtimes. The proposed LSTM can be applied to analyze multiple shifts in mealtimes with respect to their original entries. The prediction tool's data feed is thus composed of multiple instances of each meal with deliberately distinct offsets, enabling the algorithm to determine the most suitable one for predicting upcoming values of glucose.
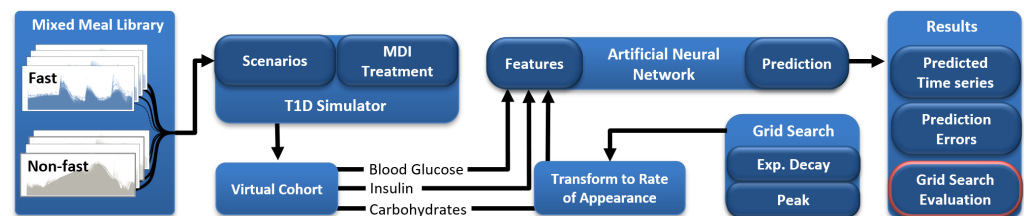

Figure 3. Graphical representation of general methodology for the identification of the exogenous glucose appearance rate response.

2.3. Modeling the Rate of Exogenous Glucose Appearance

A model was implemented to generate different RA curves to mimic real RA curves in the dataset by using a parametric curve generator. The model is based on the combination of a cubic polynomial function and an exponential decay function (see Equation (1)). The initial phase of the RA response, representing incremental blood carbohydrate uptake, is represented by the polynomial function, while the decreasing rate of carbohydrate uptake is represented by an exponential function. Thus, the model is based on two essential parameters: the time to a maximum peak of the curve and the exponential decay of the curve. The RA shapes generated by this model can represent a wide range of curves by combining both parameters. Figure 4 shows all of the curves that were generated for the experiments presented in this article. On the one hand, the parameter representing the peak time at which the meal has a maximum action is staggered at an incremental time interval (*peak* ∈ {20 min, 40 min, 1 h, 1 h 20 min, 1 h 40 min, 2 h, 2 h 20 min, 2 h 40 min, and 3 h}). On the other hand, an exponential decay parameter was configured to boost the fall in the rate of glucose appearance at six increasing rates (*decay* ∈ {0.6, 0.8, 1.05, 1.45, 2.2,

and 3.85}). The dashed line in Figure 4 captures the overall variability in the real values obtained from the mixed-food library used to generate the experimental data.

$$ShapeRA(k) = \begin{cases} p(k) & if \quad p(k) \leq p(k+1) + \lambda \\ e(k) & if \quad p(k) > p(k+1) + \lambda \end{cases} \tag{1}$$

where

$$p(k) = peak * 3k - k^3$$
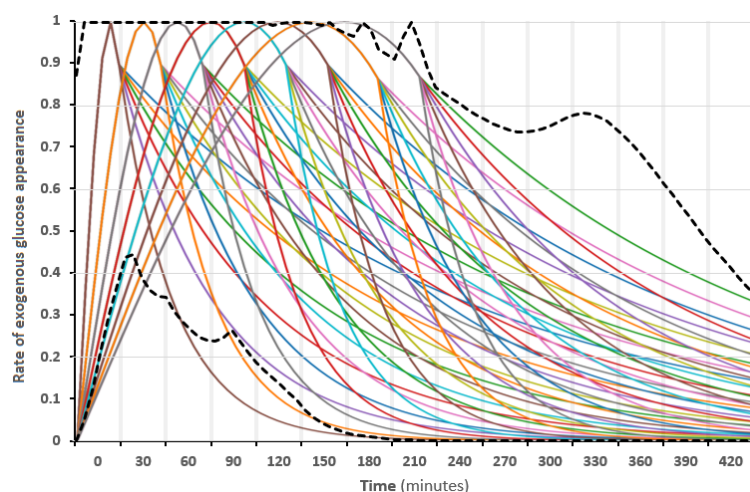$$e(k) = e^{decay * -0.04k}$$
$$\lambda = peak/3.5$$

Figure 4. This graph illustrates colored lines that depict time series data of exogenous glucose appearance rates in the blood, encompassing all combinations of [*decay*, *peak*] tuples. The dashed line represents the overall variability observed in the mixed-food library.

2.4. Technical Specifications

Matlab scripts were developed to modify the T1D simulator in [8] in order to generate the simulated patient data for experimentation and to perform all data preprocessing operations. A Python-based program was developed to implement the LSTM-based machine learning model described in the previous subsection and to compute performance metrics when fed with different RA-generated curves for the simulated patients. Python implementation used the Keras library for LSTM implementation and other data management functions belonging to the Scikit-Learn (1.2.0), Numpy (1.19.5), Pandas (1.5.2), and Matplotlib (3.8) libraries. Parallelization features from TensorFlow (2.0) were employed to improve computational times on a GeForce RTX™ 3090 (Nvidia, Santa Clara, CA, USA).

3. Results

3.1. Identification of the Carbohydrate Appearance Rate Response

The first batch of experiments was focused on the identification of the types of carbohydrates administered to the generated patients. The T1D simulator was configured so that each generated patient always consumed the same type of meal (either fast or non-fast in terms of carbohydrate absorption rates).

The LSTM machine learning model was trained with the generated RA candidate curves for each patient (10 executions per patient, 60 epochs per each generated curve inside each execution using a batch size of 8, and a validation/training ratio of 20/80). The parameters (peak time and exponential decay values) were explored exhaustively, meaning that all configurations were tested per patient. Finally, the parameters defining the RA curves achieving the best model validation accuracy per execution were selected. Figure 5 shows a scatter plot of the best parameters (peak and decay) obtained for the

corresponding prediction values. The graph shows different carbohydrate response clusters, where the overall means are represented by black and red circles. These means show values of 40.5 min peak time and 3.3 ratio of decay for fast-response carbohydrates, and values of 91 min peak time and 1.6 ratio of decay for non-fast meals. Each pair of the remaining values identified by crosses (+ or x) consists of the medians of the best-performing solutions over the total set of executions. A solution is considered to be among the best solutions if its loss value (the root mean square deviation) is within the first quartile of the overall loss values obtained by the tested models. The points are grouped by patient and labeled according to the response of the curve (fast and non-fast). In addition, Figure 6 presents the RA curves corresponding to the parameter pairs shown in the previous figure, thus presenting the best median RA curves for the overall cohort. The latter figure also presents the overall variability in the mixed-meal library in the dashed area. The RA curves fit the area defined by the library relatively tightly, although both fast and non-fast plots present points outside of the reference area. This is probably because the curves are approximations of the real curves and thus provide a lower degree of complexity with respect to the generated curves, as they lack features inherent to real meals, such as changes in the exponential decay rate, multiple peaks, etc. While the present study did not intend to evaluate the performance of the predictions itself, and no fine tuning of the methodology was performed to exploit its full potential, the predictions show feasible errors for the future possible exploitation of the model's forecast results. Table 1 shows a summary of the mean RMSE errors obtained and the related variability for all generated models.

Table 1. Mean RMSE values and their corresponding standard deviations for fast and non-fast models.

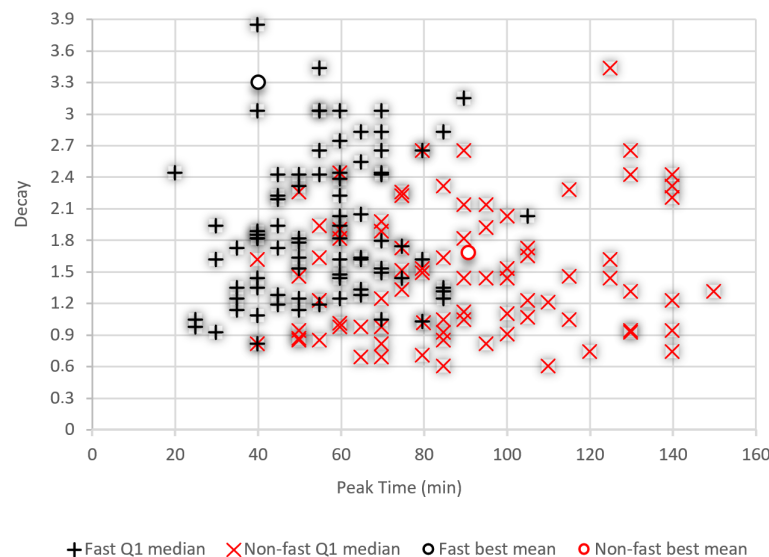|	$\overline{RMSE}_{All}$	σ_{All}	$\overline{RMSE}_{Best}$	σ_{Best}
Fast	32.09	16.64	14.02	4.38
Non-fast	15.89	7.32	12.08	5.06

Figure 5. Scatter plots of the analyzed parameters, the exponential decay, and the peak time generated by the meal. The filled shapes represent the mean value of the best solution for all patients, while the empty shapes show the median of the first-quartile solutions for each patient.
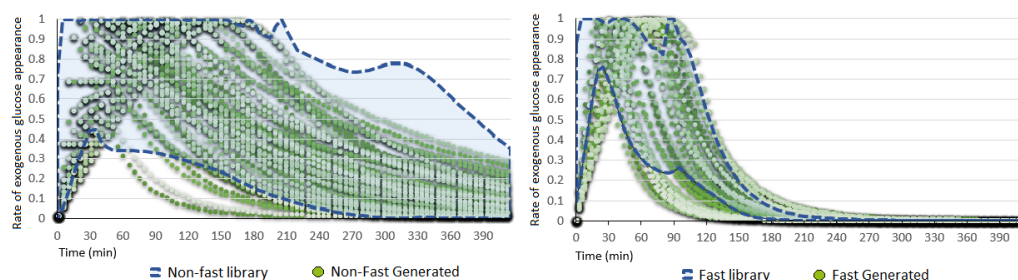
Figure 6. Best median exogenous glucose appearance rates for fast and non-fast meals, and their corresponding variability in the mixed-meal library.

3.2. Timing of Meal Intake Identification

The second strand of the experiments addressed the ability of the presented methodology to detect the mislabeling of mealtimes. The time shifts for the RA series were distributed around the original mealtimes, anticipating and delaying them by a maximum of one hour (±10 min, ±20 min, ±30 min, ±40 min, ±50 min, ±60 min, and no displacement were tested). Unlike in the previous subsection, the LSTM machine learning model was trained with the original shifted RA curves for each patient. Finally, the time-shift parameters defining the RA curves achieving the best model validation accuracy per execution were selected. Table 2 presents the experimental results of the means and medians of the best parameters. As previously stated, the best solutions are those solutions with loss values within the first quartile of the overall loss values obtained in this experiment.

Table 2. Means and medians of the best-performing parameters for the task of blood glucose prediction.

	Total		Fast		Non-Fast	
	1Q Mean	**Best**	**1Q Mean**	**Best**	**1Q Mean**	**Best**
Mean (steps)	3.53	2.53	5.76	3.60	1.29	1.45
Median (steps)	5.10	4.00	6.40	4.00	2.93	4.00
Deviation (steps)	4.35	5.01	1.31	1.95	5.12	6.67
Mean time (min)	17.63	12.63	28.78	18.00	6.47	7.25
Median time (min)	25.50	20.00	32.00	20.00	14.64	20.00
Deviation time (min)	21.73	25.07	6.55	9.73	25.61	33.34

4. Discussion and Conclusions

The relevance of the effect of carbohydrate intake in people with type 1 diabetes (TD1) is not in question; however, the monitoring of carbohydrate intake has been significantly reduced in relevance when compared with other factors, such as insulin or glucose. The complexity of its estimation, the variability in the carbohydrate content of meals, and the variability in the response of carbohydrates according to diverse factors (cooking time, cooking method, etc.) are some of the reasons that make it a diminished factor in T1D management systems. It is, therefore, essential to increase research efforts to obtain meaningful information about the food ingested by patients. In this paper, an analytical effort was made in this direction by looking at the feasibility of a system for correcting mealtime labeling information derived from meals to enhance T1D databases, either by identifying the correct labeling of mealtimes or by identifying the response curves of the rate of exogenous glucose appearance (RA) in blood.

Based on the reported results, it can be argued that carbohydrates play an important role in data-driven prediction algorithms and that the performance of machine learning (ML) techniques is closely linked to the reliability and veracity of the available meal information. This, in turn, makes it possible to propose a reverse-based system that can carry out a retrospective analysis of data, where future data from a hypothetical prediction event are already available. This would make it possible to derive details about meals by analyzing the output signal, which would correspond to the values of a continuous glucose

monitor (CGM). In this way, data could be checked for inconsistencies, or the databases could be improved by enriching them with supplementary information.

As shown in the experimentation, the RA curves generated in this study provided approximations for grouping the different types of meals due to their general response. However, the curves for real meals present more irregular shapes that are related to the type and amount of ingredients, among other factors. This fact prevents an accurate approximation of the generated curves compared with those of the actual meal. Given the recent explosion of in silico data generation techniques based on data-driven approaches, techniques such as generative antagonistic networks (GANs), which have demonstrated their ability to generate time series in various domains and, in particular, in T1D, suggest that more realistic RA curve generators could be interesting features that could complement such systems [23,24].

The results presented in this study make it clear that further research efforts should be directed towards this field, as a refined methodology would lead to significant potential applications within the realm of smart health solutions for individuals with diabetes, particularly for those afflicted with T1D. Starting with the most immediate applications, carbohydrate monitoring and classification techniques may serve to help people with T1D to estimate the impact of different carbohydrates on their blood glucose levels, providing real-time carbohydrate classification at mealtimes. This capability may also assist as an educational instrument, helping users understand the influence of diverse carbohydrates on their diabetes management. On the other hand, a substantial proportion of diabetic individuals struggle in accurately documenting the timing of their meals. The ability to analyze historical data and alert users when discrepancies or inconsistencies are detected in their meal records helps users maintain more reliable records for better diabetes management. Additionally, by integrating these capabilities, smart health solutions can provide more accurate predictions of postprandial blood glucose levels, enabling better insulin dosing decisions. Moreover, these data-driven methods can learn from individual user data to provide personalized insights and recommendations, such as mealtime adjustments based on the user's historical carbohydrate consumption patterns and corresponding blood glucose responses.

This study has obvious limitations concerning the immediate applicability of the results. On the one hand, although virtual T1D patients offer valuable opportunities for research and training, they do not always accurately represent the complexity and nuances of real patient data. Virtual patients are generated based on algorithms and assumptions, which can lead to limitations in capturing the full spectrum of clinical variability and unpredictability seen in real patient cases. Consequently, the extrapolation of results from virtual patient simulations to real clinical practice should be performed with caution, and the translation of knowledge and interventions requires further validation in real patient populations. On the other hand, to validate the results of the proposed methodology, it is necessary to have a database with reliable and accurate information on the meals consumed by patients. Therefore, future work should include obtaining datasets that allow us to validate the system in a real environment and to improve the system with an approach capable of automatically handling historical datasets for their improvement.

To conclude, this research study presented a collection of experiments focusing on the relevance of patient-collected carbohydrate information within T1D management systems, demonstrating not only the substantial contribution of machine learning models for obtaining carbohydrate information, but also providing a pathway to improve historical T1D datasets.

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Data Availability Statement: Data from virtual patients will be shared upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

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