# MACHINE LEARNING METHOD TO PREDICT AND MITIGATE REAL-TIME BLOOD GLUCOSE PREDICTION UNCERTAINTY

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## BACKGROUND AND AIMS

To maintain blood glucose levels (BGL) in the safe range, and prevent complications, it is critical for insulin requiring patients to self-administer insulin according to their fluctuating needs. Assessing the most appropriate dosing is complex and patients must make those decisions on-the-spot, using data at their disposal, personal knowledge and experience, and what they lack is a way to anticipate.

Therefore, to improve glycemic control, there is a need for a system capable of producing reliable and personalised BGL predictions, as the accurate interpretation of the data is the most relevant aspect of the patient's decision-making process.

At Hillo we have developed an accurate machine learning (ML) method to predict BGL at prediction horizons (PH) up to 2h **[A]**. But despite this good accuracy, erroneous predictions could occur and lead to bad decisions for the patient. There is a need to anticipate these events and minimize their frequency of occurence.

## MATERIALS AND METHODS

The sample included data from 14 T1DM patients: real-life BGL from CGM devices, carbs intakes and insulin injection data collected over 30 days.

| Sample Characteristics | |
|---|---|
| Group Size | n = 14 |
| M / F | 6 (43%) / 8 (57%) |
| Age (years) | 51 ± 15 |
| HbA1c (%) | 7.09 ± 0.82 |

**Table 1:** Characteristics [M ± SD, n (%)]

In the present work, patient's data sets are splitted respecting time ordering between 80% for train set and 20% for test set, and we perform 5 folds cross-validations both for model stacking, and for all grid search procedures.

We are able to build patient-specific BGL predictors. At a prediction time $t_{pred}$, a BGL predictor try to guess the BGL value $y_{t_{target}}$ at PH time $t_{target}$, depending on data available $x_{t_{pred}}$. We assume that a full probability distribution of possible BGL $p(y_{t_{target}} \mid x_{t_{pred}})$ exists at time $t_{target}$, and we want to estimate its conditional probability density. We focus on a ML approach using density models.

Let us call $q(y_{t_{pred}};\Theta)$ a family of probability distributions that may fit $y_{t_{target}} \longmapsto p(y_{t_{target}} \mid x_{t_{pred}})$, for any features $x_{t_{pred}}$. The objective is to give an estimation of the parameters $\Theta$ that best suits our target probability distribution. If $\theta_\lambda(x)$ is our ML multi-regressor, we can summarize it as follows: $p(y_{t_{target}} \mid x_{t_{pred}}) \sim q(y_{t_{target}};\theta_\lambda(x_{t_{pred}}))$, with the parameters $\lambda$ estimated using Negative Log Likelihood (NLL) as loss function:

$$NLL(\lambda) = -\sum_{i=1..N} \log(q(y_i;\theta_\lambda(x_i))$$

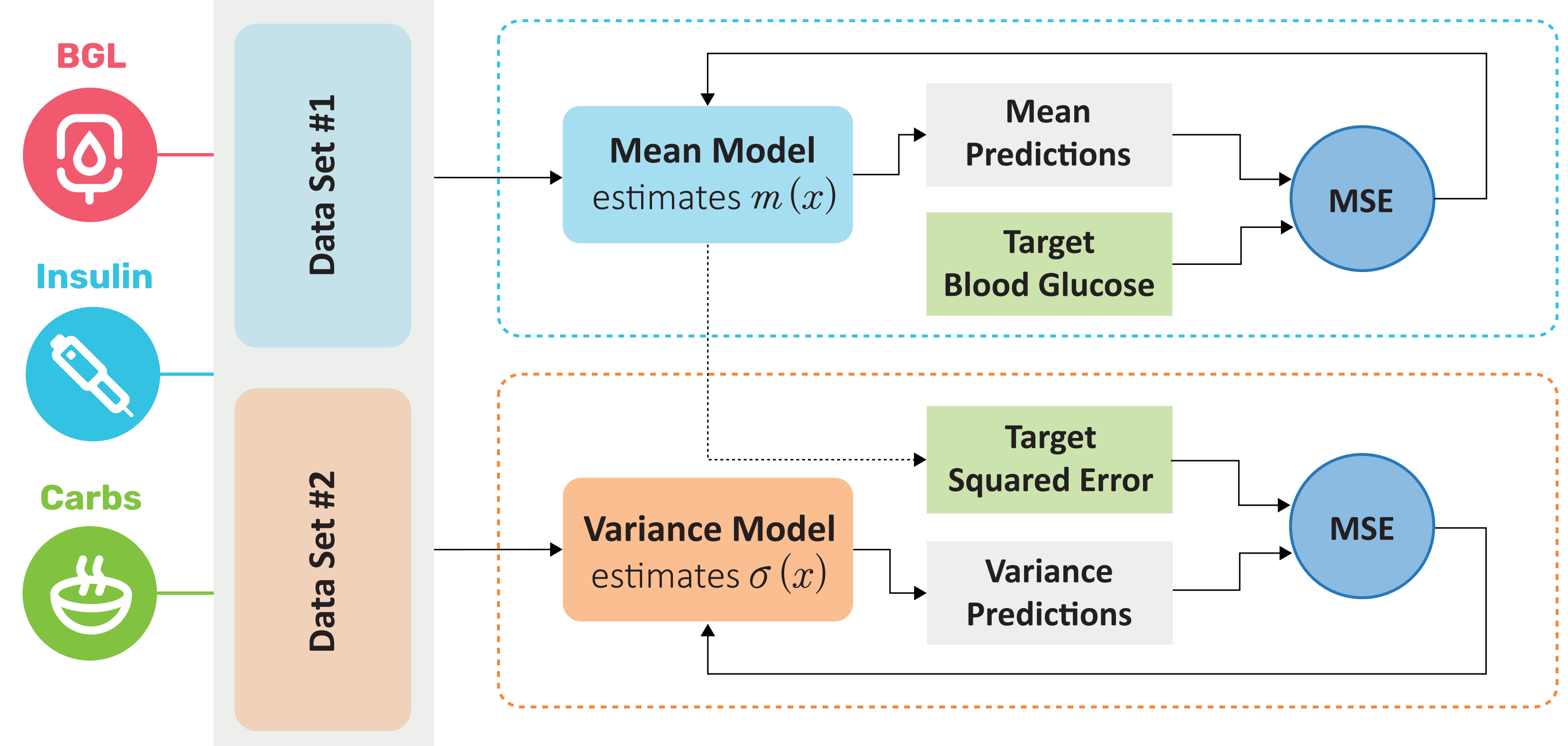

**Figure 1:** 2-Steps Gaussian Density Model

With $q$ as a gaussian density function, we simplify a bit this framework, keep NLL as evaluation metric, but train 2 different models as described in **Fig. 1**:

- A BGL predictor $m(x)$ similar to the ones described in **[A]**, that estimates the conditional expectation value $\mathbb{E}_y[Y \mid x] = \int_y yp(y \mid x)$
- A standard deviation (STD) predictor $\sigma(x)$ with the squared error $(y_{t_{target}} - f(x_{t_{pred}}))^2$ as the new target, that estimates the variance $\mathbb{E}_y[Y - \mathbb{E}_y[Y \mid x] \mid x]$.

With both mean and STD models trained, we get a conditional density estimator using Normal distribution. Our final density model is:

$$q(y_{t_{target}} \mid x_{t_{pred}}) = \frac{1}{\sigma(x_{t_{pred}})\sqrt{2\pi}} \exp - \frac{(y_{t_{target}} - m(x_{t_{pred}}))^2}{2\sigma(x_{t_{pred}})^2}$$

BGL predictors can be evaluated using Parkes Error Grid Analysis (EGA), which breaks down a scatterplot of reference and predicted BGL into 5 regions (A to E). The gold standard is to have less than 1% of points that fall in regions C, D and E, referred to as zone PC⁺ **[A]**.

With the conditional BGL probability density estimation, we can compute a PC⁺ probability estimation as described in **Fig. 2**:

$$Q(PC^+(m(x)) \mid x) = \int_{y \in PC^+(m(x))} q(y \mid x)\, dy$$

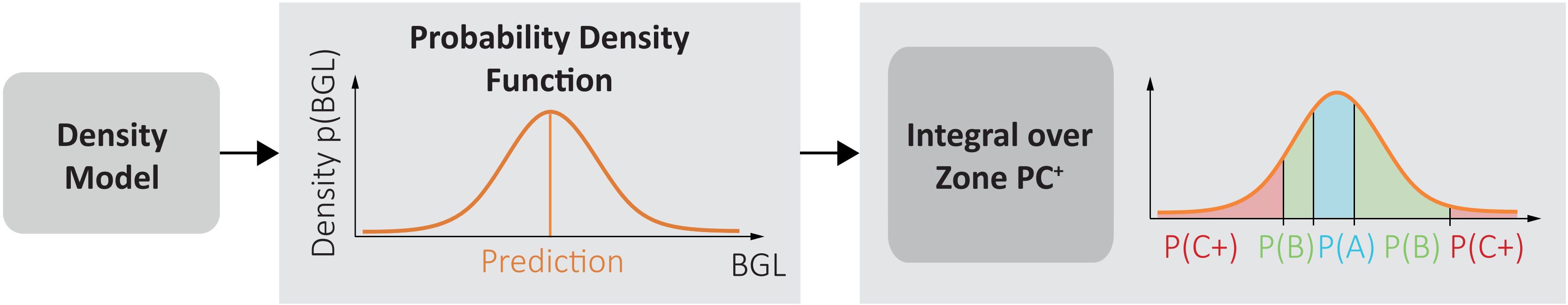

**Figure 2:** Parkes Zone Probability

## RESULTS AND DISCUSSIONS

| Performances | |
|---|---|
| PH (min) | NLL (log(mg/dL)) |
| 30 | 4.1154 ± 0.2165 |
| 60 | 4.7491 ± 0.2289 |
| 90 | 5.0504 ± 0.2394 |
| 120 | 5.2062 ± 0.2462 |

**Table 2:** Performances of the Gaussian Density Model [M ± SD]

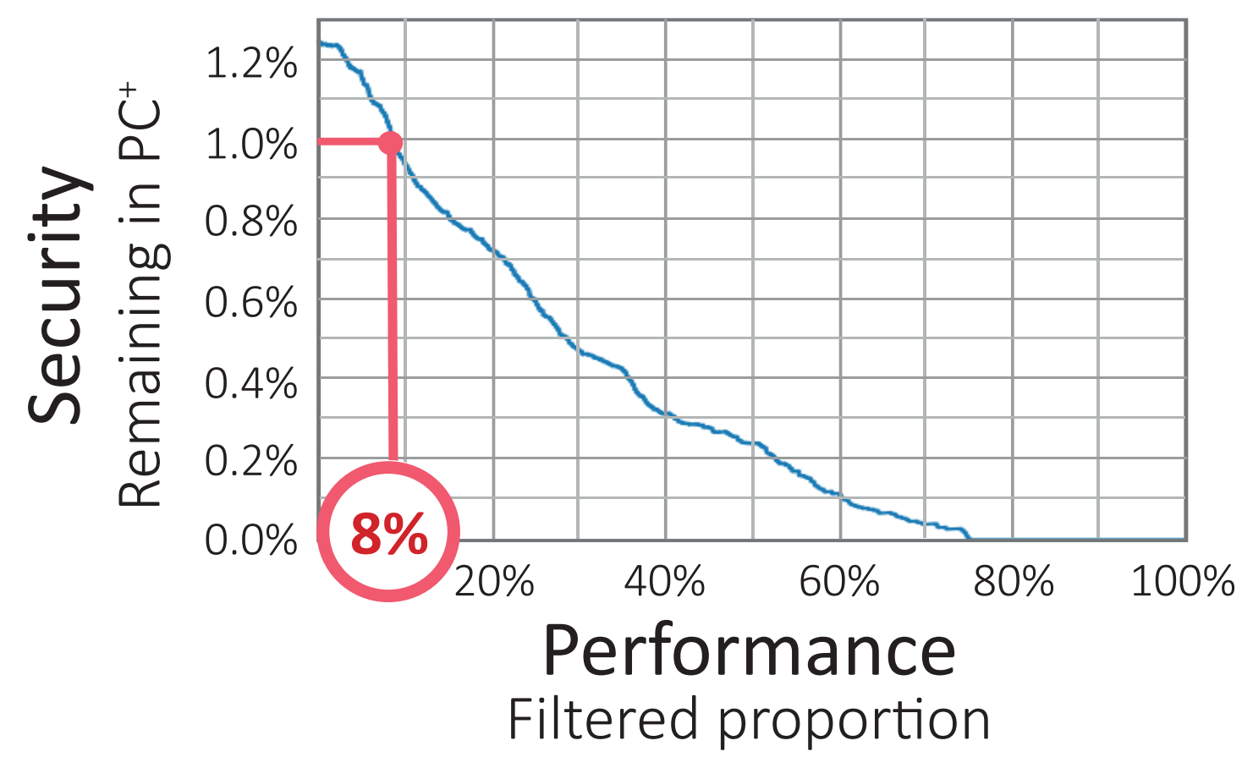

**Figure 3:** Filtering trade-off (PH=60 min)

To our knowledge, there is no equivalent procedure in the literature on which we could compare our performances presented in **Table 2**. These scores could instead be a baseline for later improvements in the BGL conditional density estimations.

Our density model calculates a probability to fall in zone PC⁺ associated with each BGL Predictions. We can determine a threshold above which predictions should be filtered. The graph in **Fig. 3** shows the proportion of filtered predictions associated with a the proportion of points that still fall in zone PC⁺. With our data, it basically means that with PH=60 min, if we keep all the predictions, 1.2% of them will fall in zone PC⁺. We need to filter 8% of the predictions to have a remaining probability to fall in PC⁺ < 1%.

## CONCLUSION

We showed a method to anticipate and mitigate risky stuations. The density model methodology can be improved by using a different distribution-model and by adding a calibration step.

## REFERENCES

**[A]** S. Bidet, N. Caleca, E. Renard, T. Camalon, L. De La Brosse, M. Rehn, O. Diouri and J. Place. First assessment of the performance of a personalized machine learning approach to predicting blood glucose levels in patients with Type 1 diabetes: The CDDIAB study. *ATTD 2019.*