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Unannounced Meal Detection for Artificial Pancreas Systems Using Extended Isolation Forest

Fei Zheng^{1,2}, Stéphane Bonnet², Emma Villeneuve², Maeva Doron², Aurore Lepecq² and Florence Forbes¹

Abstract—This study aims at developing an unannounced meal detection method for artificial pancreas, based on a recent extension of Isolation Forest. The proposed method makes use of features accounting for individual Continuous Glucose Monitoring (CGM) profiles and benefits from a two-threshold decision rule detection. The advantage of using Extended Isolation Forest (EIF) instead of the standard one is supported by experiments on data from virtual diabetic patients, showing good detection accuracy with acceptable detection delays.

I. INTRODUCTION

Currently, the most used Artificial Pancreas (AP) system implements an hybrid closed-loop requiring patients with Type 1 Diabetes (T1D) to declare both the time and the amount of their carbohydrates (CHO) intakes. Consequently, such systems are prone to CHO underestimations due to missing declarations and may lead to inadequate insulin dosing, and expose the subjects to hyperglycemia risk [1]. Unannounced meal detection and quantification is thus an essential task to reduce such risk as well as to achieve an accurate fully automated closed-loop AP system.

Studies have been devoted to unannounced meal detection with a majority of them implementing physical model-based detection methods. The minimal model [2] or Medtronic Virtual Patient (MVP) model [3], [4] are modified for the application of different prediction algorithms, for example Unscented Kalman Filter [5], [6], Moving Horizon Estimation [7] or Sliding Mode Observer [8] to estimate the states (specifically glycemia and meal appearance rate). Some linear state-space models are adjusted also for describing the pharmacodynamic response of insulin and glucose appearance, so that Kalman Filter [9] or Variable State Dimension [10] can be applied for the states estimation. Then, detections are made by comparing the residuals between the estimated and observed states to a threshold [8], by calculating their cross-covariance [6], or by applying further decisions rules, for example hypothesis testing [9] or statistical analysis [7].

Besides the model-based detection approaches, data-driven methods have the advantage that their performance is much less dependent on the identification accuracy of the applied physical model. Three data-driven methods are studied in [11] for insulin pump fault detection, showing that Isolation Forest (IF) [12] outperforms the other two density-based outlier detection methods. Inspired by [11], our work adapts the application of IF to unannounced meal detection. We

propose suitable features for individual Continuous Glucose Monitoring (CGM) profiles, and a two-threshold-based rule for risk evaluation and detection. More importantly, the replacement of the standard IF by its recent generalization named Extended Isolation Forest (EIF) [13] is explored and shows promising performance on a virtual data set for this specific unannounced meal detection task.

The remaining of the paper is organized as follows: Section II presents the proposed EIF based detection method, Section III shows the superiority of EIF compared to standard IF and evaluates the performance of the method on a virtual data set; finally, Section IV concludes the work and draws some perspectives.

II. METHODS

A. Isolation Forest & Extended Isolation Forest

Isolation forest (IF) is an approach to detect anomalies that explicitly isolates anomalies rather than profiles normal instances [12]. Let $\mathbf{X} = \{\mathbf{x}_1, \dots, \mathbf{x}_N\}$ denote the training set, where $\mathbf{x}_n \in \mathbb{R}^d$. $\mathbf{X}_\psi[m]$ denotes a randomly sampled subset of size ψ from \mathbf{X} with $m \in \{1, \dots, M\}$ represents the subset size. An isolation tree (iTree) recursively divides $\mathbf{X}_\psi[m]$ by randomly selecting at each node an attribute among d features and a split value. The process is stopped for a node when it contains only one instance or when the instances are with the same value.

We denote by $h(\mathbf{x})$ the so-called “path length” of \mathbf{x} which is the number of edges that \mathbf{x} traverses from the root node to the external node of an iTree. In practice, the path length is limited to the depth $l = \text{ceil}(\log_2 \psi)$. Then, the Anomaly Score (AS) is defined by:

$$s(\mathbf{x}) = 2^{-\frac{E[h(\mathbf{x})]}{c(N)}}. \quad (1)$$

$c(N)$ is the theoretical average path length which is only related to the training set size N [12]. $E[h(\mathbf{x})]$ represents the expectation of path length of instance \mathbf{x} , which can be approached by averaging over M iTrees. The AS takes its value in $(0, 1]$. A score close to one indicates that the corresponding instance \mathbf{x} is easy to isolate and could then be considered as an outlier.

As a variant of IF, Extended Isolation Forest (EIF) creates nodes by randomly selecting an hyper-plane in the feature space. It can thus provide relatively more consistent anomaly scores, as well as more accurate detection of the feature structure [13]. When applying EIF, different extension levels can be chosen related to the number of feature axes that hyper-planes intersect, ranging from 1 (intersect 1 feature,

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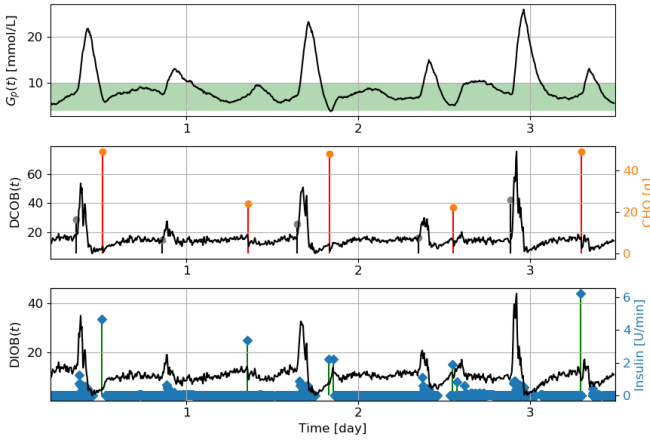


Fig. 1: Feature time waveform. Green area in top figure shows the ideal glycemia range. Gray stems in middle figure show unannounced meal and orange stems are announced ones. Insulin doses (basal + bolus) are displayed by blue stems in bottom figure.

leads to the standard IF) to d (intersect d features, fully extended).

B. Features for Unannounced Meal Detection

Considering the unannounced meal detection problem, inspired by [11], $d = 3$ features are chosen such that $\mathbf{x} = [G_p(t), \text{DCOB}(t), \text{DIOB}(t)]$. $G_p(t)$ represents plasma glucose which is approximated by CGM measurement, while DCOB, DIOB are defined as follows:

$$\text{DCOB}(t) = \frac{\alpha \exp(\gamma \dot{G}_p(t))}{\omega \text{COB}(t) + 1}, \text{DIOB}(t) = \frac{\beta \exp(\gamma \dot{G}_p(t))}{v \text{IOB}(t) + 1}. \quad (2)$$

$\dot{G}_p(t)$ represents the time derivative of $G_p(t)$ [mmol/L], $\text{COB}(t)$ [mmol] and $\text{IOB}(t)$ [mU] are CHO on board and insulin on board respectively. COB and IOB are calculated using declared CHO (if any) and injected insulin through a modified MVP model (see Section V for details) identified on a training set. Doing so, the MVP model parameters as well as the features can adapt to specific profile. The description of the virtual patient simulator is in Section III. The hyper parameters are manually tuned and set as: $\alpha = \beta = 15$, $\gamma = 5$, $\omega = 8 \times 10^{-4}$ and $v = 10^{-4}$.

An example of features from a virtual patient is illustrated in Fig. 1. It is worth noticing that the computation of $\dot{G}_p(t)$ requires the knowledge of $G_p(t+1)$, if 2nd order accurate central difference is applied as in this work, which leads to a minimum detection delay of one sample interval, = 5 min.

C. Risk levels & Detection Decision

Outlier detection is usually performed using a single threshold. We propose a more reliable decision rule using two thresholds related to two unannounced meal risk levels, low and high, respectively. They are defined as:

$$\text{thr}(\eta) = \begin{cases} F^{-1}(\eta) & 0 \leq \eta \leq 1 \\ 1 - (2 - \eta)(1 - F^{-1}(1)) & 1 < \eta \leq 2 \end{cases}, \quad (3)$$

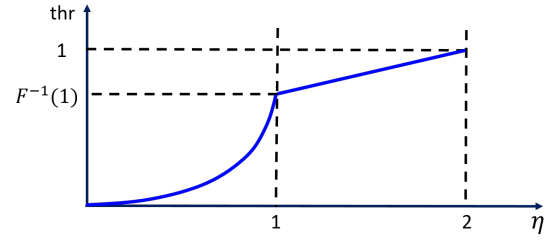


Fig. 2: Anomaly Score (AS) threshold.

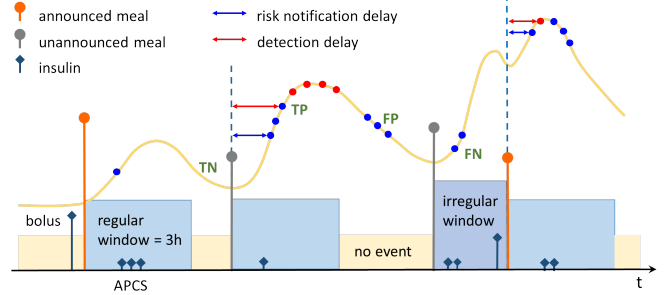


Fig. 3: Example of anomaly detection and evaluation (yellow curve shows the glycemia). TP: True Positive, TN: True Negative, FP: False Positive, FN: False Negative.

where $F^{-1}(\cdot)$ represents the empirical quantile function of AS values from a training set (with all meals announced), $\eta \in [0, 2]$ is the parameter of the threshold. When $\eta \leq 1$, $\text{thr}(\eta)$ is the empirical quantile of order η of the training set AS values. While the threshold is linear with respect to η when $\eta > 1$, As seen on Fig. 2. We then define the low risk and high risk thresholds using parameters $\eta = \{\eta_l, \eta_h\}$. An alarm of unannounced meal is then raised when either: 1) one high risk appears ($\text{AS} > \text{thr}(\eta_h)$); 2) or three successive low risks are observed ($\text{AS} > \text{thr}(\eta_l)$). See Fig. 3 for an illustration. To summarize, the meal detection process for individual subject consists of a training and testing step as follows:

- Training: 1) a MVP model is first identified using a training dataset. 2) EIF is trained on the training feature set and AS thresholds are defined.
- Testing: 1) The MVP initial state of the tested scenario is estimated; 2) for each coming sample, its AS is computed and the announced meal risk is evaluated with the following appropriate detection decision.

For evaluation, the regular detection window is set to 3h (maximum detection delay) except when two meals are less than 3h apart (see irregular window in Fig. 3).

III. EXPERIMENTAL RESULTS

A. Virtual Patient Data Set

The proposed method is tested on four virtual patients simulated from SIM-HOV¹ based on Hovorka model [14]. The data includes CGM measures, insulin doses and announced meals with a sample rate of 5 min. In addition, SIM-HOV

¹SIM-HOV is a Python simulator developed by DiabeLoop S.A.

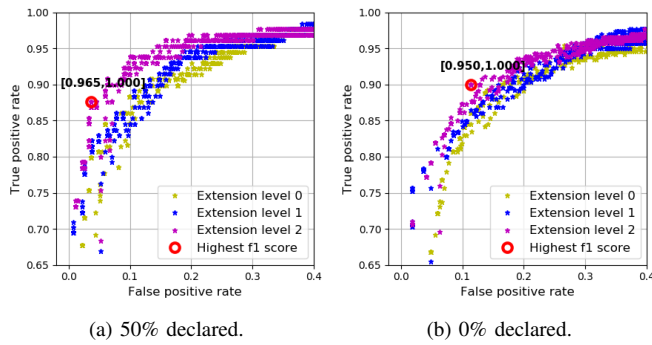


Fig. 4: ROC surfaces for different IF extension levels with respect to different thresholds (annotation shows the value of η which gives the best f_1 score).

considers that the data is contaminated by a Gaussian noise with a standard deviation (sd) of $0.012 \times G_p(0)$ mmol/L, where $G_p(0)$ is the initial glycemia value. The patients have various physiologies, such as different insulin sensitivity and digestion speed. Simulated scenarios correspond to an average of 3.4 meals per day, with time and size of the meals randomly sampled from the DiabeLoop WP7 data set² (median meal size: 40g CHO and interquartile 35g). Thus the virtual patients have similar eating behaviour to the real patients. Their glycemia was continuously regulated in closed-loop by an AP Controller for Simulation (APCS) designed by Algorithms Teams from DiabeLoop S.A and CEA. APCS adjusts in real-time the insulin bolus and basal infusions according to a certain strategy in order to maintain glycemia in a healthy range. As we can see in Fig. 1, some compensation insulin doses are delivered after meals. However, APCS does not realise any meal detection.

In the experiment, for each virtual patient, a 5-day scenario (with all meals announced) of data is simulated for training, and two scenarios of 20 days are available for testing. One scenario includes 50% of declared meals, to mimick the case where meals are irregularly announced by patients. Another scenario has 0% meal declared to mimick a fully automatic meal detection case.

B. Performance

The procedure described in Section II-C is applied for unannounced meal detection to each virtual subject. The MVP model is identified through a non-linear least-square method. Then, EIF with a certain extension level is trained on the 5-day scenario training set. The parameters of EIF are set empirically to $\psi = 256$ and $M = 100$. Various thresholds are tried with η_l in $[0.6, 1.2]$ and η_h in $[\eta_l, 1.2]$ with a 0.05 step. When $\eta_l = \eta_h$, the decision is degraded to the commonly used single threshold case. Testing is conducted on the two scenarios with 50% and 0% declared meal. The initial state of the MVP model is estimated using the initial 5-hour data. The detection is then processed “real-time” like,

²DiabeLoop WP7 study [15] is a 12-weeks nationwide (France) randomized crossover trial study concerning 63 T1D patients.

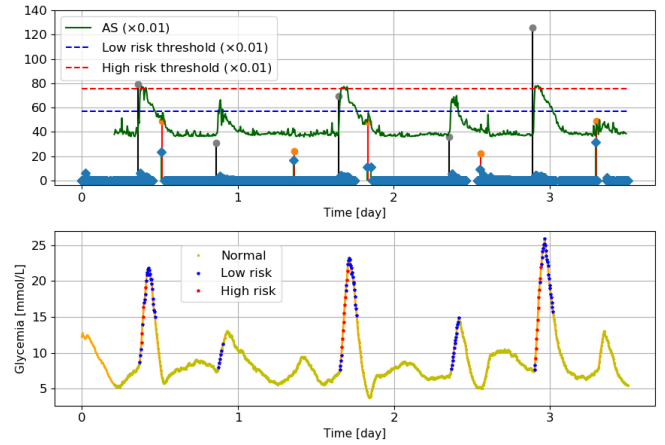


Fig. 5: An example of detection result. Risks are shown on glycemia (bottom), with corresponding meal [g] and insulin ($5 \times$ original value) [U/min] information, AS and AS thresholds (top).

sample by sample, calculating the AS value through trained EIF, measuring the risk and taking a subsequent decision, as illustrated in Fig. 3.

ROC surfaces of the detection performance for different choices of η are illustrated in Fig. 4. From it we can conclude that under the proposed detection framework, EIF with the highest extension level outperforms the other extension levels as expected. The thresholds chosen by f_1 score [16] in the test of 50% and 0% meal declaration are close to each other and both with $\eta_l < \eta_h$. This shows the interest of the two threshold decision.

To further assess the detection performance, we detail the fully extended IF case (extension level 2) with $\eta = [0.950, 1.000]$. Table I reports the performance matrix, which shows for both 50% and 0% meal declaration cases, that EIF reaches a high true positive detection rate around 90%. The false alarm rate of the all unannounced meal case is 11.47% while it is 6.2% for the 50% declaration case. This is probably due to the continuous abnormal behavior affected by dense unannounced meals. Around 39% announced meals are detected as unannounced, which may mean that, measured by the trained EIF, the delivered insulin regulated by APCS is not adequate to compensate the effect of the announced meal. Indeed, the proposed method is tested

TABLE I: Performance (detection rate average (sd)) for the fully extended IF with $\eta = [0.95, 1.00]$.

Event	Unannounced meal	Announced meal	No event
50% declared	90.8% (8.0%)	38.9% (17.5%)	6.2% (4.1%)
0% declared	90.0% (2.1%)	–	11.47% (6.8%)

TABLE II: Detection delay (average (sd) min)

Delay	Unannounced meal		Announced meal
	50% declared	0% declared	
Detection	39.0 (22.8)	35.1 (16)	31.1 (16.6)
risk notification	30.2 (22.3)	26.3 (15)	22.4 (15.4)

under a harder condition than the pure open-loop case, since less evidence is observed thanks to the compensation from APCS. The standard deviations shown in brackets confirm an acceptable performance variance in between subjects.

Table II reports the delays of detection which are within 40 min on average, and risk notification are within 31 min for all cases. It happens for the virtual patients that some unannounced meals raise risks that maintain longer than their irregular detection windows, and are detected as an alarm of the following announced meal. This phenomena leads to a shorter detection delay concerning announced meals as observed in Table II.

The detection result from a virtual patient with 50% declared meals is illustrated on its glycemia record in the bottom figure of Fig. 5. The corresponding meal and insulin intake, estimated AS values and risk thresholds are depicted in the figure above. The good performance of the proposed detection method can be visualized. Running on a 3.6 GHz CPU, the MVP identification and EIF training take 197 s, then the risk evaluation of each sample takes only 0.005 s.

IV. CONCLUSIONS & PERSPECTIVES

An Extended Isolation Forest (EIF) based method is proposed to detect unannounced meals for artificial pancreas. The method captures differences in individual profiles, with real-time applicability. The detection performance is illustrated on virtual patients data simulated from SIM-HOV. It shows the superiority of using EIF over the standard Isolation Forest (IF) and the interest brought by the introduced two threshold decision rule.

Future work includes: 1) MVP update for adapting the physiological dynamics of a subject; 2) safe thresholds decision strategy for real patients individually; 3) meal size estimation and compensation bolus calculation for fully closed-loop AP, possibly using the estimated AS from EIF.

V. APPENDIX

A. Modified Medtronic Virtual Patient Model

The modified MVP model [3], [4] with a complexity trades off between minimal models and maximal ones is defined by:

$$\begin{aligned} \text{CHO} \quad & \begin{cases} \dot{D}_1(t) &= A_G U_m(t) - D_1(t)/\tau_D \\ \text{absorption} \quad \dot{D}_2(t) &= D_1(t)/\tau_D - D_2(t)/\tau_D \end{cases} \\ \text{insulin} \quad & \begin{cases} \dot{S}_1(t) &= U_i(t) - S_1(t)/\tau_S \\ \text{absorption} \quad \dot{S}_2(t) &= S_1(t)/\tau_S - S_2(t)/\tau_S \\ \dot{I}_P(t) &= S_2(t)/(V_I \tau_S) - k_e I_P(t) \end{cases} \end{aligned}$$

$$\dot{I}_{eff}(t) = -p_2 I_{eff}(t) + p_2 S_I I_P(t)$$

$$\dot{G}_p(t) = -[p_1 + I_{eff}(t)] G_p(t) + p_1 G_b + D_2(t)/(V_G \tau_D)$$

The model considers 2 inputs, CHO intake $U_m(t)$ [mmol/min], insulin delivery $U_i(t)$ [mU/min], and 7 states, amount of glucose in remote compartments $D_1(t)$, $D_2(t)$ [mmol], amount of insulin in remote compartments $S_1(t)$, $S_2(t)$ [mU], plasma insulin concentration $I_P(t)$ [mU/L], insulin effect $I_{eff}(t)$ [1/min] and plasma glucose $G_p(t)$ [mmol/L]. The 10 parameters are: CHO utilization A_G , CHO and insulin absorption delay τ_D , τ_S [min], insulin

elimination rate k_e [1/min], insulin and glucose distribution volume V_I , V_G [L], insulin sensitivity S_I [L/mU/min], glucose effectiveness at zero insulin p_1 [1/min], rate of disappearance of insulin effect p_2 [1/min], and basal glucose G_b [mmol/L].

Based on the MVP model, $COB(t) = D_1(t) + D_2(t)$ and $IOB(t) = S_1(t) + S_2(t)$ for features in (2).

The estimated parameters of the subject in Fig. 5 are: $A_G = 0.86$, $\tau_D = 51.7$ min, $\tau_S = 97.6$ min, $k_e = 0.09$ /min, $V_I = 12.3$ L, $V_G = 6.5$ L, $S_I = 3.96 \times 10^{-4}$ L/mU/min, $p_1 = 0.026$ /min, $p_2 = 0.01$ /min, $G_b = 8.62$ mmol/L.

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