hillo

Unlocking Precision Diabetes Care with AI and Digital Twin Technology

ÉCOLE POLYTECHNIQUE UNIVERSITÉ PARIS-SACLAY · HEC PARIS · NVIDIA INCEPTION PROGRAM · Microsoft for Startups · AI FOR HEALTH BY ARTEFACT · TECH CARE PARIS PARIS&CO · La FRENCH TECH · Agoranov · FUTURE 4 CARE

The team

Stéphane BIDET

CEO & Co-founder

Master's degree from UTC

Worked as software engineer in a Californian mobile/web software Start-up, and as sales manager and business unit director in a leading European consulting firm.

Fields of expertise: mobile app development, sales and business development

Nicolas CALECA

CSO & Co-founder

Master's degree from Ecole Polytechnique and ENSAE

Worked at AREVA for 6 years as project manager., and then as Technical Director in a leading European consulting firm.

Fields of expertise: simulation, mathematics, project management

Hillo's mission: transform diabetes management with AI

AI-based Digital Twins *trained with real-world patient generated data*

1. **Simulation and prediction**
   Anticipate how changes in lifestyle or treatment plans might impact blood glucose control
2. **Advanced data analysis**
   Pinpoint specific triggers or patterns that lead to high or low blood glucose levels
3. **Personalized Medicine**
   Personalized dose recommendation & Tailored treatment plans to maximize glucose control

One-stop-shop: Hillo's platform

AI-based technology, patented and clinically validated
Supported by world-renowned KOL

Digital twin

A digital twin can be described as a mathematical representation of one or more of the patient's physiological processes. In our case, it serves as a virtual copy of the glucose homeostasis.

Descriptive Models

Based on rules, equations, or logic derived from human understanding of the subject matter.

$$
\begin{array}{lcll}
\dot{G}_p(t) & = & EGP(t) + R_a(t) - U_{ii}(t) - E(t) - k_1.G_p(t) + k_2.G_t(t) & G_p(0) = G_{pb} \\
\dot{G}_t(t) & = & -U_{id}(t) + k_1.G_p(t) - k_2.G_t(t) & G_t(0) = G_{tb} \\
G(t) & = & \frac{G_p(t)}{V_G} & G(0) = G_b
\end{array}
$$

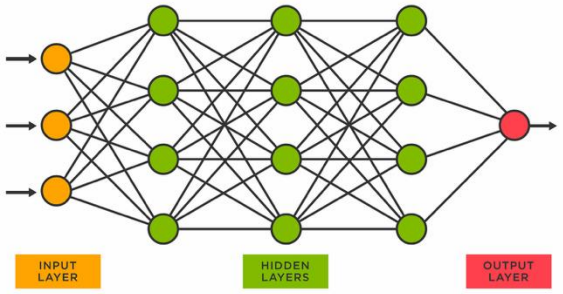
$$
\begin{array}{lcll}
\dot{I}_l(t) & = & -(m_1 + m_3(t))).I_l(t) + m_2.I_p(t) & I_l(0) = I_{lb} \\
\dot{I}_p(t) & = & -(m_2 + m_4).I_p(t) + m_1.I_l(t) + R_i(t) & I_p(0) = I_{pb} \\
I(t) & = & \frac{I_p(t)}{V_I} & I(0) = I_b
\end{array}
$$

$$m_3(t) = \frac{HE(t).m_1}{1 - HE(t)}$$

$$HE(t) = -m_5.R_i(t) + m_6 \quad HE(0) = HE_b$$

Data-Driven Models

Use algorithms and statistical techniques to uncover patterns, relationships, and insights directly from the data.



Flexibility and Adaptability

- Descriptive models may face challenges in dynamic systems where predefined rules or theories struggle to capture all nuances.
- Data-driven models excel in adapting to complex, nonlinear, or evolving situations as they learn directly from the data.

Prediction and Generalization

- Descriptive models may not excel in predicting outcomes for new scenarios unless explicitly accounted for in existing rules or theories.
- Data-driven models excel at making predictions on new, unseen data by generalizing patterns learned from the data to predict outcomes for new instances.

Required data

CGM data

Mainly data from:

- **Abbott FSL**: data manually imported from LibreView, or
- **Dexcom**: shared via an API (with a 3-hour time lag)

Insulin data

Data from insulin pumps or connected pens is easily retrievable via APIs

Insulin data is automatically classified and labeled according to its type:

- ***meal bolus***
- ***correction bolus***

Carbs data

Estimation of the amount of carbohydrates in meals or sugar intakes:

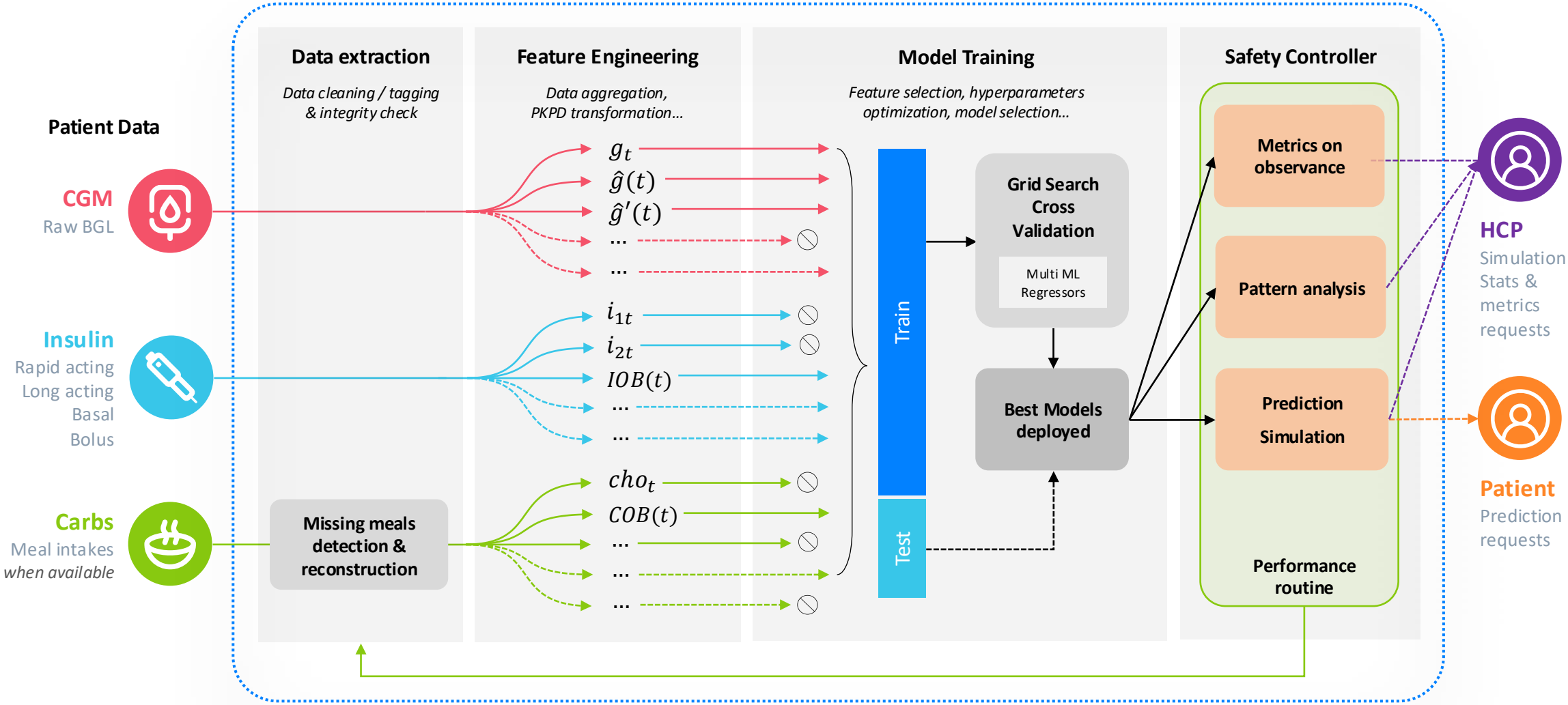
- Manual entry by the patient into a digital logbook, and shared via an API
- Reconstruction from CGM and insulin data using an in-house ML algorithm

Carbs data is automatically classified and labeled according to its type:

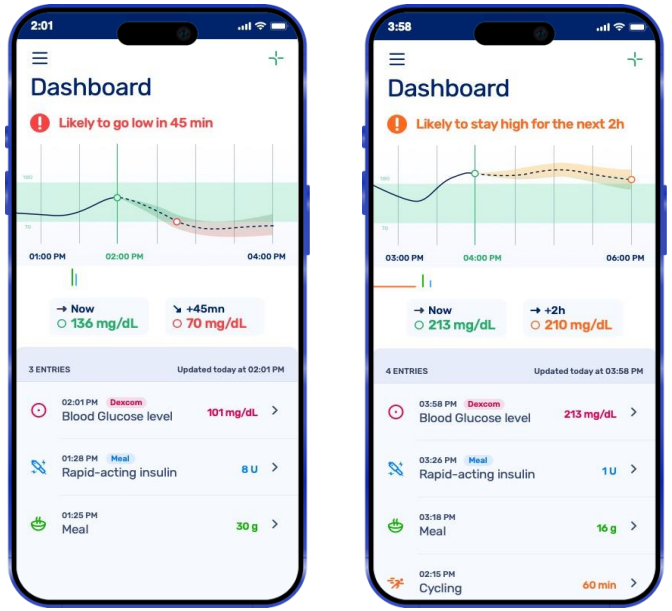
- ***meal***
- ***sugar intake***

Model training requires an average of 9 days of collected data

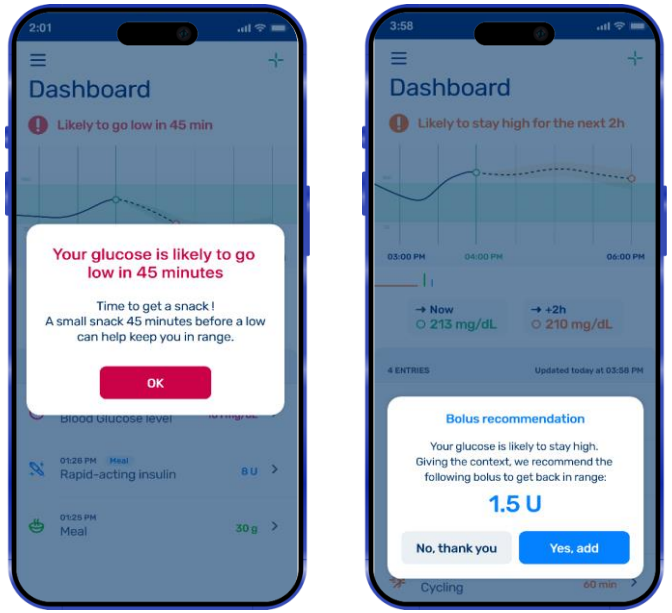
Digital Twin training process



Digital twin for real-time prediction to support patients



Real-time prediction of blood glucose levels to anticipate risks of hypo & hyperglycemia

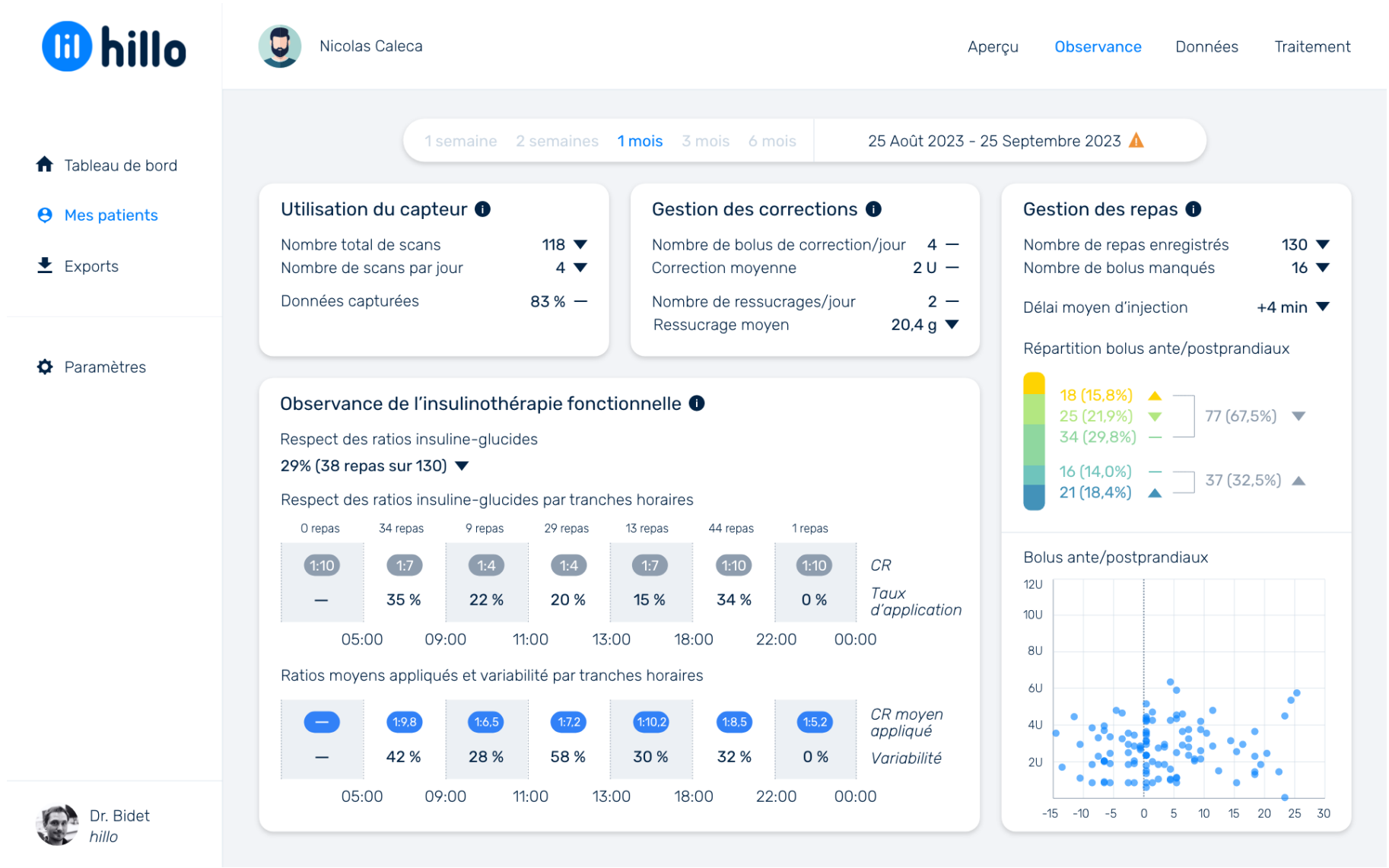


Smart personalized recommendations of preventive actions, including insulin doses and fast-acting carbs

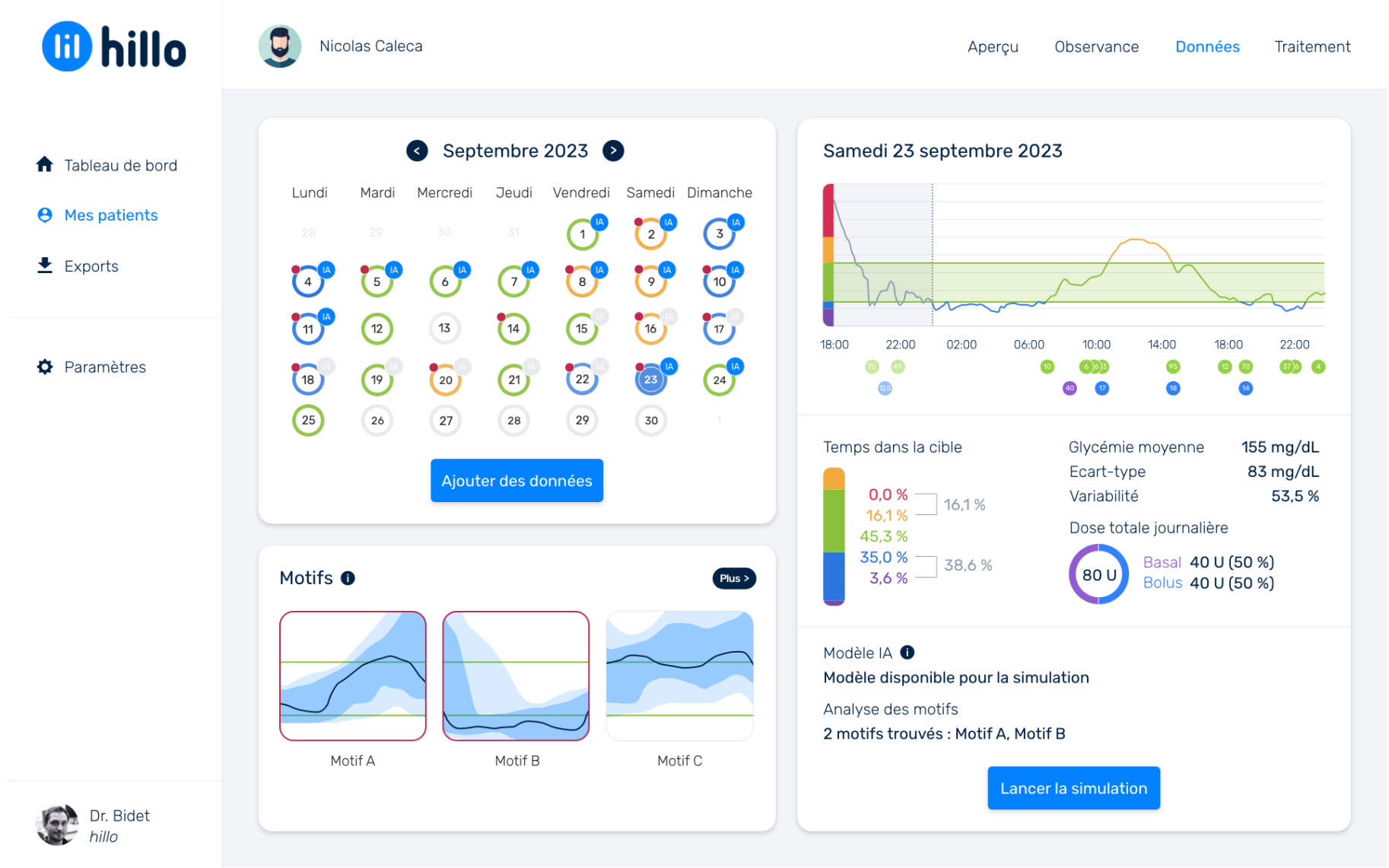
Hillo fills a critical gap in existing digital tools with real-time glucose prediction and help prevent 85% of glycemic excursions[1]

1. Supported by clinical data: Hillo CDDIAB study @ ATTD 2020

Digital twin boosts HCPs efficiency

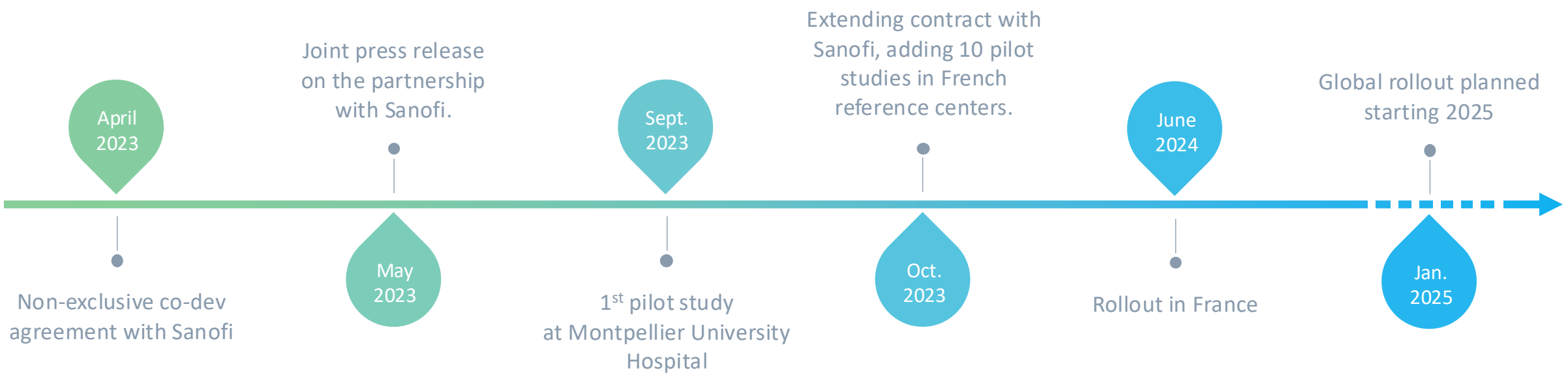


Digital twin boosts HCPs efficiency



Digital twin boosts HCPs efficiency

Co-development and deployment partnership with Sanofi



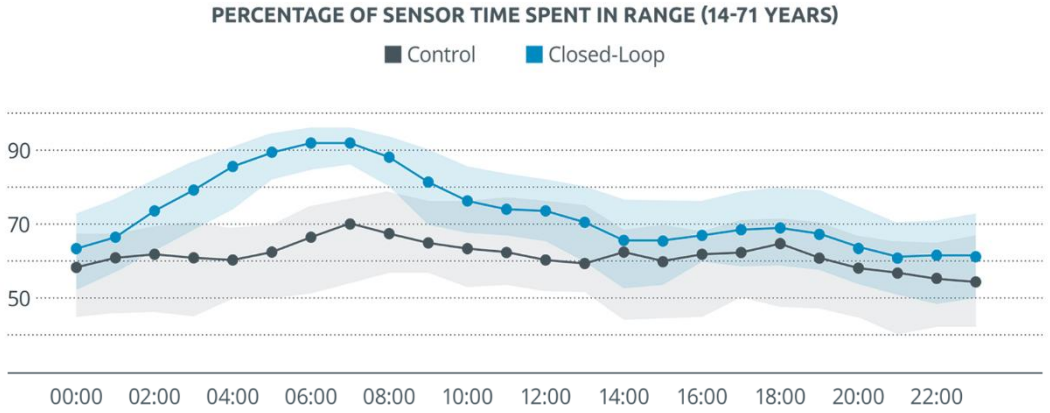
Digital twin for Closed-Loop enhancement

State of the art on closed-loop systems

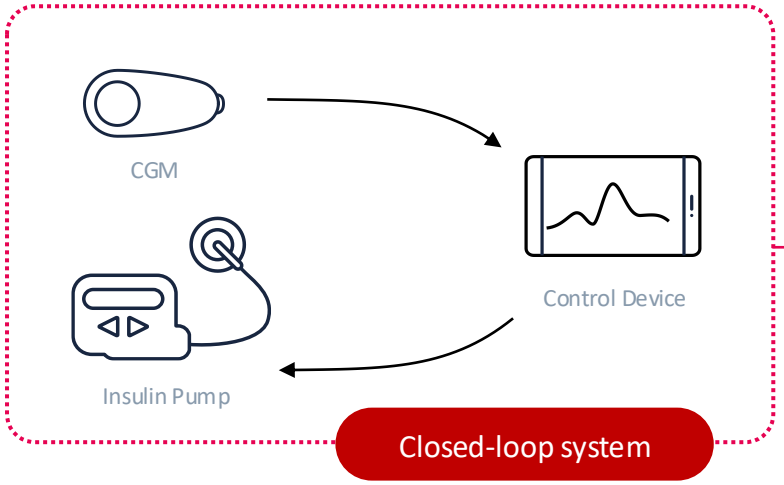
Automatic adjustment of insulin administration based on CGM signals in line with dosing algorithms.

Perform well during stable phases, but patients still experience excursions during rapid glucose changes such as meals, exercises…

Personalization and accurate BGL prediction are necessary key factors to significantly improve existing systems



*Closed-Loop group: N=112 (t:slim X2 pump and Dexcom G6 with automation)**
Control group: N=56 (t:slim X2 pump and Dexcom G6 without automation)



Adapt infusion strategy to the context and patient's individual glycemic response

*Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes - 2019

Award-winning technology

hillo

X-Grant Price

20k€ price from Ecole Polytechnique Foundation

Challenge + Program

The project has been accepted in the HEC program

Winners of France is AI 2018 contest

Second batch Future4Care

Leading and highly selective European start-up accelerator program

Winners of i-LAB 2017 contest

150k€ grant from French Ministry of Research to fund R&D of breakthrough innovation

CES 2019 Innovation Award

Honoree in category Fitness, Sports and Biotech

Winners of Innov'Up Leader 2018 contest

500k€ grant as part of the "Investing for the Future" program, which supports potential future leaders

Finalist of Innovation & Galien

Challenges

Hillo among the top 100 start-ups in which to invest

Observational studies

CDDIAB study (2018)

Evaluate accuracy of Hillo prediction technology

Sample characteristics	
Group Size	n = 14 (T1D)
M / F	6 (43%) / 8 (57%)
Age (years)	51 ± 15
A1c	7.09 ± 0.82

Publication at ATTD 2019

First assessment of the performance of a personalized machine learning approach to predicting blood glucose levels in patient with T1D

S. BIDET, N. CALECA, Pr. E. RENARD, T. CAMALON, L. DE LA BROSSE, M. REHN, O. DIOURI and J. PLACE

CDDIAB extension (2019)

Assess relevance of prediction for decision-making

Sample characteristics	
Group Size	n = 15 (T1D)
M / F	6 (40%) / 9 (60%)
Age (years)	45 ± 15
A1c	7.32 ± 0.66

Publication at ATTD 2020

Assessment of the relevance of predicted blood glucose curves as a support to decision making in patients with T1D

S. BIDET, N. CALECA, P. CALMELS, T. CAMALON, L. DE LA BROSSE, M. REHN, O. DIOURI, J. PLACE and Pr. E. RENARD

Observational studies

Prediction Accuracy

CDDIAB + Extension [Mean ± SD]

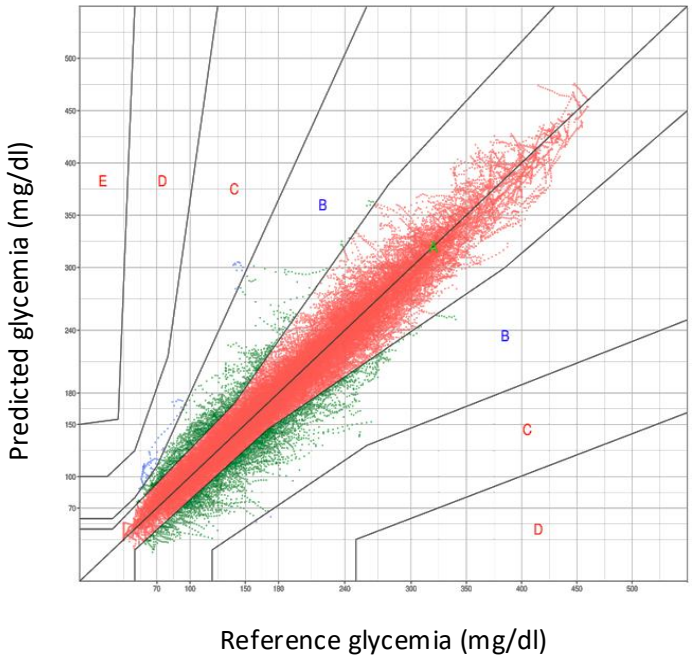
	MARD** (%)	RMSE (mg/dL)	Parkes* A+B (%)
30min	6.80 ± 1.26	14.74 ± 2.73	99.95 ± 0.08
60min	15.01 ± 3.77	30.70 ± 6.59	98.34 ± 1.74
90min	20.53 ± 4.53	41.21 ± 9.12	96.38 ± 2.59
120min	24.88 ± 5.84	48.15 ± 10.96	94.36 ± 3.95

Prediction Relevance

CDDIAB Extension only

	Nb. of events	Action taken relevant	Action taken not relevant
High BGL	42 (67%)	34 (81%)	8 (19%)
Low BGL	21 (33%)	19 (90%)	2 (10%)
Total	63	53 (84%)	10 (16%)

Parkes error grid analysis (PH=30)



* ISO15197:2015 guideline: common performance metric for CGM device, to be considered safe must have 99% of points in zones A and B

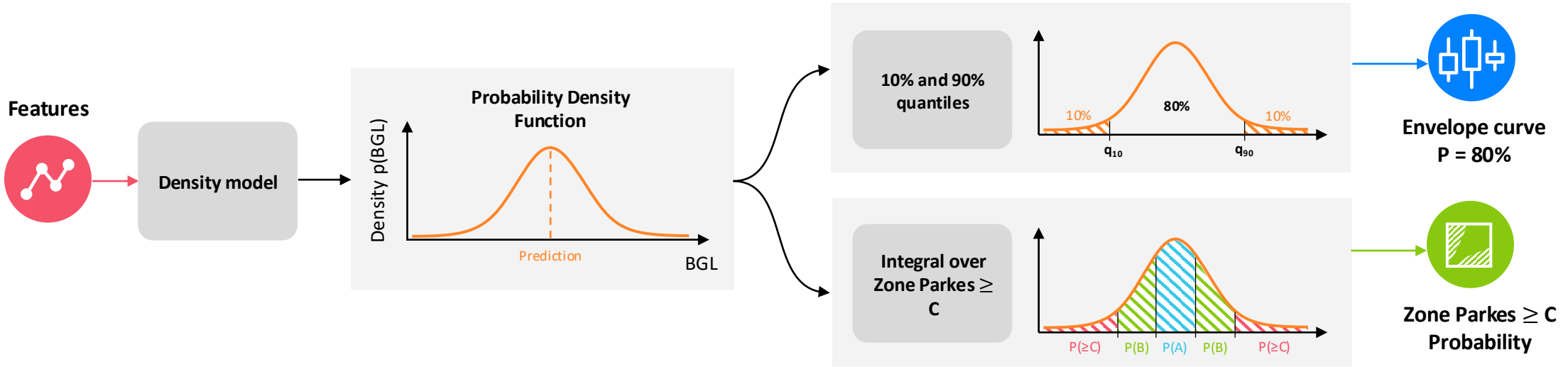
** Mean Absolute Relative Deviation

Safety Controller

Anticipate the error of the model when calculating a prediction

To enhance the safety controller and filter predictions that could drive bad decisions, and to increase the confidence in the prediction:

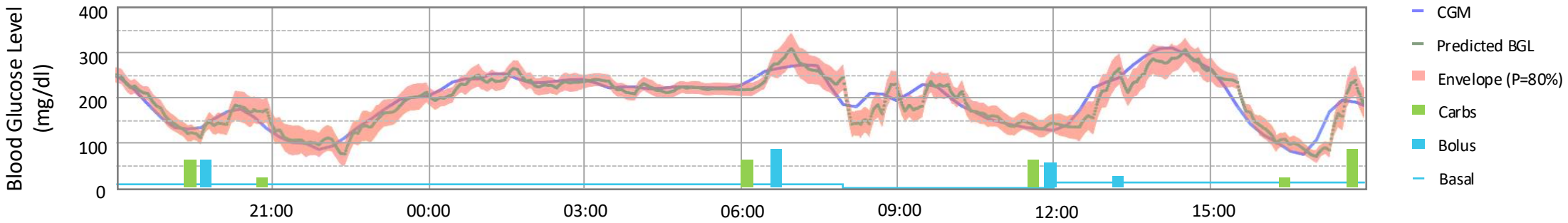
- Calculate a confidence interval (high probability for the real BGL to fall within min/max values)
- Calculate probability to fall in zones C, D or E of a Parkes grid (PC+)



Safety Controller

Example of envelope curve

CDDIAB P#01 – Sample 2018/03/18 – (PH=30)



Envelope curve P=80% performances

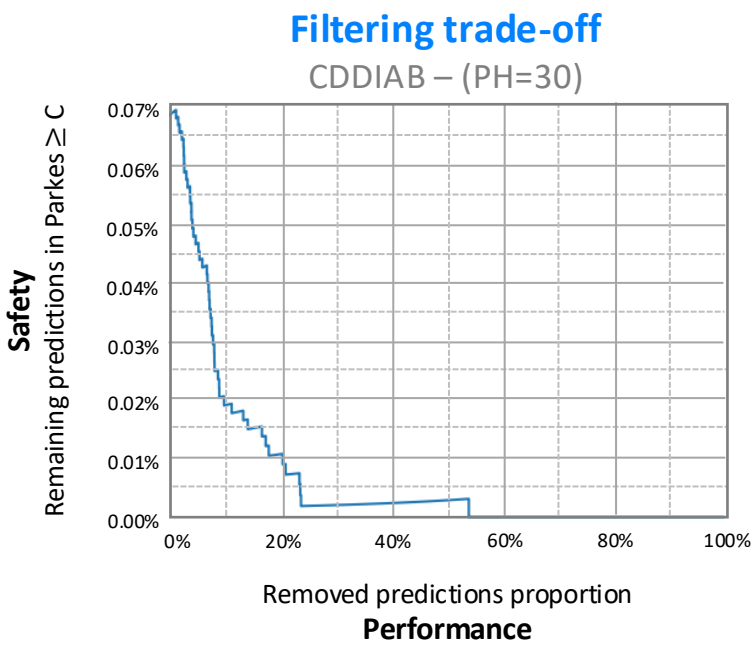
CDDIAB [Mean]

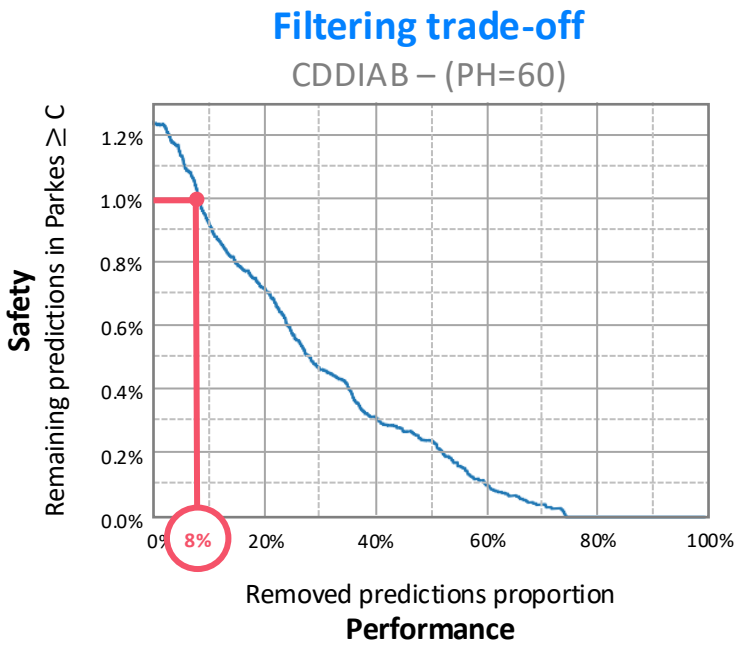
	Average width (mg/dL)	Inside proportion (%)
30min	38.96	81.78
60min	75.20	81.37
90min	101.54	81.04
120min	115.90	81.50

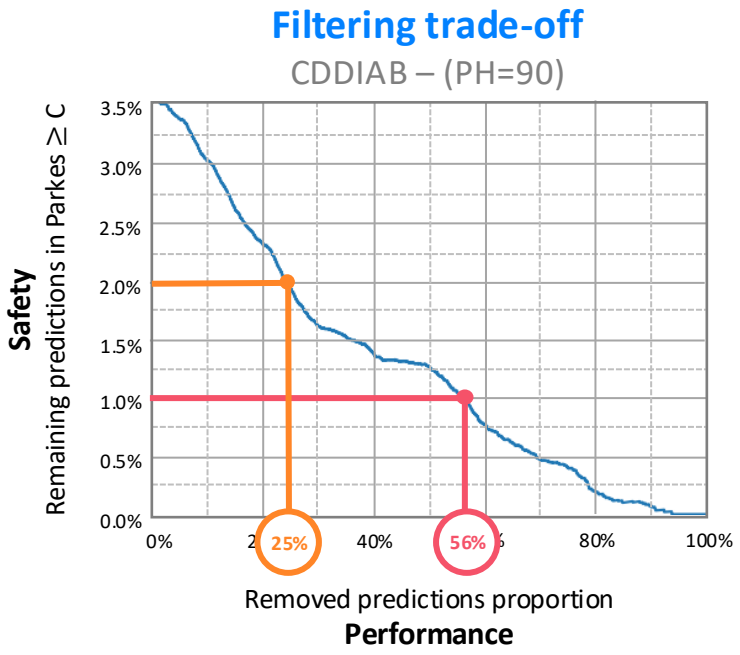
Safety Controller

Anticipate and Filter predictions that may drive bad decision for the patient

Filtering PC+ predictions requires to remove a greater number of predictions. For each threshold above which predictions are removed, a proportion of removed predictions is associated with a reduction of points that still fall in zone PC+







Publications

1. *First assessment of the performance of a personalized machine learning approach to predicting blood glucose levels in patient with T1D* - Hillo, ATTD 2019

2. *Assessment of the relevance of predicted blood glucose curves as a support to decision making in patients with T1D* - Hillo, ATTD 2020

3. *Machine learning method to predict and mitigate real-time blood glucose prediction uncertainty* - Hillo, ATTD 2022

4. *Novel AI-based algorithm to detect and reconstruct meal real-time using CGM data* - Hillo, ATTD 2022