“Making a Glucose Sensor Smarter for Managing Diabetes: Where We Are And Where to Go”

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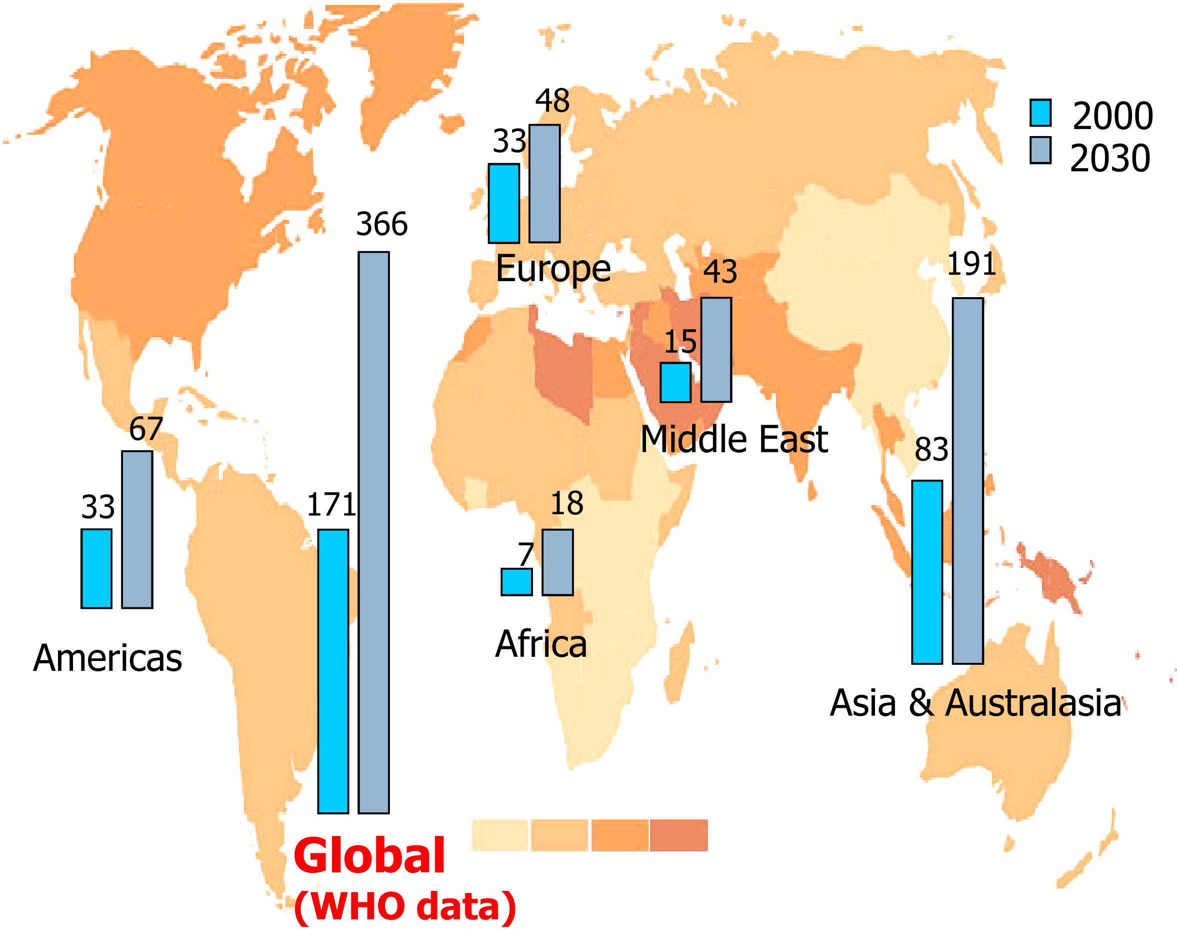
Where we are
(Giovanni Sparacino)

Diabetes: a socio-health emergency of the 3rd millennium



Nearly **200 million people** (3 million in Italy) are estimated to be **presently** affected by **diabetes (50% undiagnosed)**

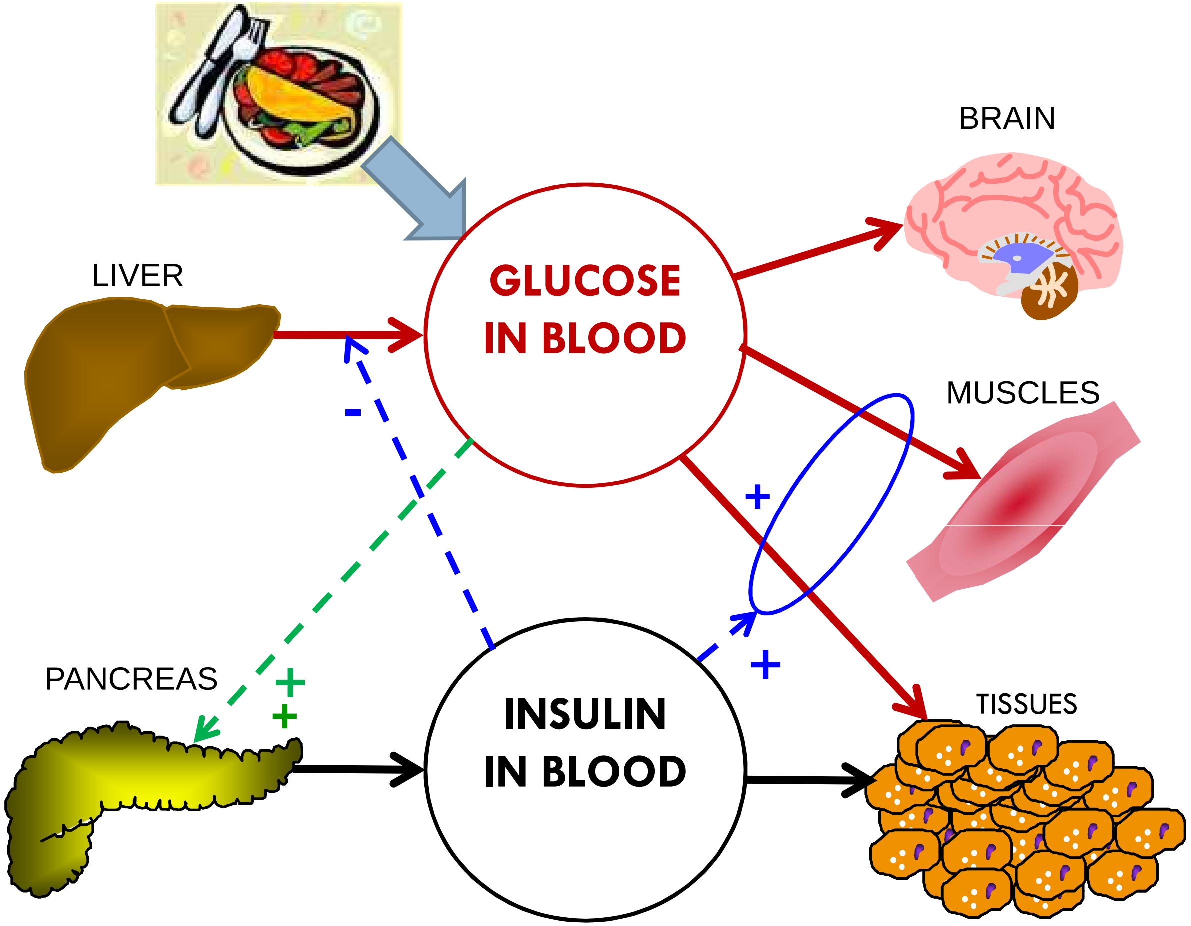
Due to aging populations, sedentary lifestyles and increasing obesity there is the prospective of approaching **400 million cases in 2030**

4 million deaths per year

Cost of diabetes is around **10%** of the budget of national health systems in western countries (in 2011, **Italy** spent **10 billion Euros**)

Impact of innovative methodologies/technologies (including sensors) for diabetes monitoring and treatment can be **extremely high**, with a potential market of **several billions of Euros**.

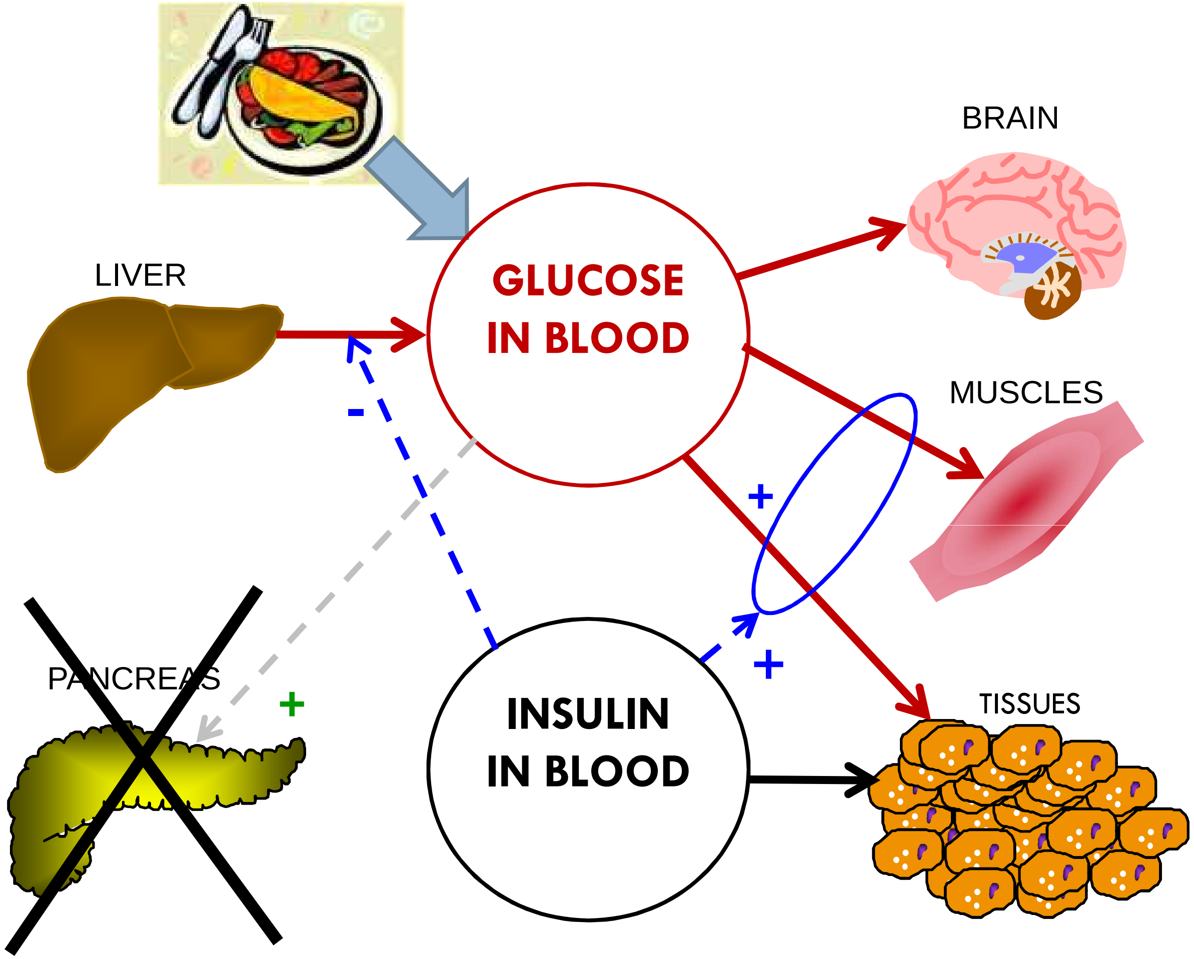
Glucose regulation in healthy subjects



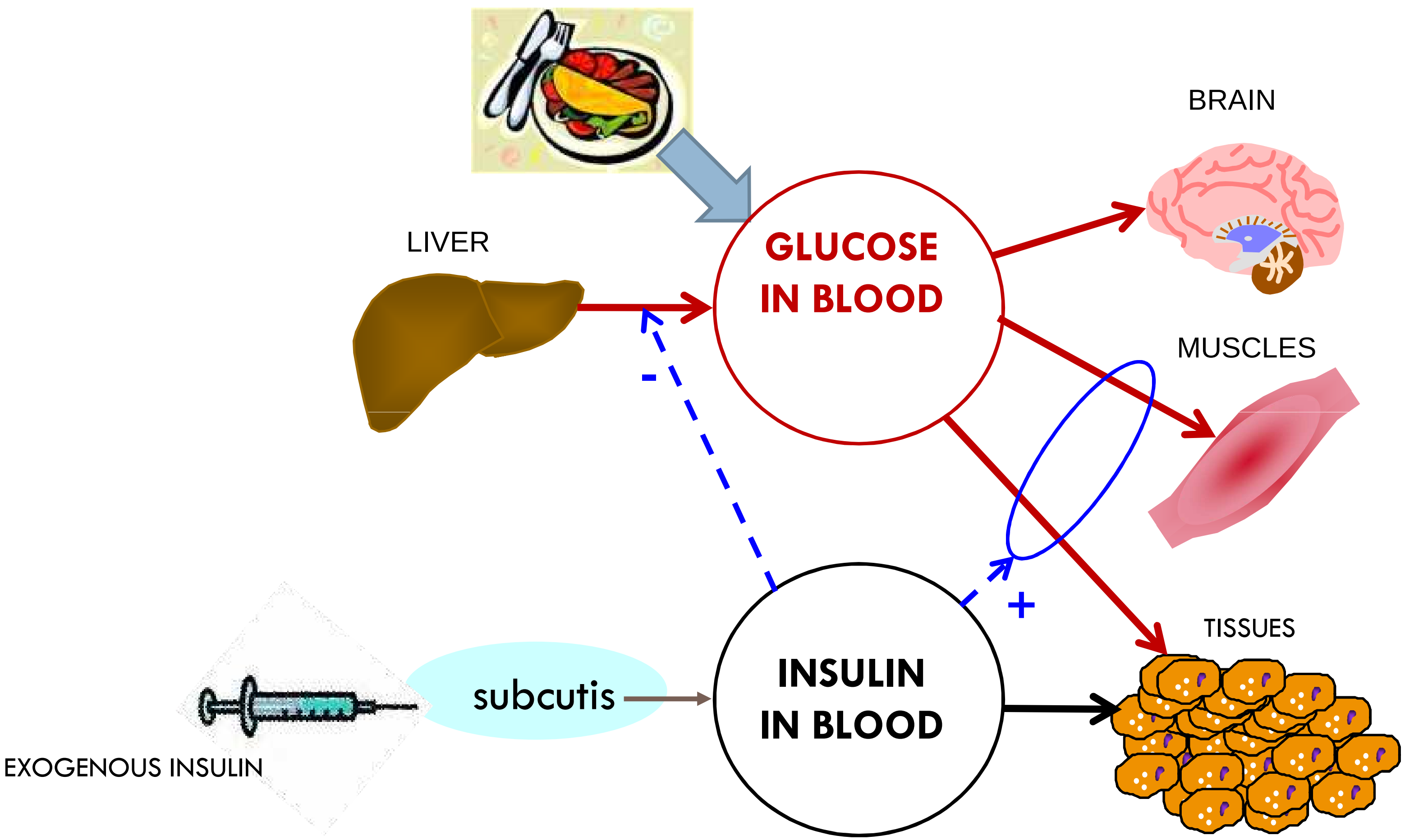
Physiology behaves as a **negative feedback control system**

In diabetics, problems in both **insulin secretion** and **insulin action** occur (type 2 diabetes) or the pancreas does not secrete insulin (type 1 diabetes)

Type 1 Diabetes (T1D)



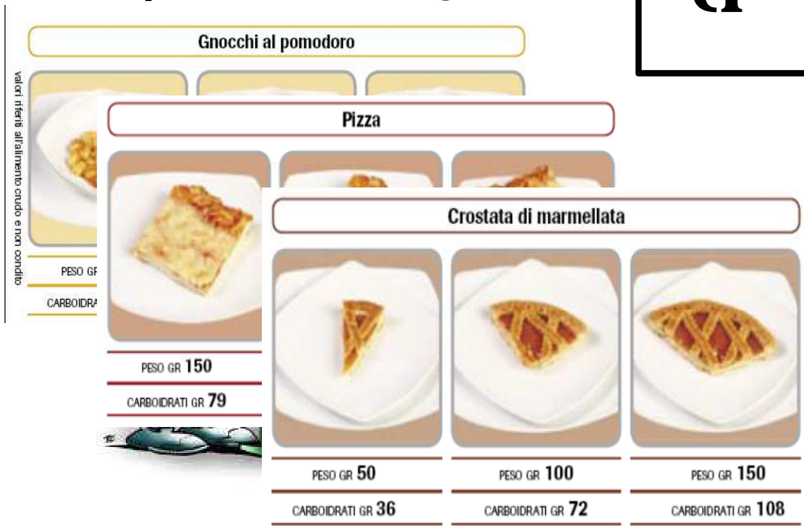
T1D conventional therapy



Tuning of T1D conventional therapy

Glucose "fingerstick" blood measurement (typically before meal)

Carbohydrate Counting

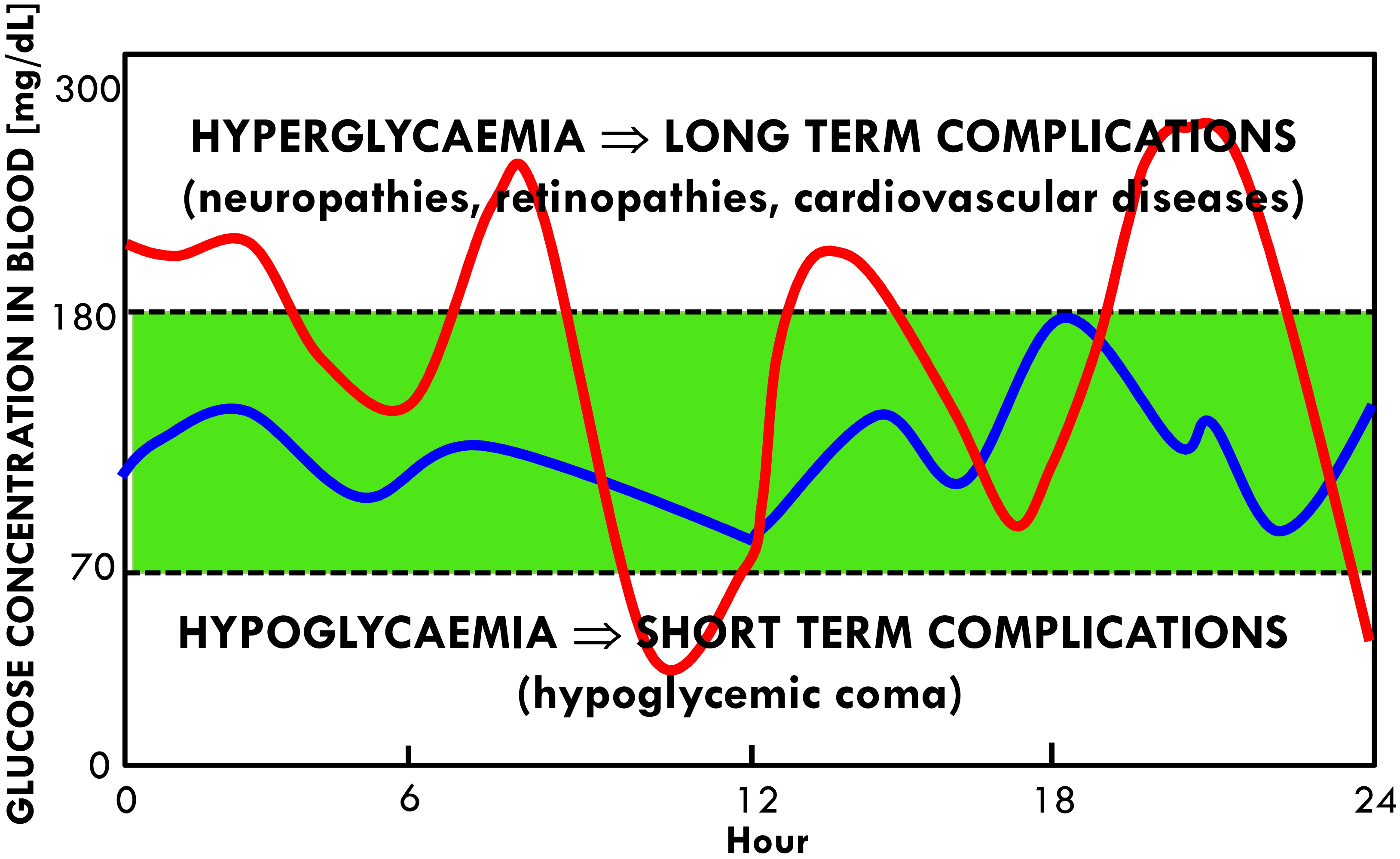


EMPIRICAL TABLES (personalized*)

Doses and Times of Insulin Injections

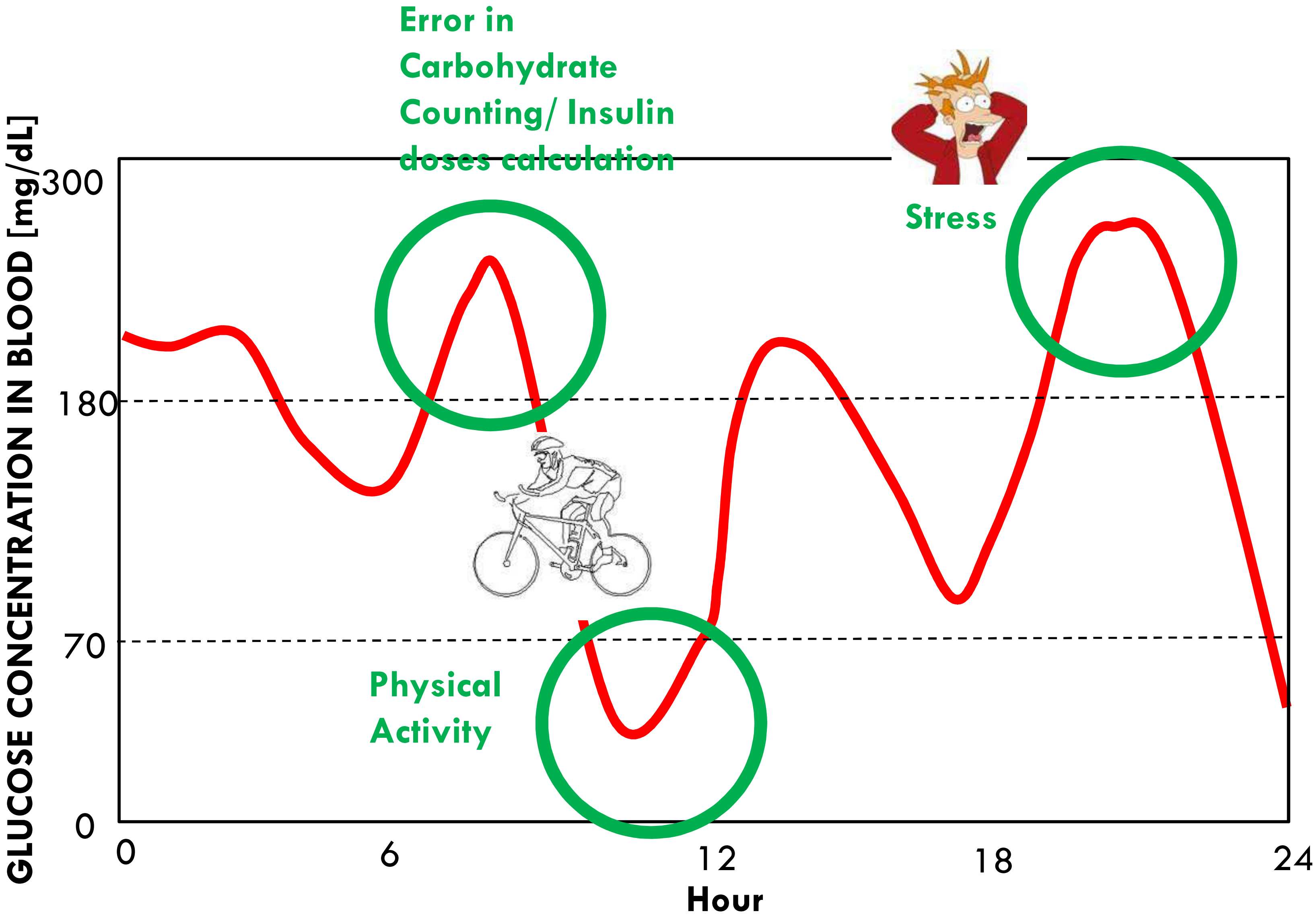
*Indivdual therapeutic plan is revised by the physician during periodical visits (every 2-4 months)

Conventional diabetes therapy is often far from optimality

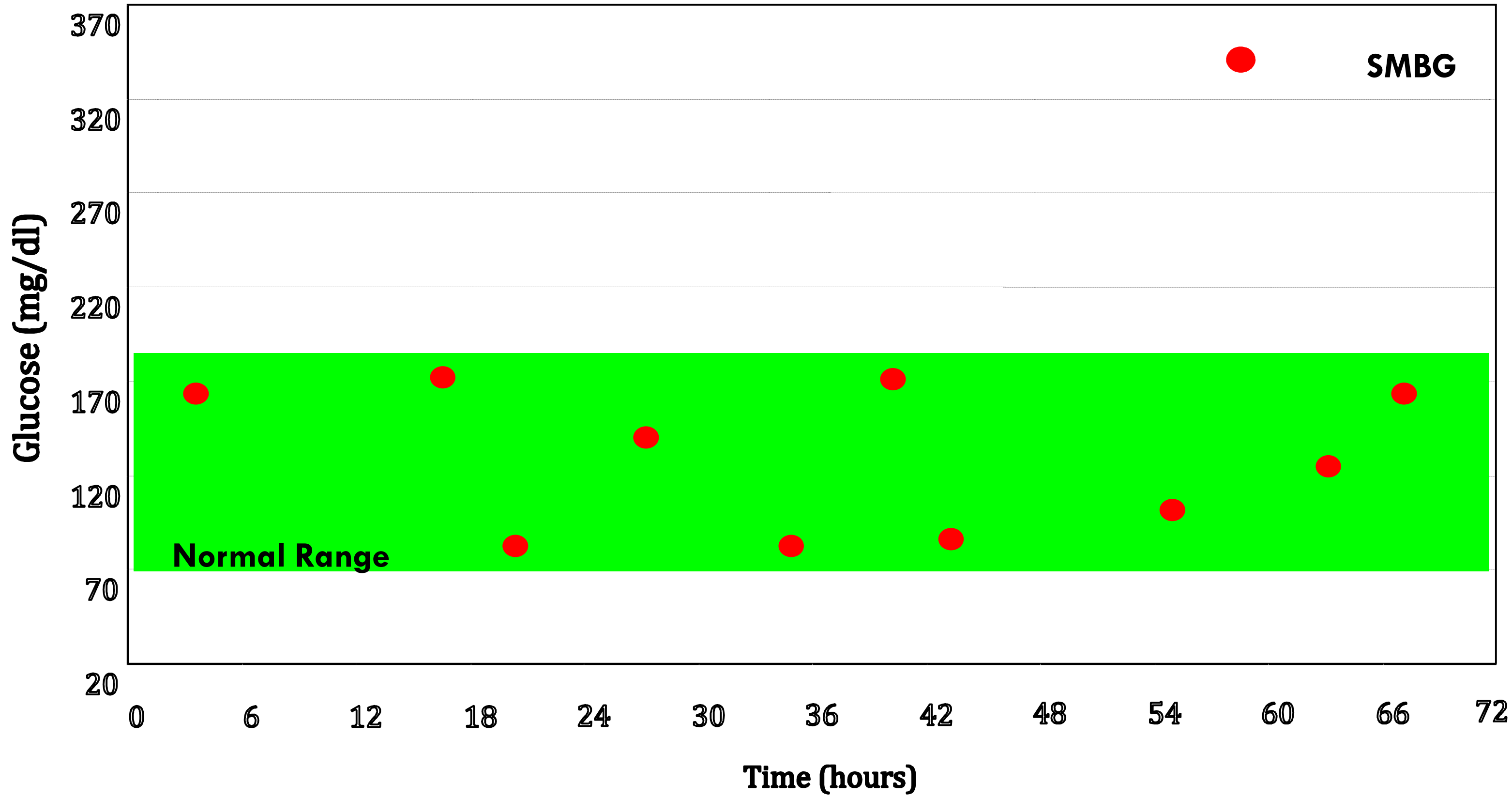


Difficulty in maintaining euglycaemia

LARGE INTER-INDIVIDUAL AND INTRA-INDIVIDUAL VARIBILITY



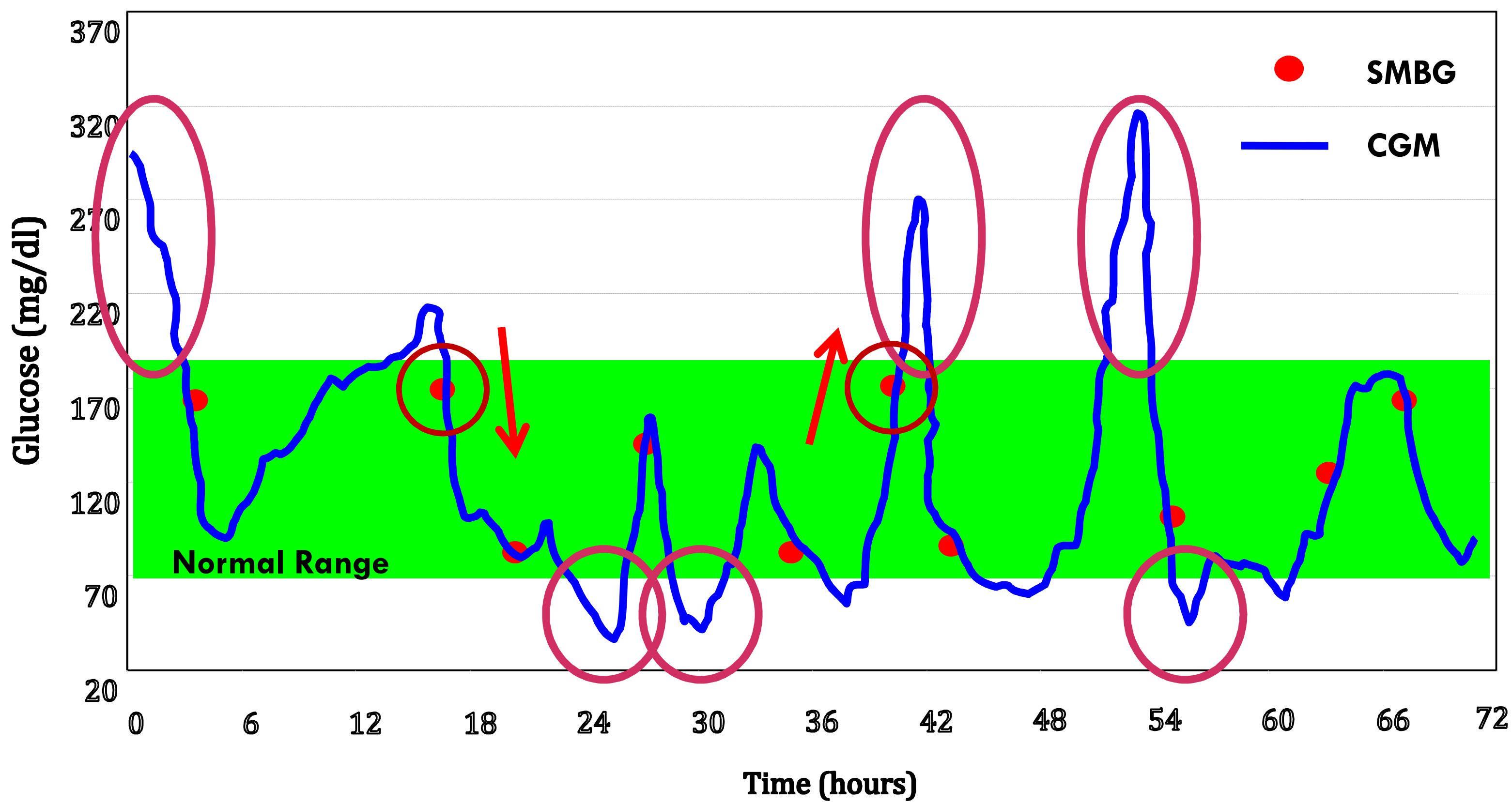
The crux of the matter: decisions drawn on the basis of Self Monitoring Blood Glucose



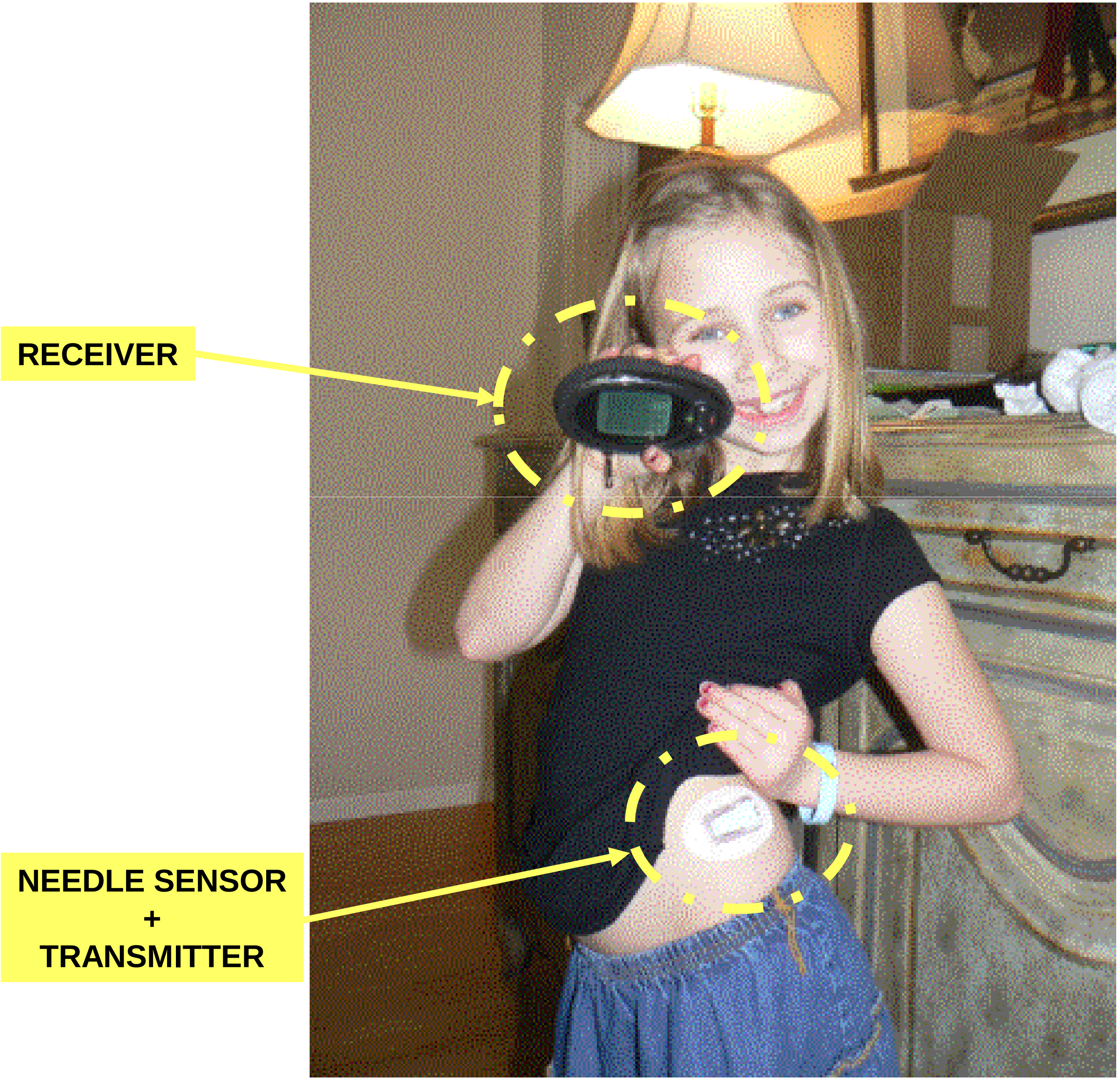
SMBG is **sparse**: usually performed **3-4 times a day** $\Rightarrow$ the feedback control loop is almost always open …

Sensors for Continuous Glucose Monitoring (> 2000)

Comparison: SMBG vs CGM

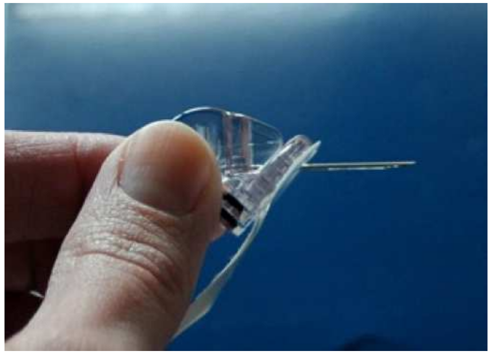


External look of a CGM sensor



Components of a CGM sensor

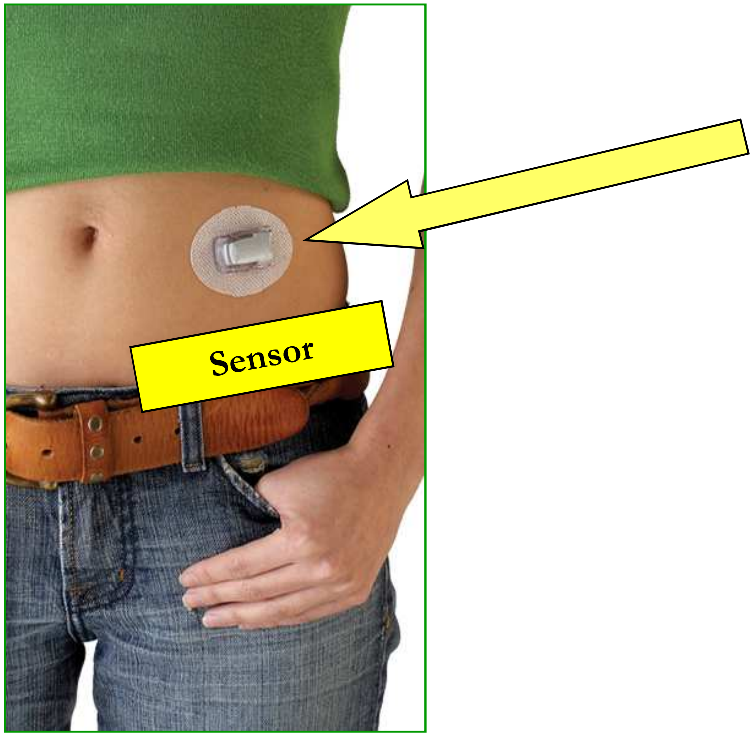
Needle sensor



Transmitter (containing a data process unit), hosting the needle sensor, applied on the abdomen or on the arm

Receiver (visualize data)

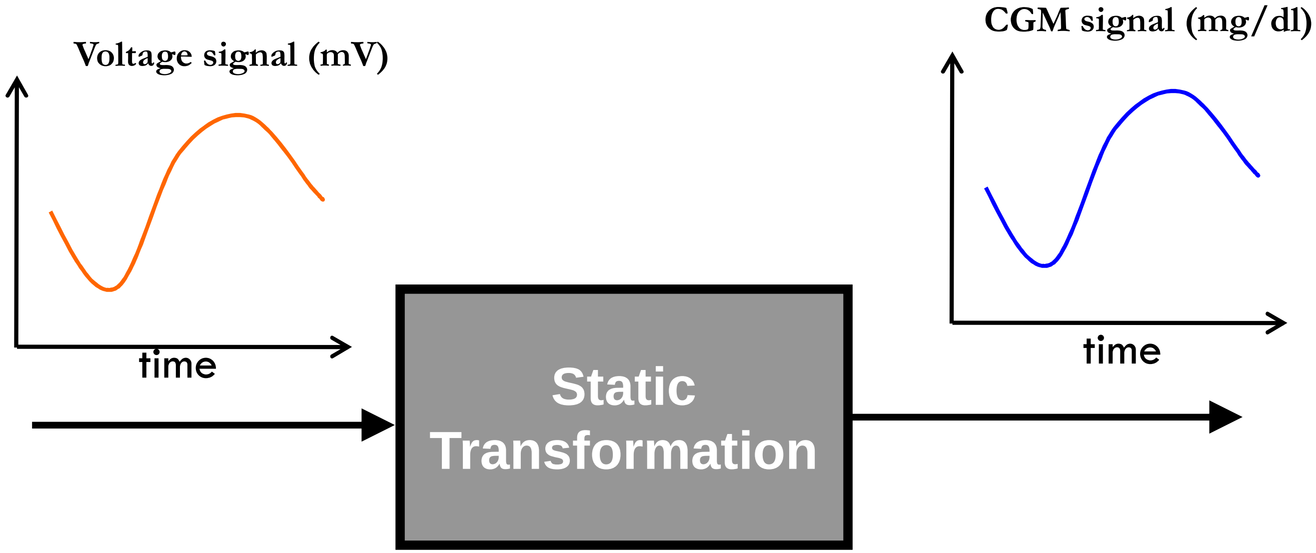
The transduction process



$$\text{glucose} + O_2 \xrightarrow{\text{glusoce oxidase}} \text{gluconic acid} + H_2O_2$$

$$O_2 + 4H^+ + 4\,e^- \rightarrow 2H_2O$$

$$H_2O_2 \rightarrow O_2 + 2H^+ + 2e^-$$



Features of today's CGM sensors

- **Minimally invasive** (limited pain)
- **Real-time readings**
- Sampling period: **from 1 to 5 minutes** (depending on the device)
- Several days of consecutive monitoring (**up to 7-10 days**)

CGM manufacturers active in the market

- **Medtronic** (Nortridge, MA)
  - CGMS (1999)
  - Guardian RT (2005)
  - iPro (2012)
- **Abbott** (Alameda, CA)
  - FreeStyle Navigator (2008)
- **Dexcom** (San Diego, CA)
  - Seven (2007)
  - Seven Plus (2009)
  - G4 Platinum (2012)

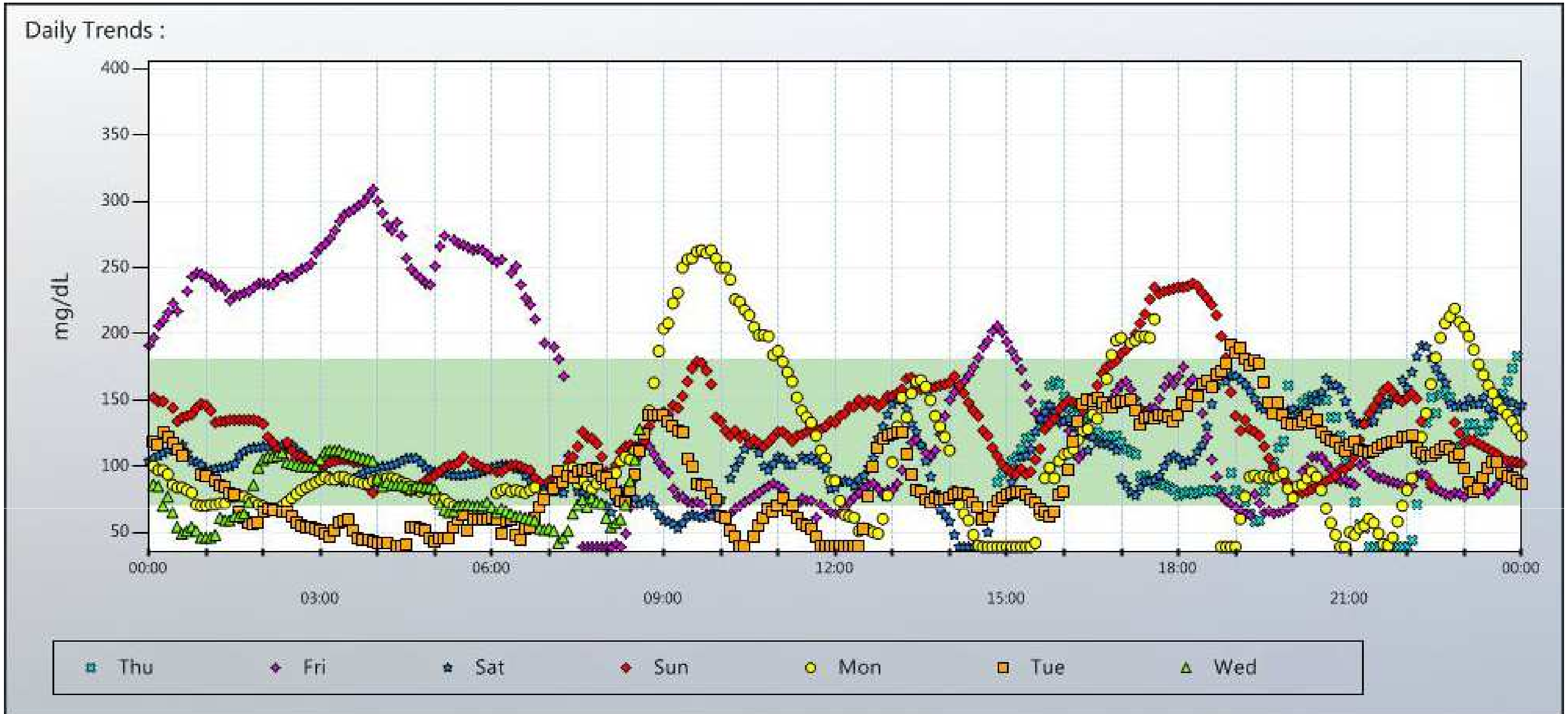
Implantable needle sensors (everyday use)

- **Roche** (Mannheim, Germany)
  - SCGM 1 (2014?)
- **Menarini Diagnostics** (Firenze)
  - Glucoday (2002)

Microdialysis probes with sensor (clinical use)

Where We Are:
Proposed CGM Applications
(Off - line, more clinically established)

Retrospective Analyis



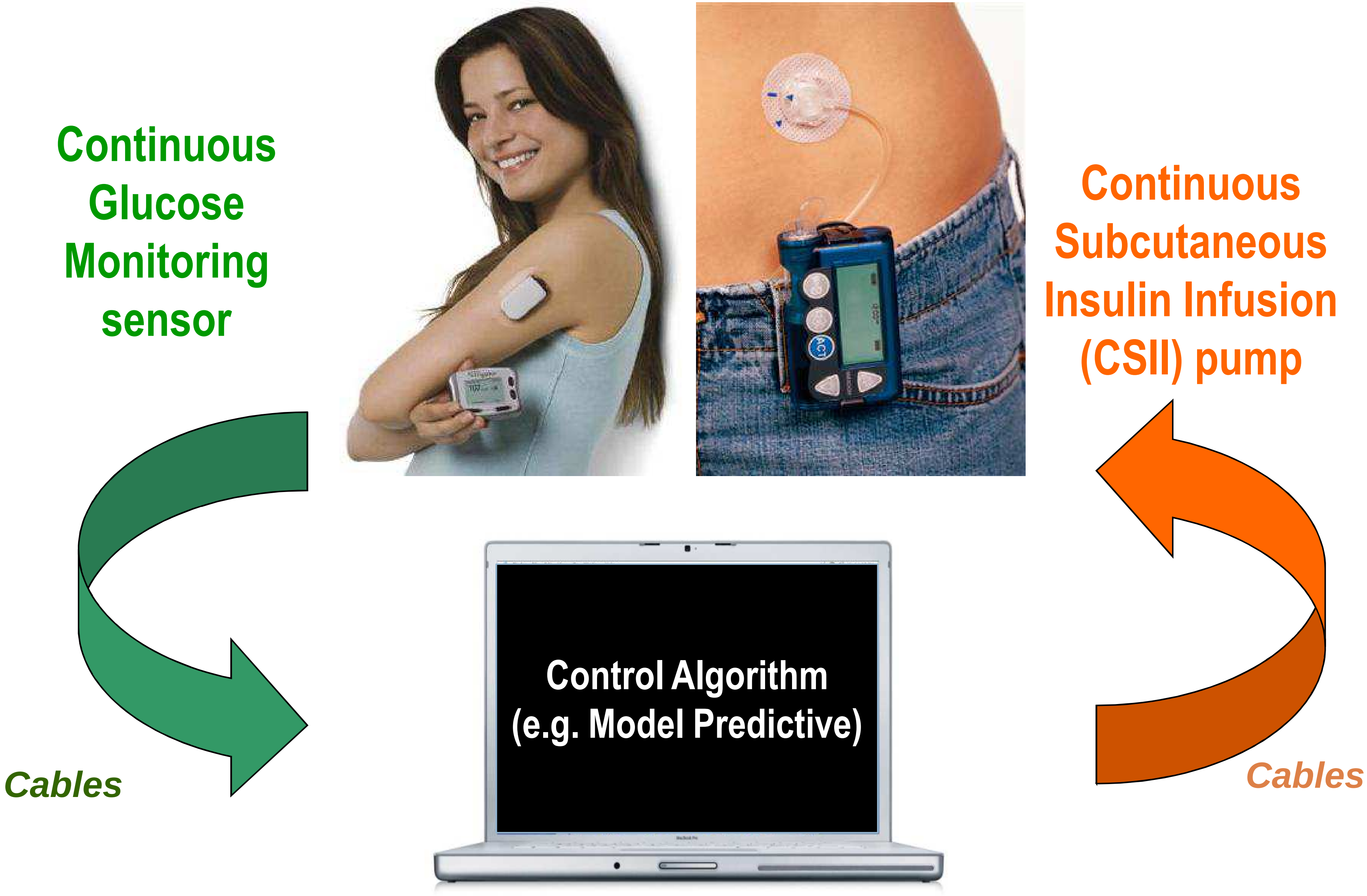
Statistic	Totals	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23
# of Readings	1609	67	71	71	72	72	68	66	69	67	59	58	59	60	60	61	71	72	66	64	72	72	72	68	72

Empirical tables for insulin administrations can be personalized and more finely tuned by the physician

Glycaemic variability (a risk factor for diabetes complications) can be quantitatively assessed (dozens of indices available) and therapy revised accordingly

Where We Are:
Proposed CGM Applications
(On - line, piooneristic)

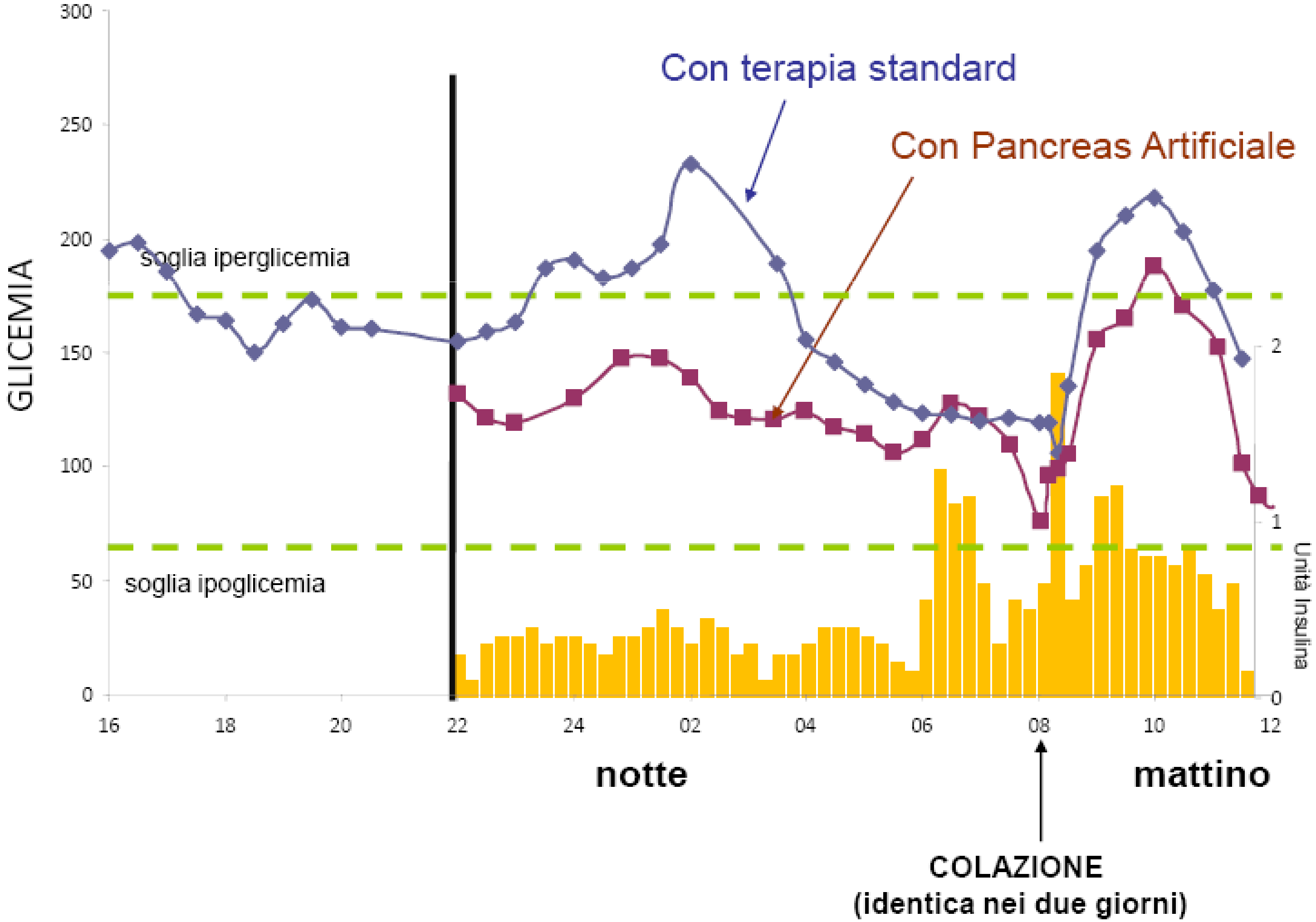
Artificial Pancreas (2008 layout)



First Trial in the Hospital (Padova, 2008)

First Trial in the Hospital (Padova, 2008)

Results

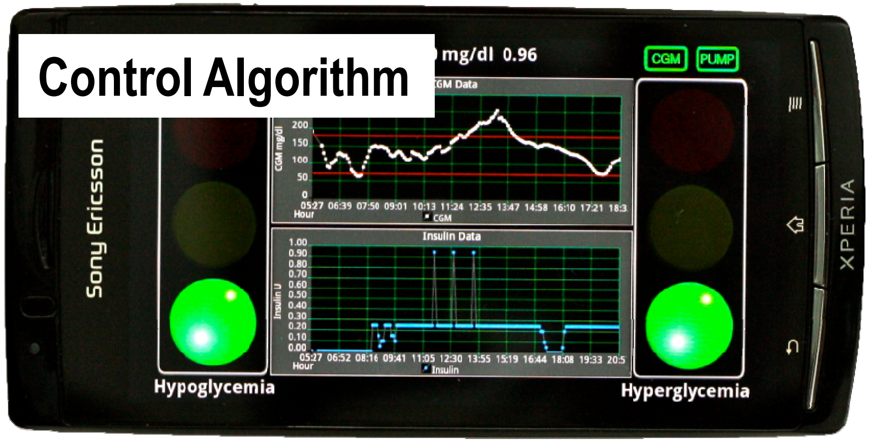


Artificial Pancreas (2011 layout)

Continuous Glucose Monitoring sensor

Continuous Subcutaneous Insulin Infusion (CSII) pump

Wireless

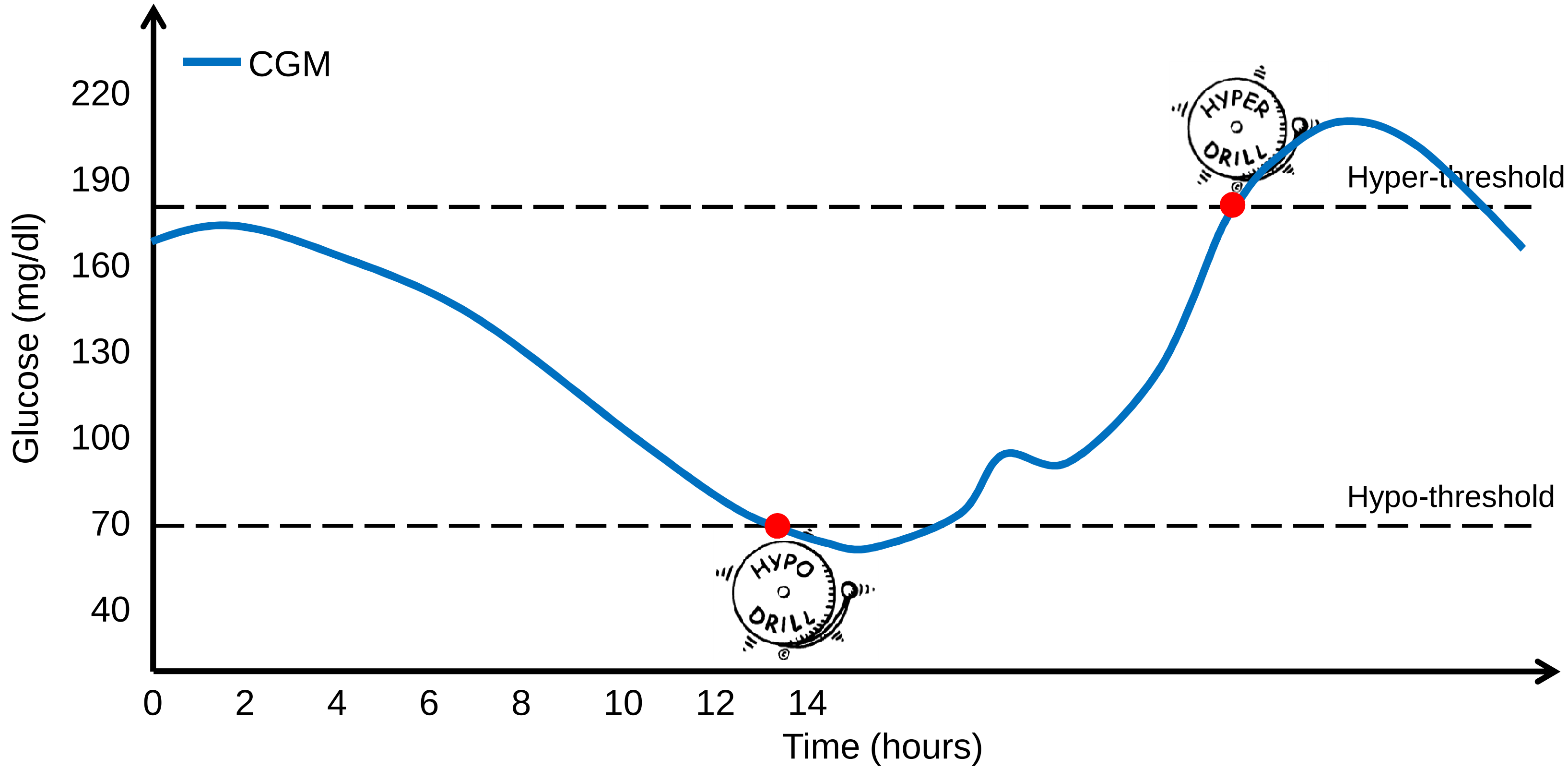


Wireless

Toward an AP@ home: study in hotel... (Padova, 2011)

Real-time hypo/hyperglycemic alerts

CGM sensors embed **VISUAL / ACOUSTIC ALARMS** which alert the patient (in real-time) when hypo/hyperglycemic threshold are reached



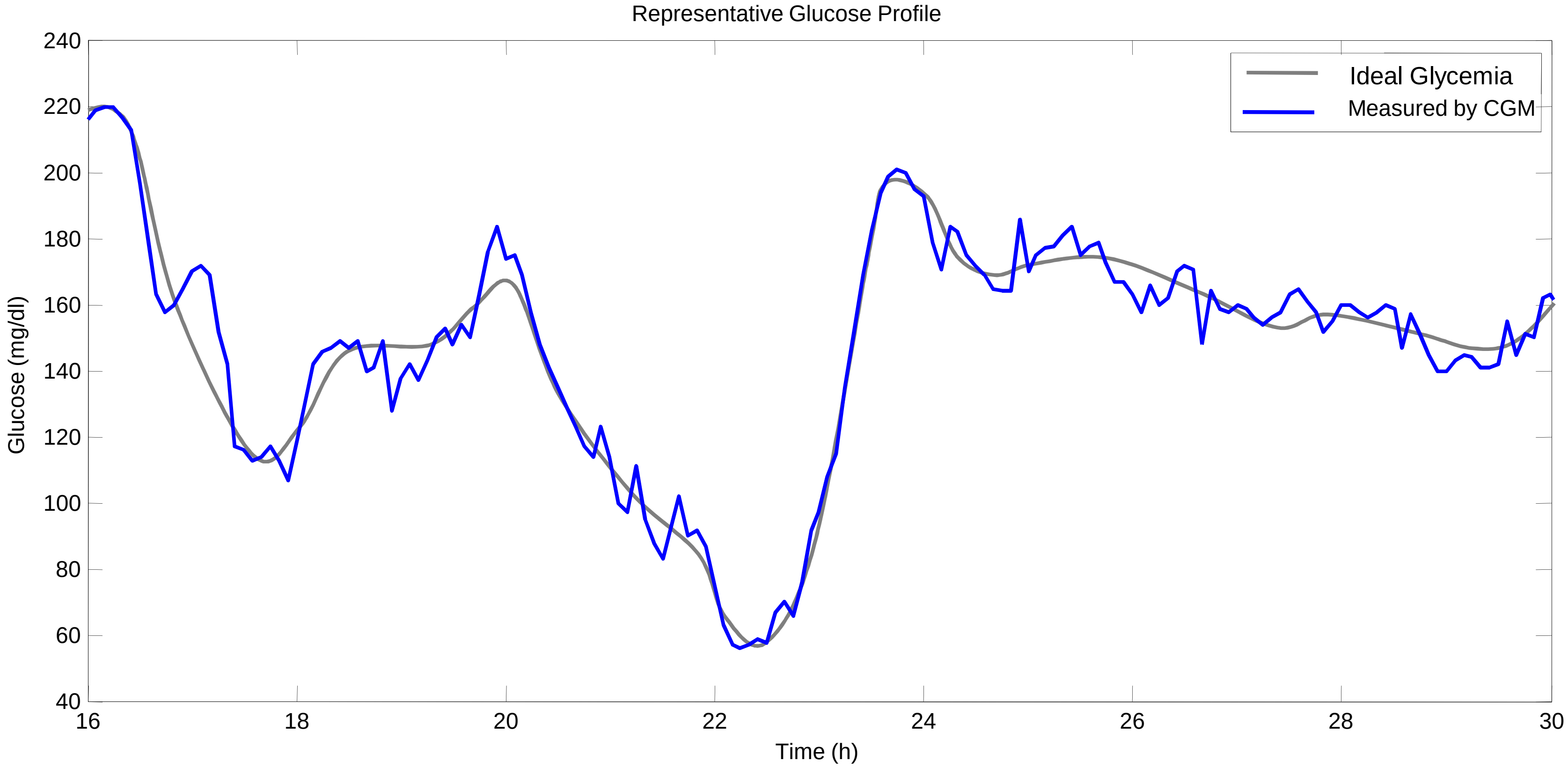
Where We Are:
(Selection of) Open Problems

Garbage IN, Garbage OUT

In order to drive the AP and generate alerts properly, it is fundamental to have **a “good” CGM signal**

- **limited bias**
- **small uncertainty**

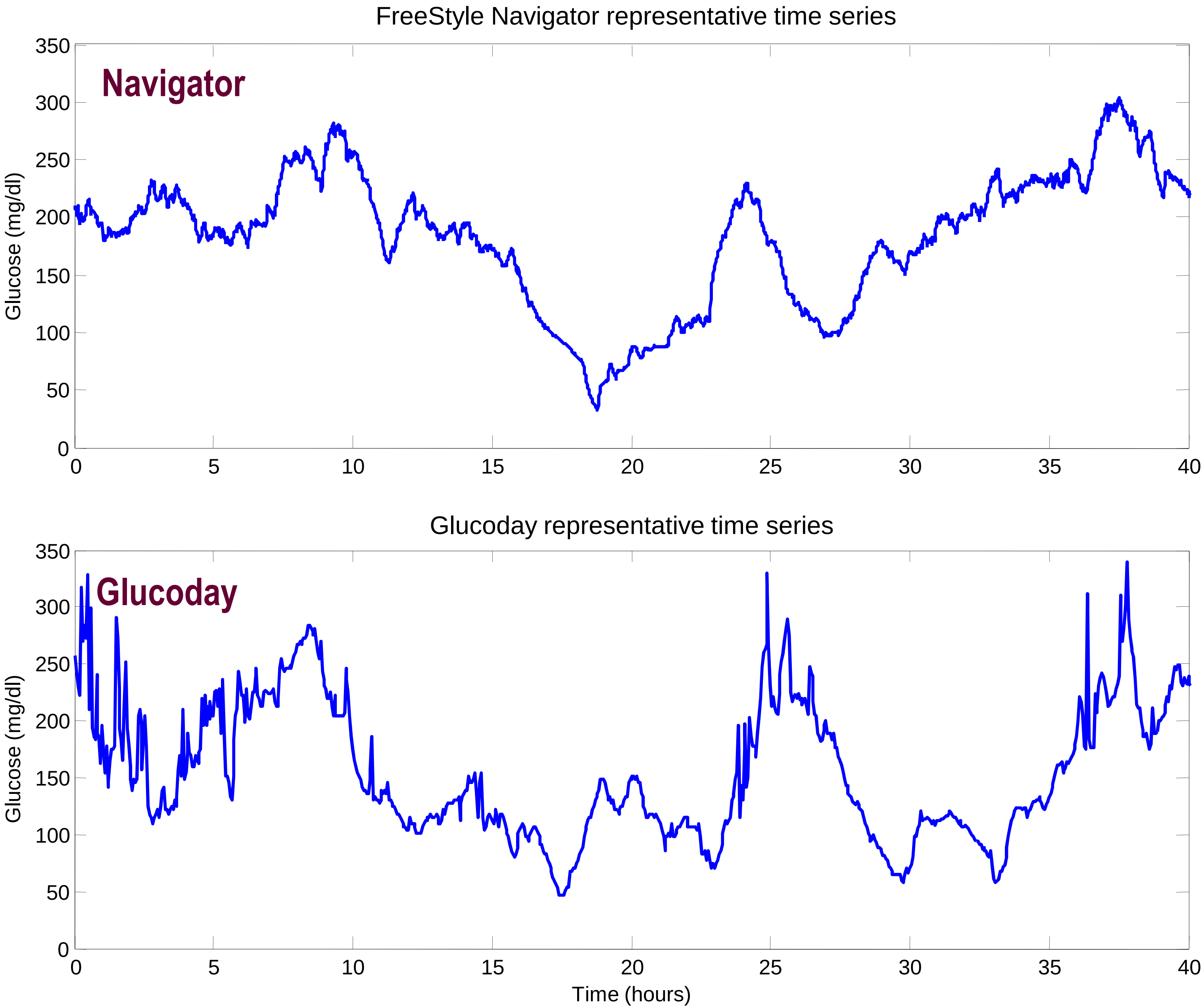
Open Issue #1: Precision



Glucose concentration readings are **uncertain**

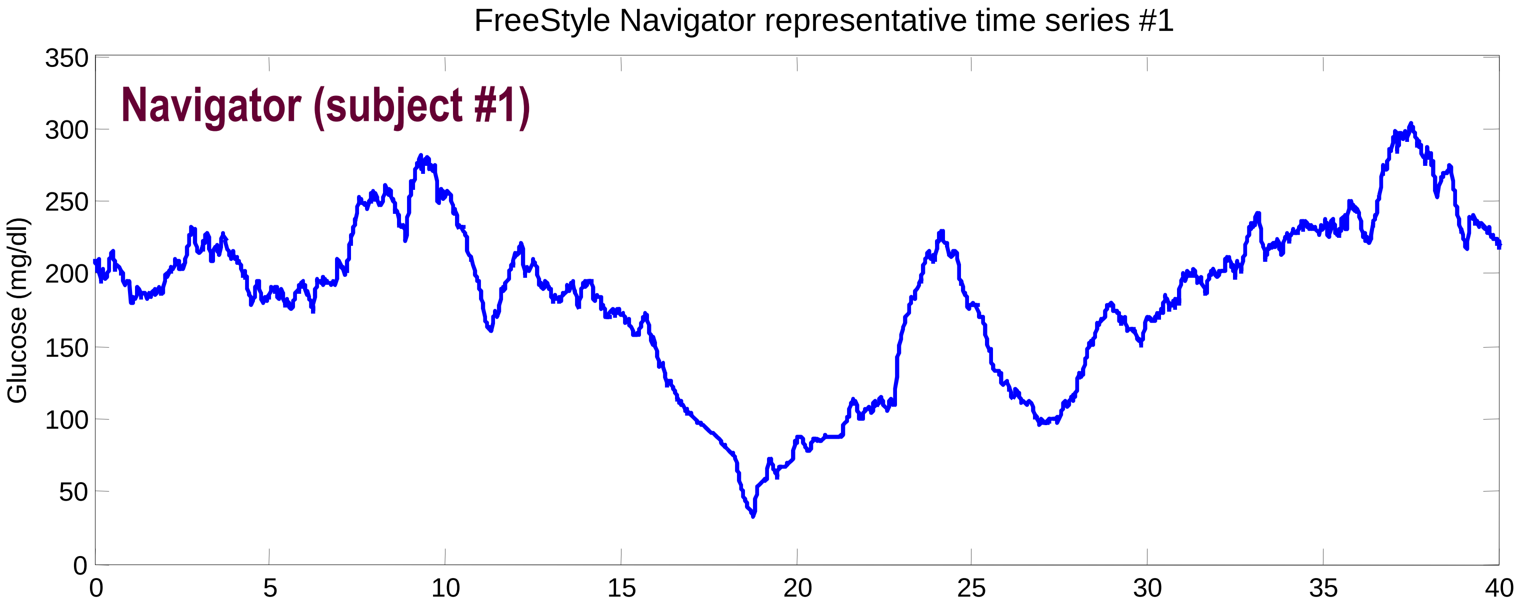
Denoising must be tackled with in **real-time**

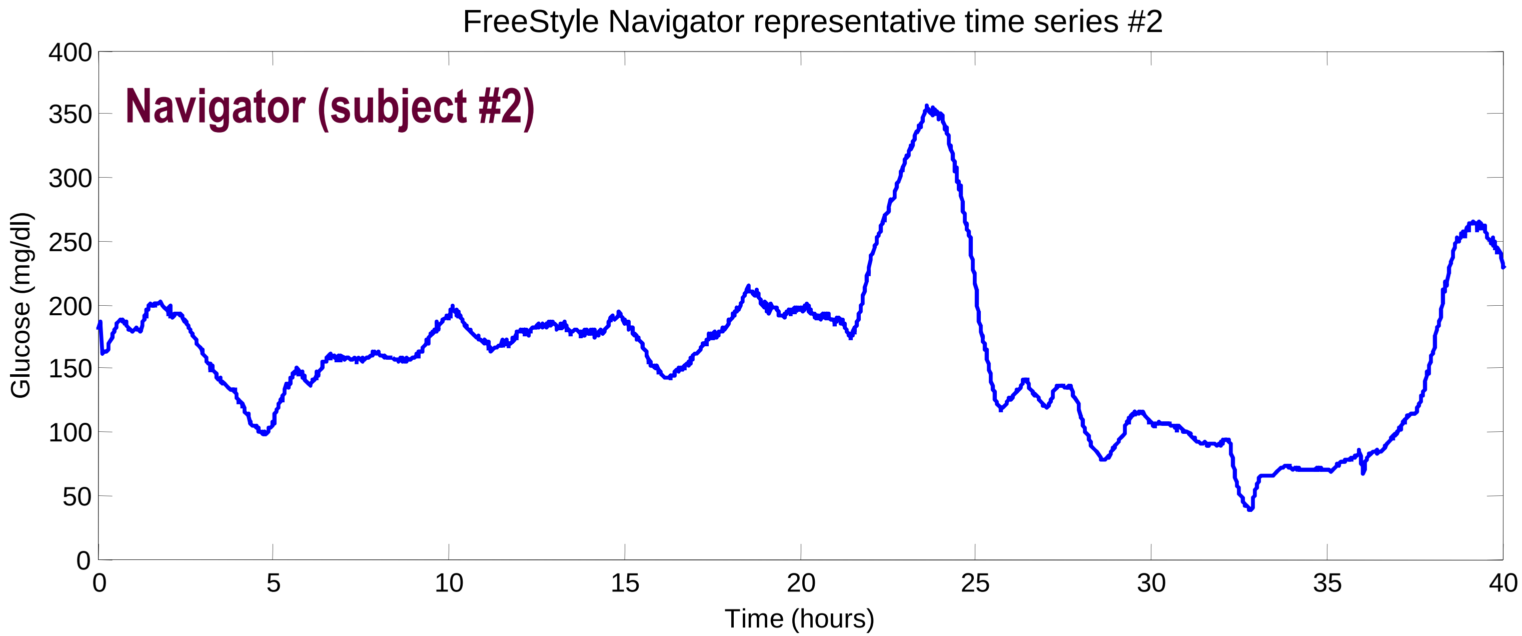
Sensor-to-sensor SNR variability



SNR in the Glucoday time-series seems worse than in the Navigator time-series

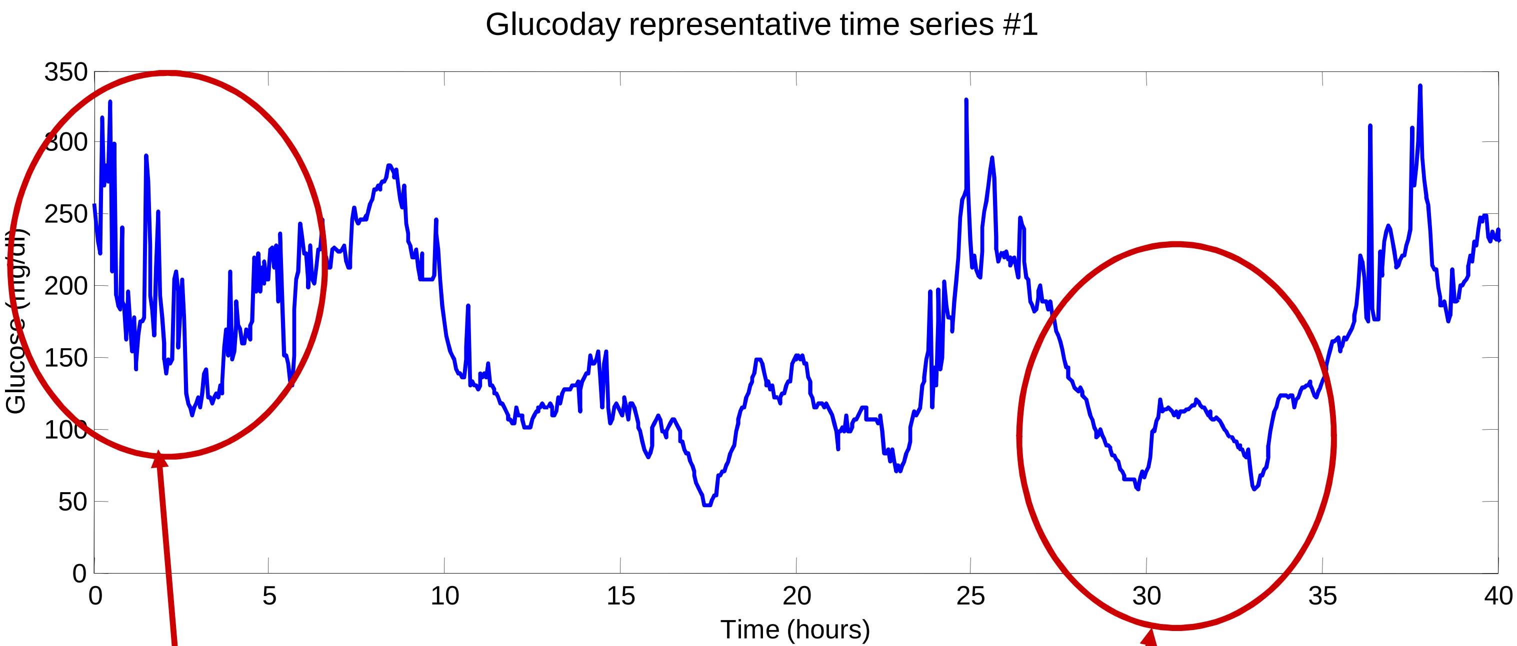
Inter-individual SNR variability





SNR in Navigator #1 is worse than in Navigator #2

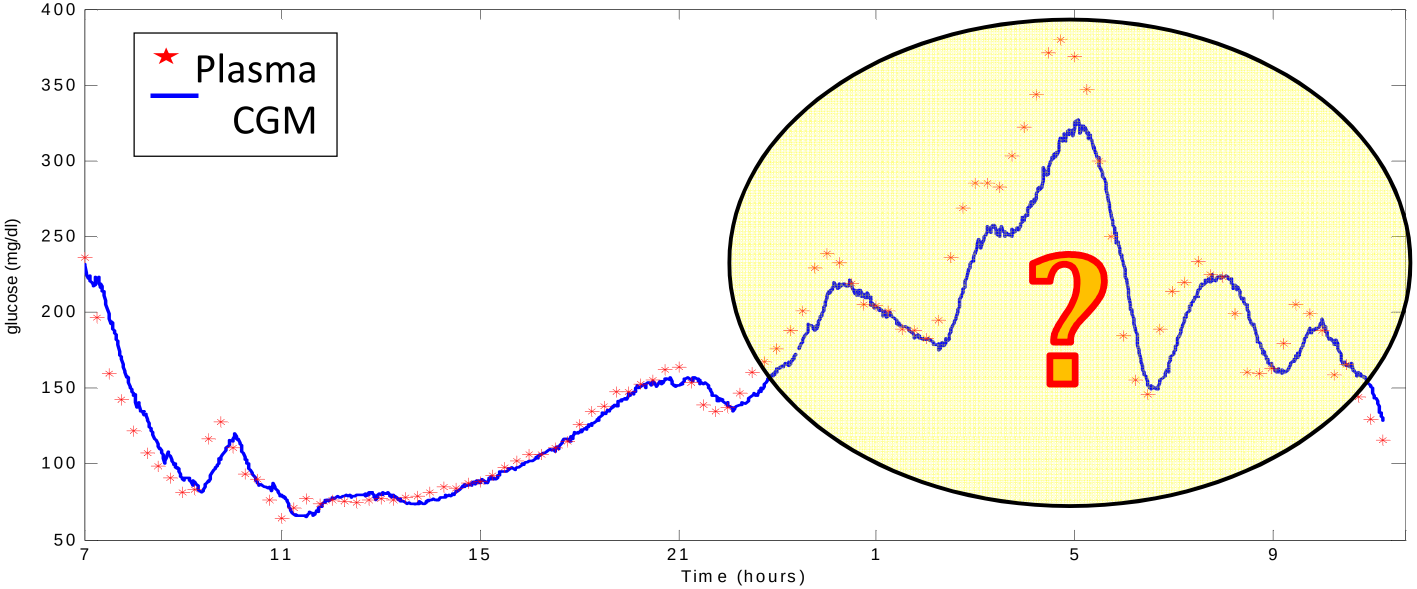
Intra-individual SNR variability



“very low” SNR

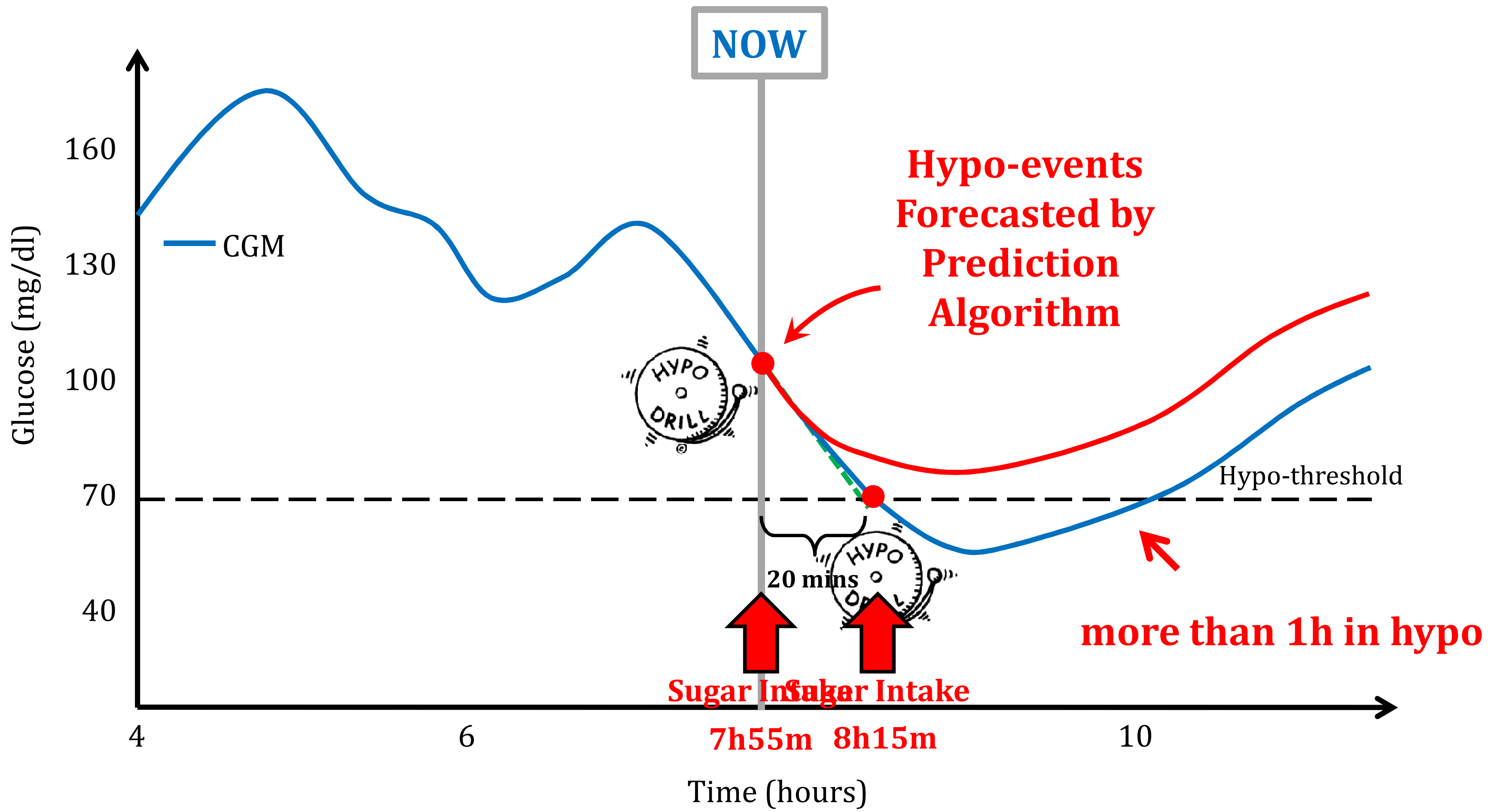
“better” SNR

Open Issue #2: Accuracy

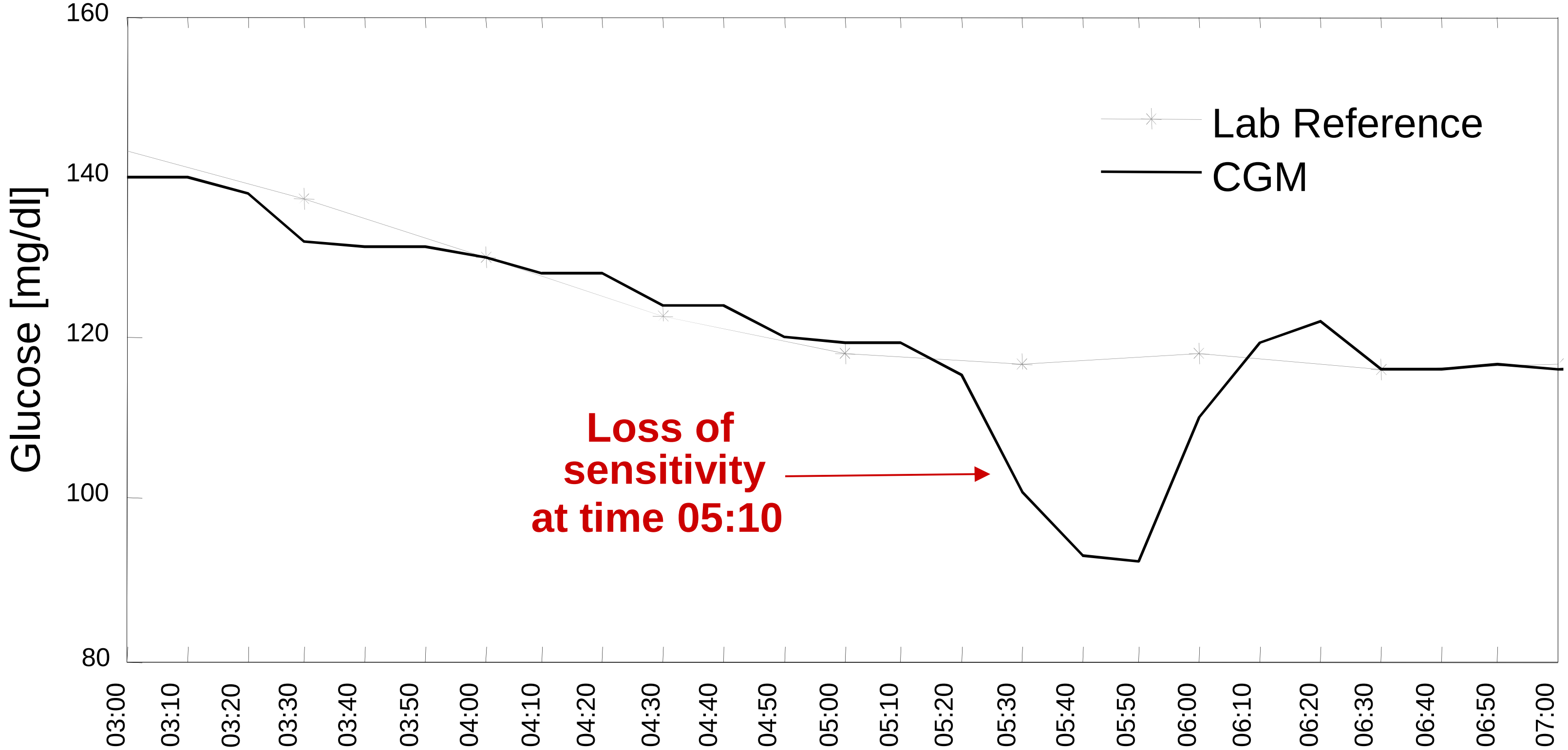


Calibration may **deteriorate** during the monitoring because undesirable interactions between the sensor surface and the biological medium

Open Issue #3: Preventing better than simply detecting hypo/hyper-events



Open Issue #4: Fault Detection



Other open issues (non algorithmical)

•easiness of implantation
•discomfort
•miniaturization

•rejection of the sensor by the body
•in-vivo calibration & stabilization time
•long-term stability

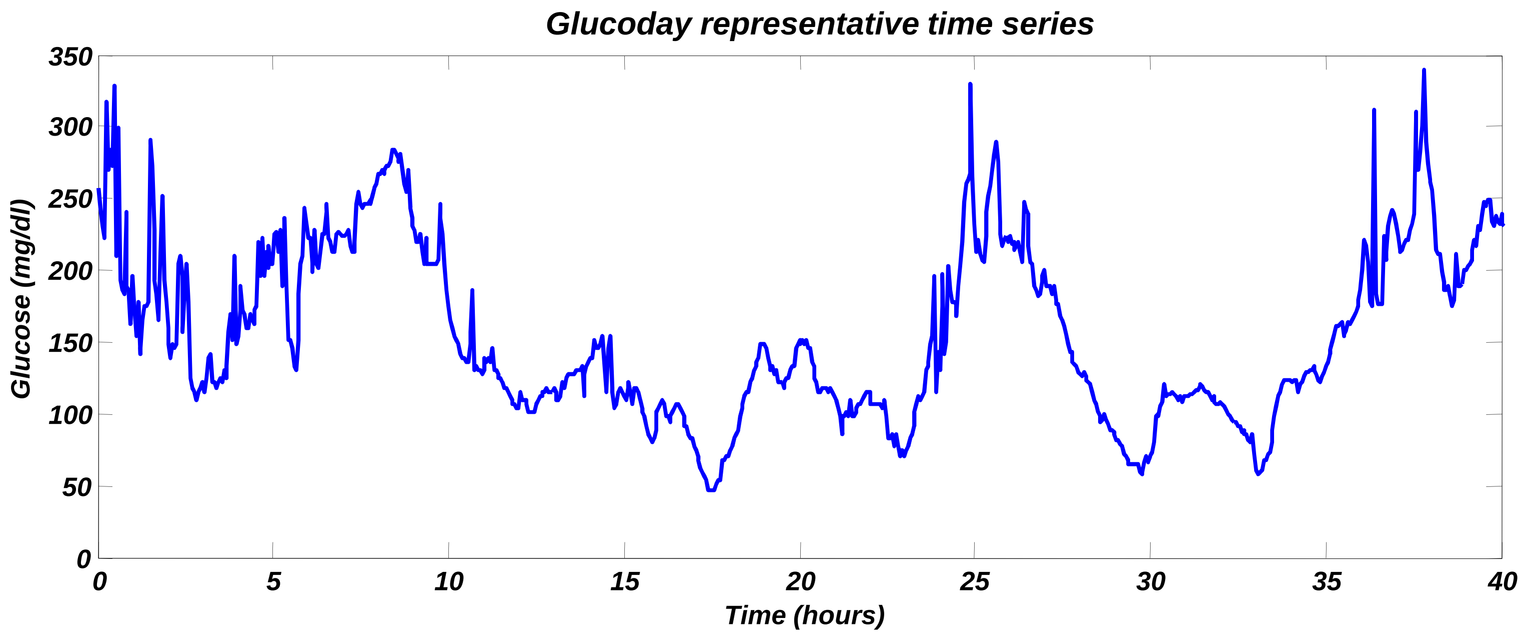
•power source/battery consumption

•…

Where to go:
“Algorithmically Smart” Sensor
(Andrea Facchinetti)

Denoising of CGM time series

Denoising: the problem



- ***CGM time series are noisy***
- ***The signal-to-noise ratio (SNR) varies from sensor to sensor, from individual to individual, and within the same monitoring***
- ***Consequences: alerts generated on the bases of CGM data can be false, impossible to perform an efficient/accurate real-time prediction, etc.***
- ***Solution → Real-time filtering of CGM data (denoising) to reduce the amplitude to noise overlapped to true glycemia***

Denoising: state of the art

Most of CGM devices embedded real-time filters with fixed parameters, e.g. FIR filter of order M

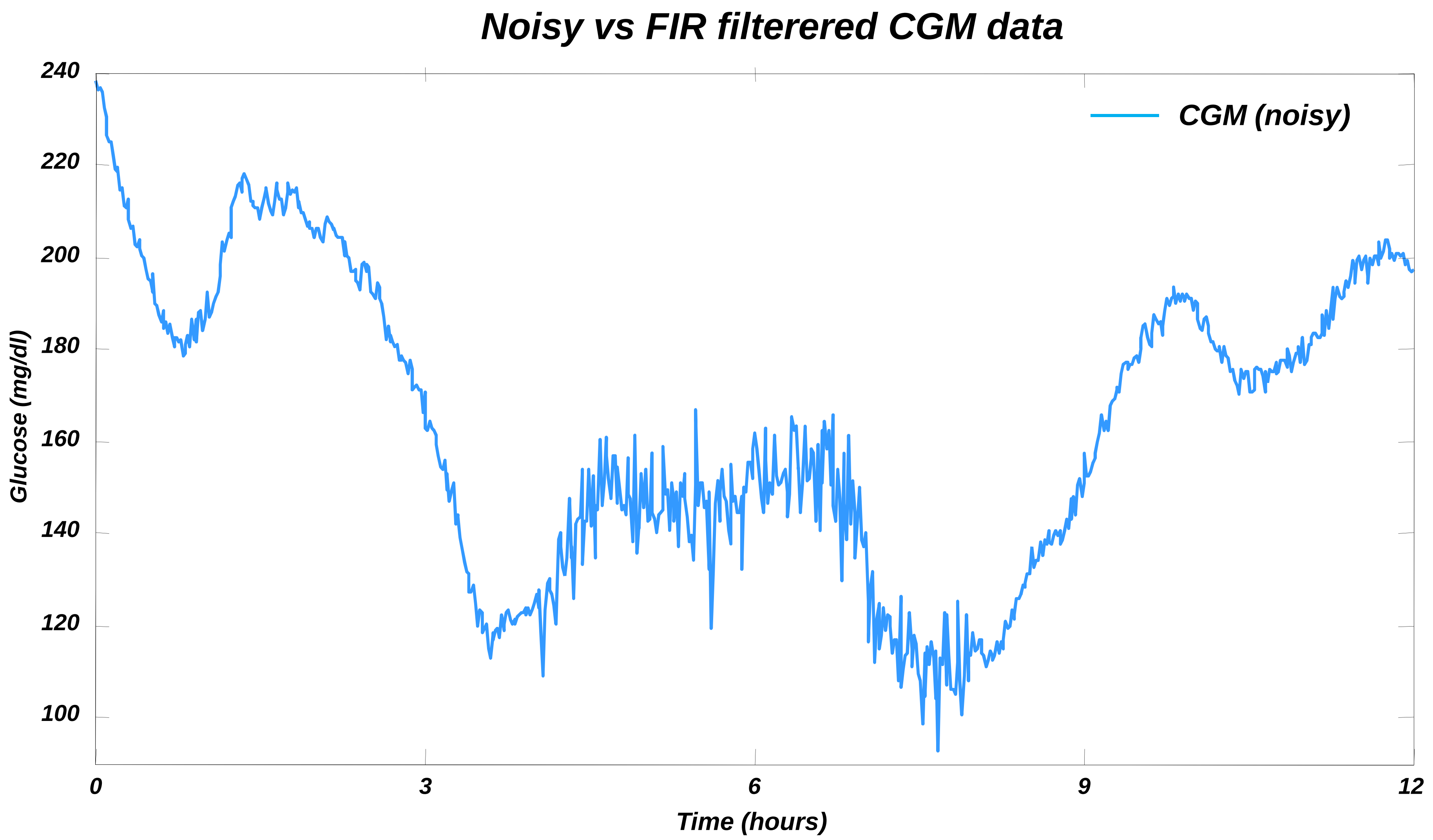
$$\hat{u}(t) = \frac{1}{\sum_{i=1}^{M} w(t)} \left(w(1)y(t) + w(2)y(t-1) + \ldots + w(M)y(t-M+1) \right)$$

$w(i)=\mu^i$

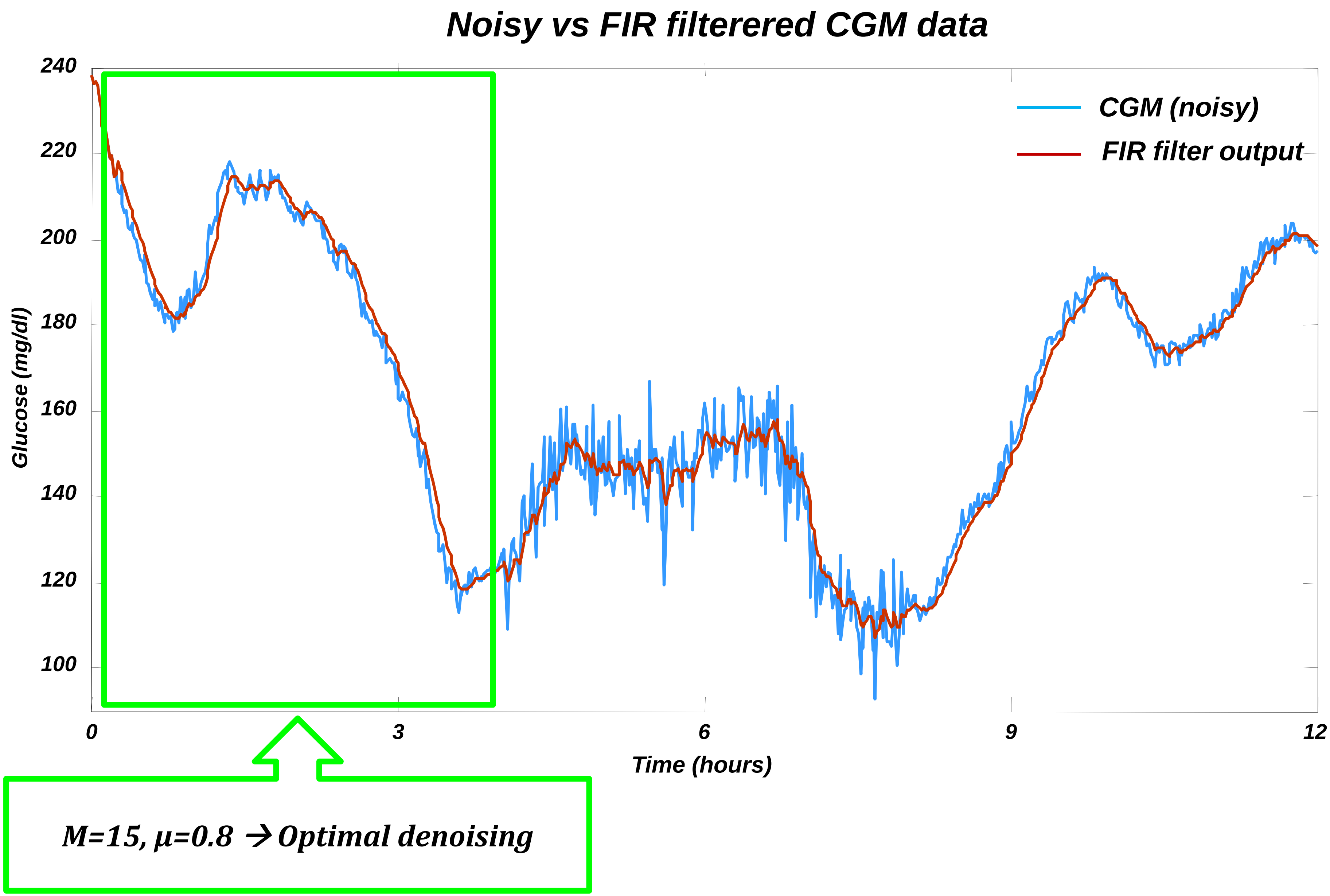
where y(t) is the noisy CGM measurement given at discrete time t, û(t) is the output of the filter at time t, w(1),…,w(M) are the parameters (weights) of the filter, and 0<µ≤1.

Given the variability of the SNR, a filter with fixed structure and parameters, i.e. a "universal denoising filter", will be suboptimal.

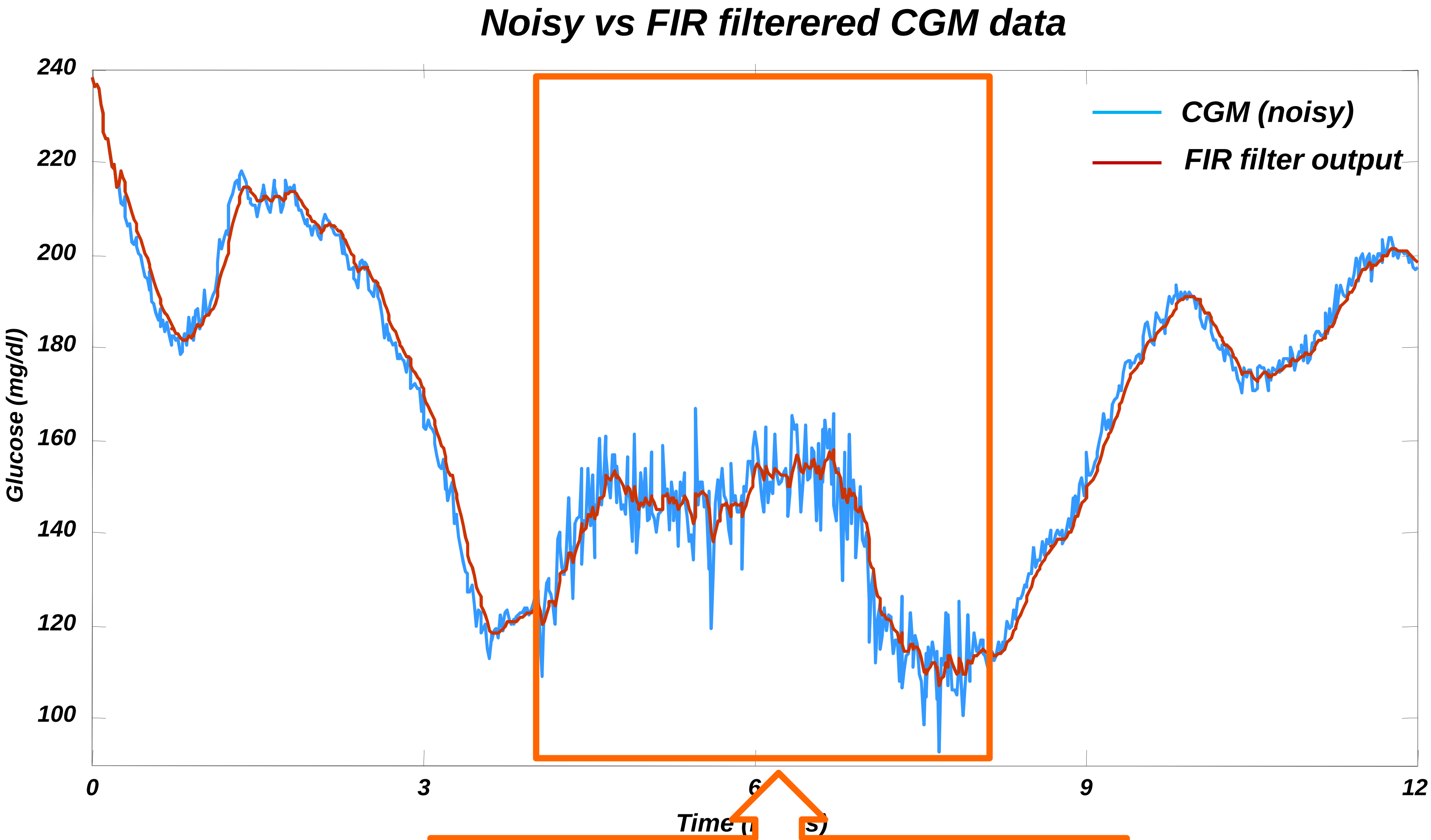
Denoising: application of FIR filter



Denoising: application of FIR filter

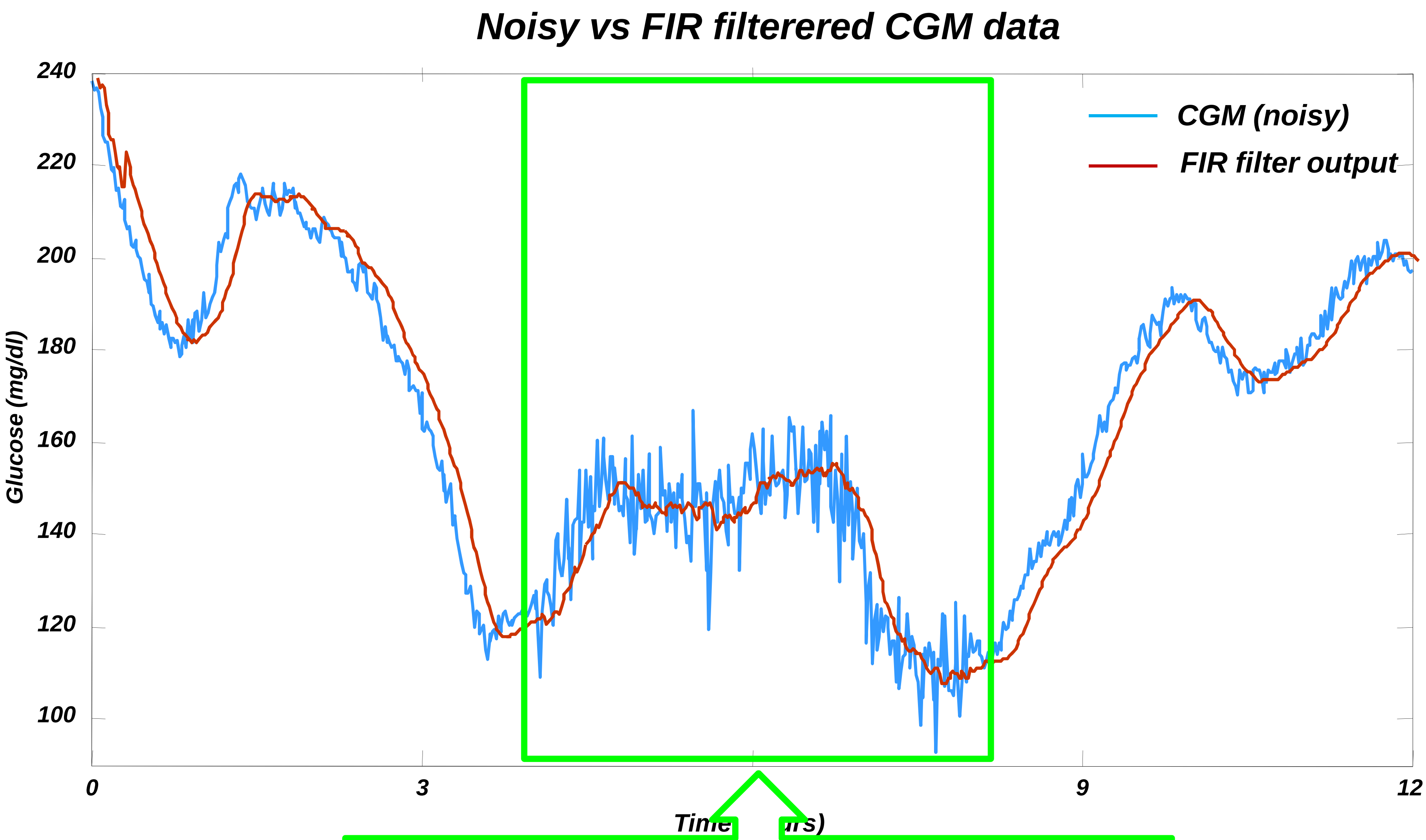


Denoising: application of FIR filter



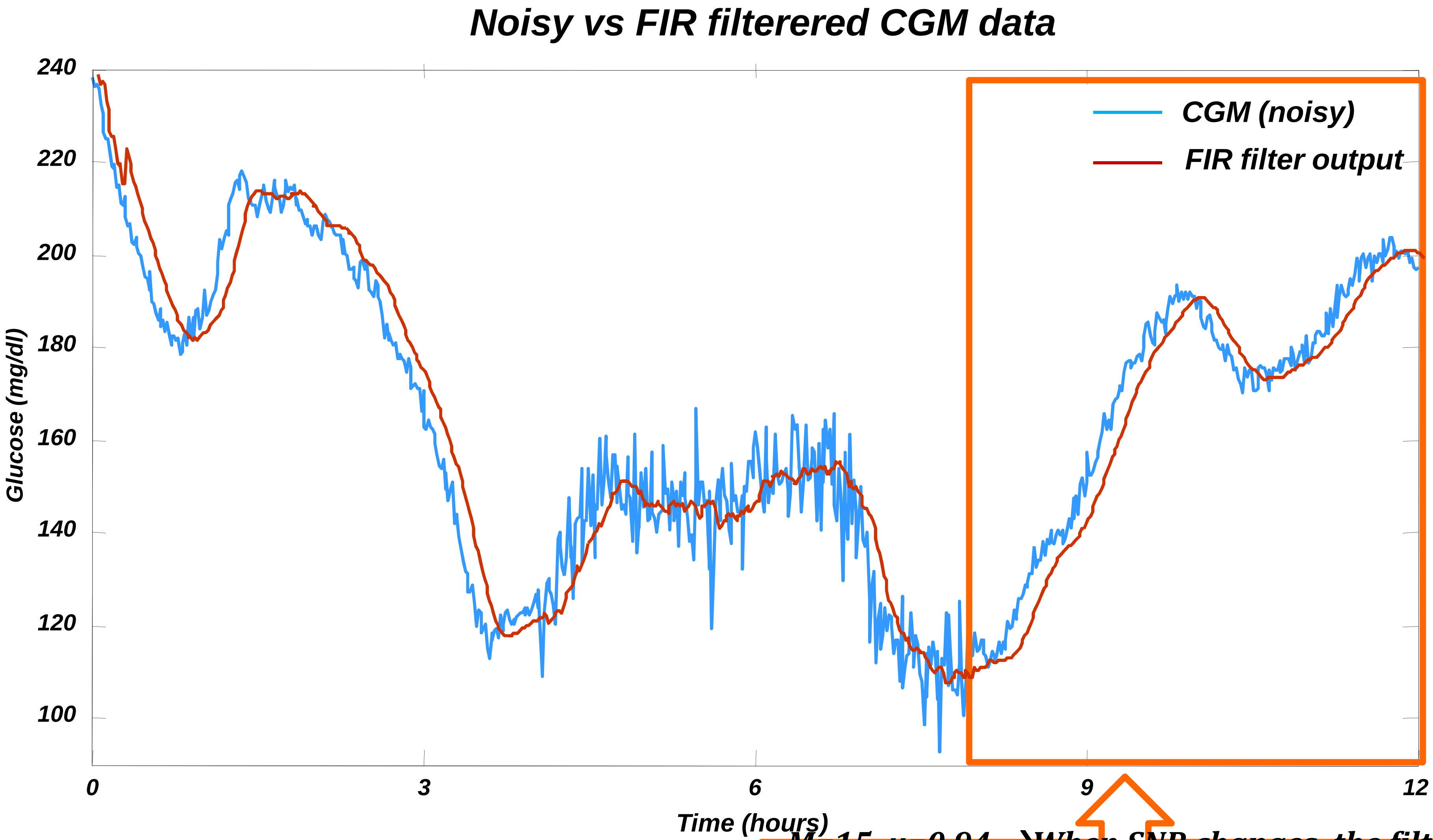
M=15, μ=0.8 → When SNR changes, the filter performs suboptimally (spikes still present)

Denoising: application of FIR filter



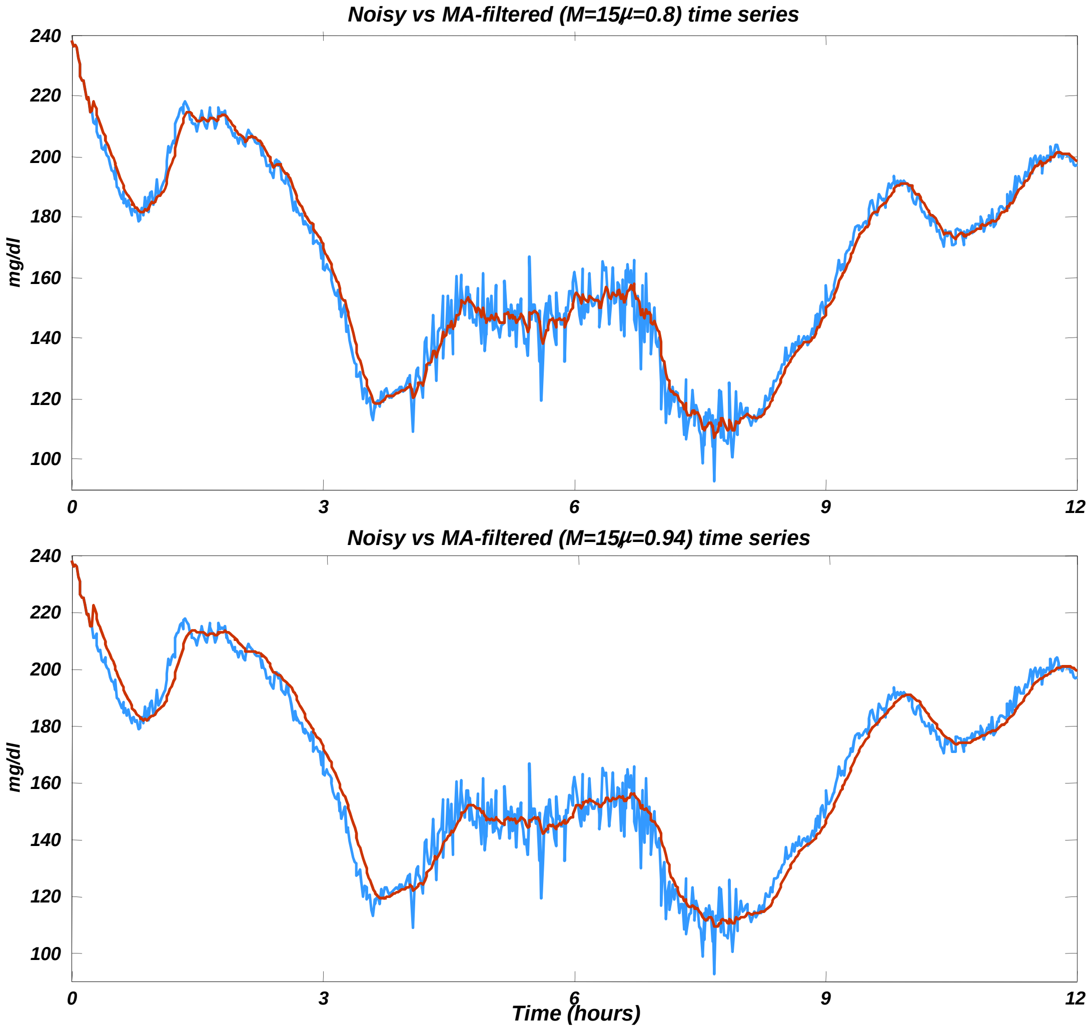
M=15, μ=0.94 →Optimal denoising
(parameters tuned on data with this SNR level)

Denoising: application of FIR filter



M=15, μ=0.94 →When SNR changes, the filter performs suboptimally (delay in displaying data, which makes untimely any alert generation)

Some Comments



- ***Each time series should have its own M and μ***
- ***No statistically-based criteria available to fix M and μ***
- ***Suboptimal values of M and μ may cause under/oversmoothing***

IDEA: ***to develop a filter with simple structure but able to automatically adapt its parameters online, depending on how the SNR varies.***

The Problem

Given the measured noisy CGM value at time t, here called y(t):

$$y(t) = u(t) + v(t)$$

Measured CGM signal — ***true glucose*** — ***noise***

We want to estimate u(t), the glycemia "without noise"

The denoising approach

***A priori knowledge* exploited within the filter:**

- ***Model of the measured CGM signal:***

$$y(t) = u(t) + v(t)$$

Measured CGM signal *true glucose* *noise*

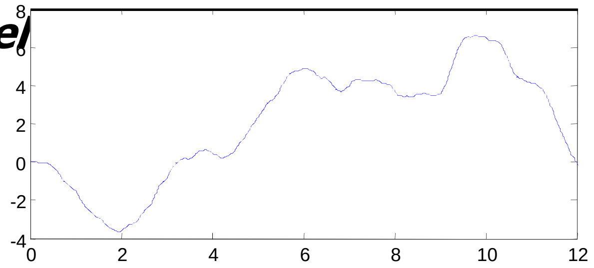
The noise process v(t) is uncorrelated, with unknown variance σ^2

- ***u(t) is continuous, together with its first and second time derivatives***

Integrated random walk model

$$u(t+1) = 2u(t) - u(t-1) + w(t)$$

$$w(t) = N(0, \lambda^2)$$



The only unknown parameter of the model is λ^2, which needs to be estimated from the data

Facchinetti et al. IEEE Trans Biomed Eng 2
Facchinetti et al. IEEE Trans Biomed Eng 2

The denoising approach

Model of the measured CGM signal $y(t) = u(t) + v(t)$ $\qquad v(t) = N(0, \sigma^2)$

Measured CGM signal $\quad$ *true glucose* $\quad$ *noise*

Model equation: $u(t+1) = 2u(t) - u(t-1) + w(t)$ $\quad w(t) = N(0, \lambda^2)$

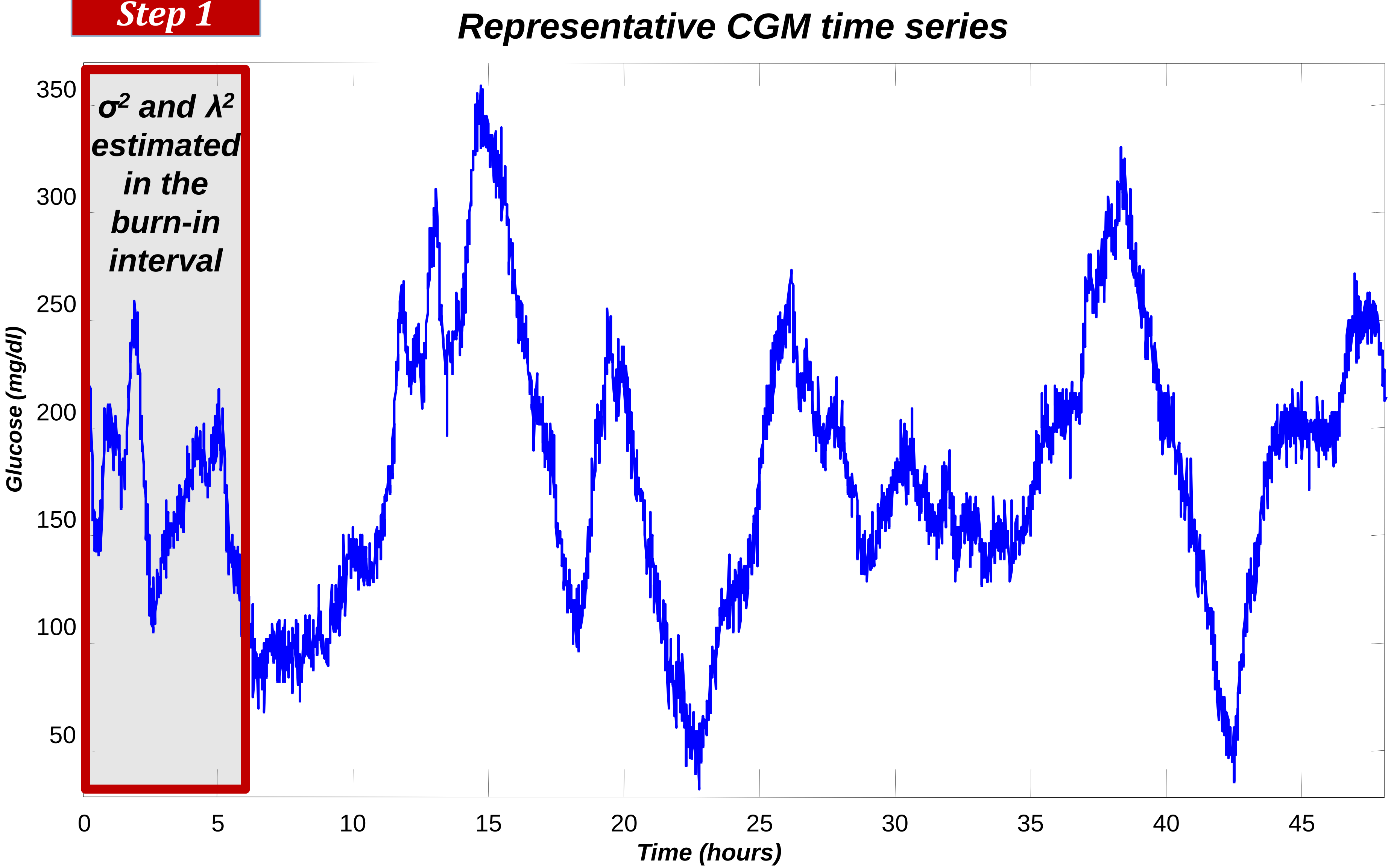
2-step (causal) implementation:

1. ***the determination of unknown parameters σ^2 and λ^2 is performed in a burn-in interval through a Bayesian smoothing approach based on maximum likelihood criterion***

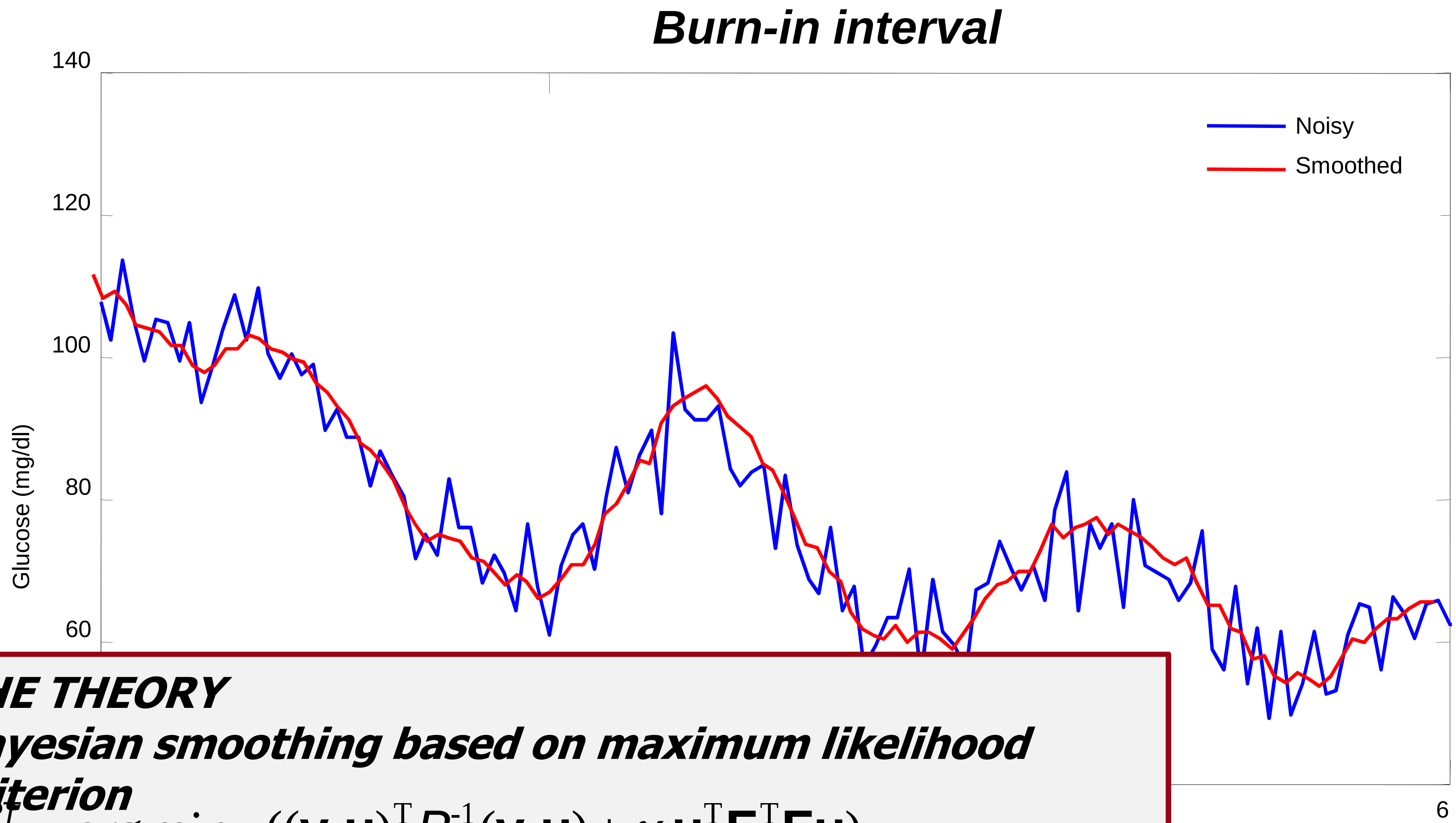
2. ***the filtered glucose level $\hat{u}(t)$ is estimated via Kalman Filtering (recursive equations→ online implementations with low-cost hardware)***

The denoising approach (overview)

Step 1



Step 1: estimation of σ^2 and λ^2



THE THEORY

Bayesian smoothing based on maximum likelihood criterion

$$\hat{\mathbf{u}}^{PT} = \arg\min_{\mathbf{u}} \left((\mathbf{y}-\mathbf{u})^{T} B^{-1} (\mathbf{y}-\mathbf{u}) + \gamma\, \mathbf{u}^{T} \mathbf{F}^{T} \mathbf{F} \mathbf{u} \right)$$

→ The degree of regularization depends on the so-called regularization parameters $\gamma=\sigma^2/\lambda^2$

Step 1: estimation of σ^2 and λ^2

How to set the regularization parameter

The expected value of the weighted residuals sum of squares is:

$$E[\mathrm{WRSS}] = \sigma^2 \{ N - \mathrm{trace}(B^{-1/2} (B^{-1} + \gamma F^T F)^{-1} B^{-1/2}) \}$$

$$\gamma = \frac{\sigma^2}{\lambda^2}$$

The expected value of the weighted estimates sum of squares is:

$$E[\mathrm{WESS}] = \lambda^2 \mathrm{trace}(B^{-1/2} (B^{-1} + \gamma F^T F)^{-1} B^{-1/2})$$

γ^{OPT} is obtained by resolving:

$$\frac{\mathrm{WRSS}(\gamma)}{N - \mathrm{trace}(B^{-1/2} (B^{-1} + \gamma F^T F)^{-1} B^{-1/2})} = \gamma \frac{\mathrm{WESS}(\gamma)}{\mathrm{trace}(B^{-1/2} (B^{-1} + \gamma F^T F)^{-1} B^{-1/2})}$$

Once γ^{OPT} is evaluated, then both σ^2 and λ^2 can be obtained as:

$$\hat{\sigma}^2 = \frac{\mathrm{WRSS}(\gamma^{OPT})}{N - \mathrm{trace}(B^{-1/2} (B^{-1} + \gamma^{OPT} F^T F)^{-1} B^{-1/2})}$$

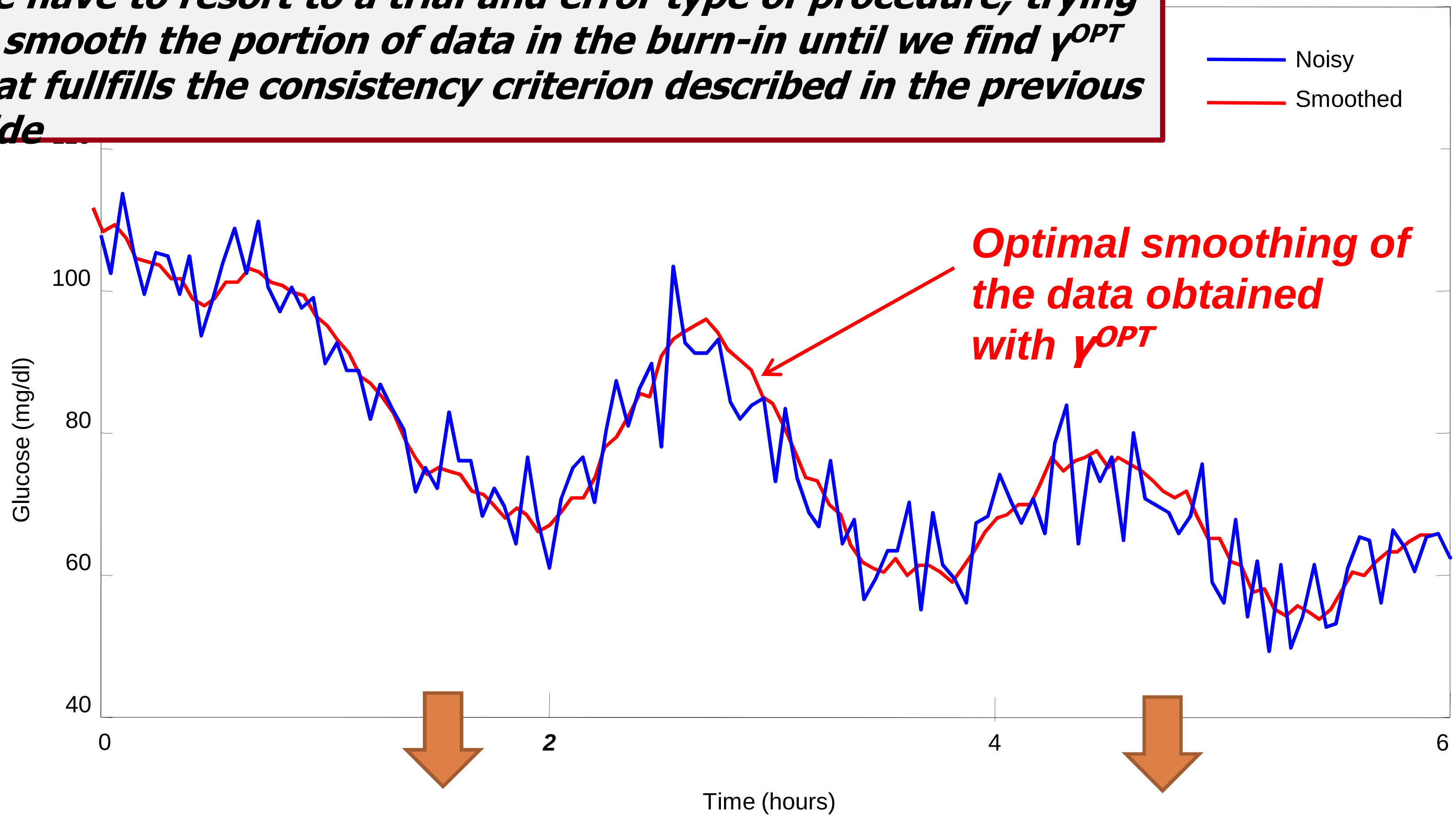
$$\hat{\lambda}^2 = \frac{\hat{\sigma}^2}{\gamma^{OPT}}$$

Sparacino et al. IEEE Trans Biomed Eng 1996
De Nicolao et al. Automatica 1997

Step 1: estimation of σ^2 and λ^2

THE PRACTICE

We have to resort to a trial and error type of procedure, trying to smooth the portion of data in the burn-in until we find γ^{OPT} that fullfills the consistency criterion described in the previous slide



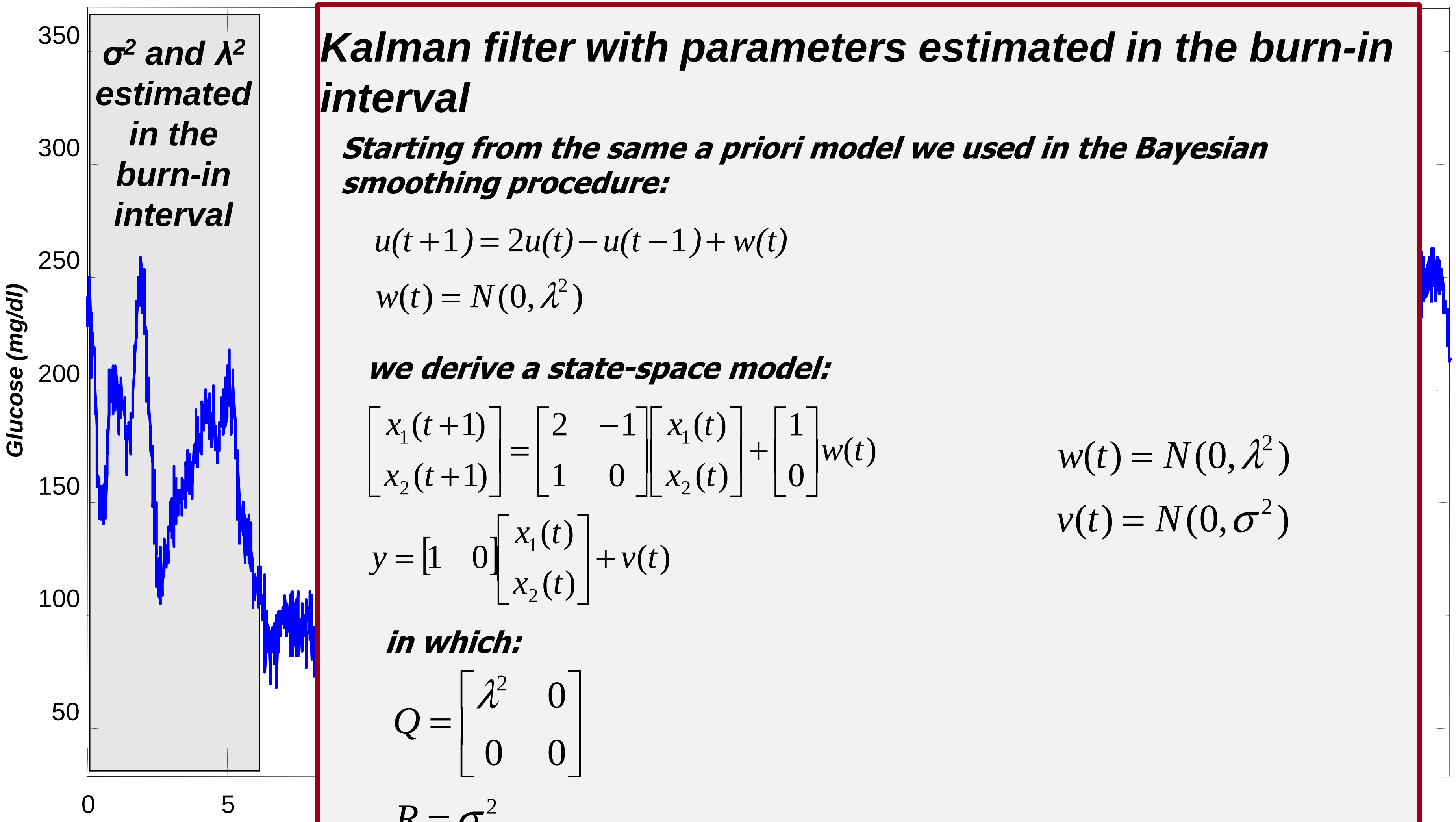
$$\hat{\sigma}^2 = \frac{\mathrm{WRSS}(\gamma^{\mathrm{OPT}})}{\mathrm{N} - \mathrm{trace}\left(\mathrm{B}^{-1/2}\left(\mathrm{B}^{-1} + \gamma^{\mathrm{OPT}}\mathrm{F}^{\mathrm{T}}\mathrm{F}\right)^{-1}\mathrm{B}^{-1/2}\right)}$$

$$\hat{\lambda}^2 = \frac{\hat{\sigma}^2}{\gamma^{OPT}}$$

The denoising approach (overview)

Step 1 **Step 2**

Representative CGM time series



Kalman filter with parameters estimated in the burn-in interval

Starting from the same a priori model we used in the Bayesian smoothing procedure:

$$u(t+1) = 2u(t) - u(t-1) + w(t)$$

$$w(t) = N(0, \lambda^2)$$

we derive a state-space model:

$$\begin{bmatrix} x_1(t+1) \\ x_2(t+1) \end{bmatrix} = \begin{bmatrix} 2 & -1 \\ 1 & 0 \end{bmatrix} \begin{bmatrix} x_1(t) \\ x_2(t) \end{bmatrix} + \begin{bmatrix} 1 \\ 0 \end{bmatrix} w(t)$$

$$y = \begin{bmatrix} 1 & 0 \end{bmatrix} \begin{bmatrix} x_1(t) \\ x_2(t) \end{bmatrix} + v(t)$$

$$w(t) = N(0, \lambda^2)$$

$$v(t) = N(0, \sigma^2)$$

in which:

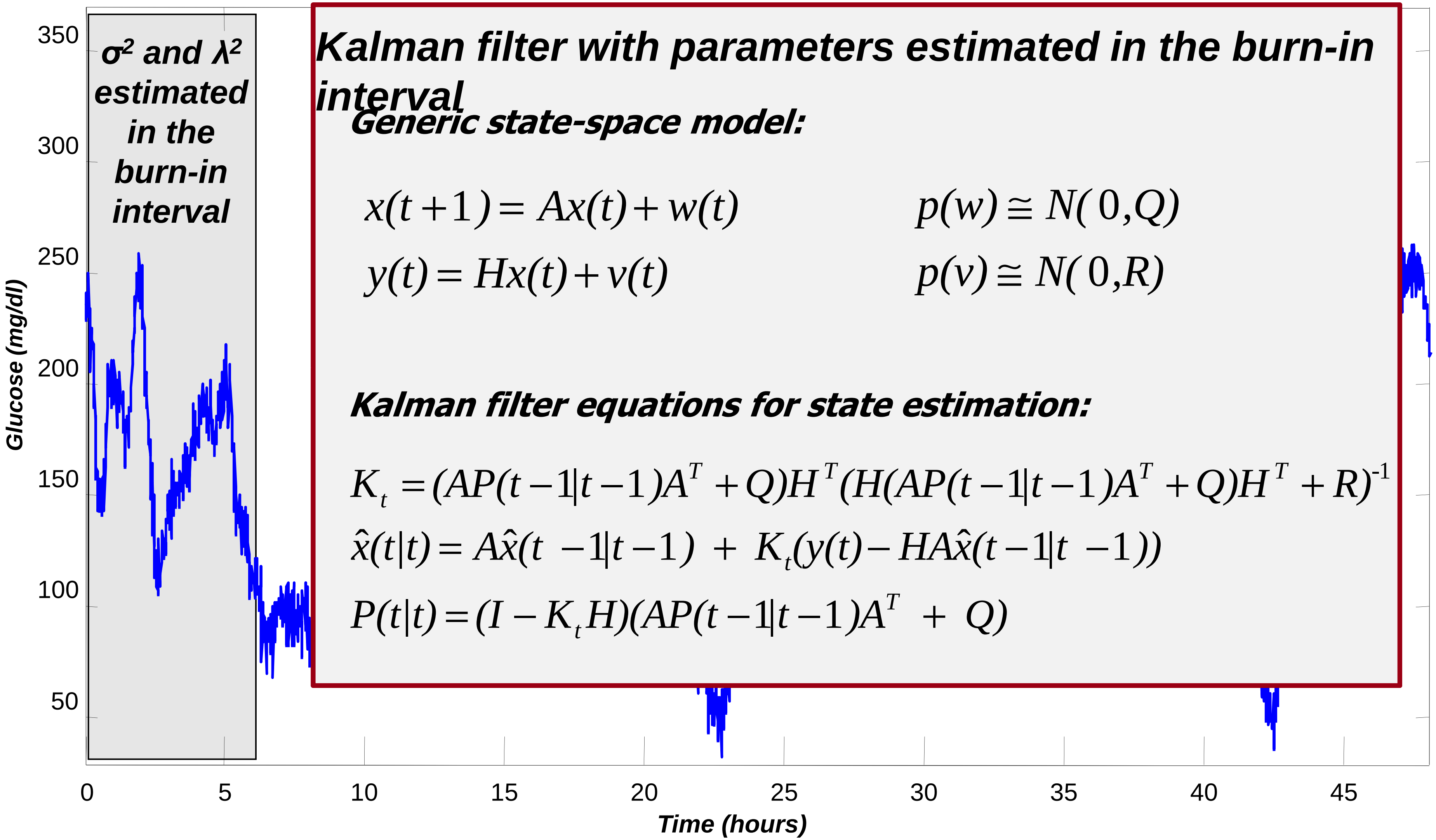
$$Q = \begin{bmatrix} \lambda^2 & 0 \\ 0 & 0 \end{bmatrix}$$

$$R = \sigma^2$$

The denoising approach (overview)

Step 1 **Step 2**

Representative CGM time series



Kalman filter with parameters estimated in the burn-in interval

Generic state-space model:

$$x(t+1) = Ax(t) + w(t) \qquad p(w) \cong N(0,Q)$$

$$y(t) = Hx(t) + v(t) \qquad p(v) \cong N(0,R)$$

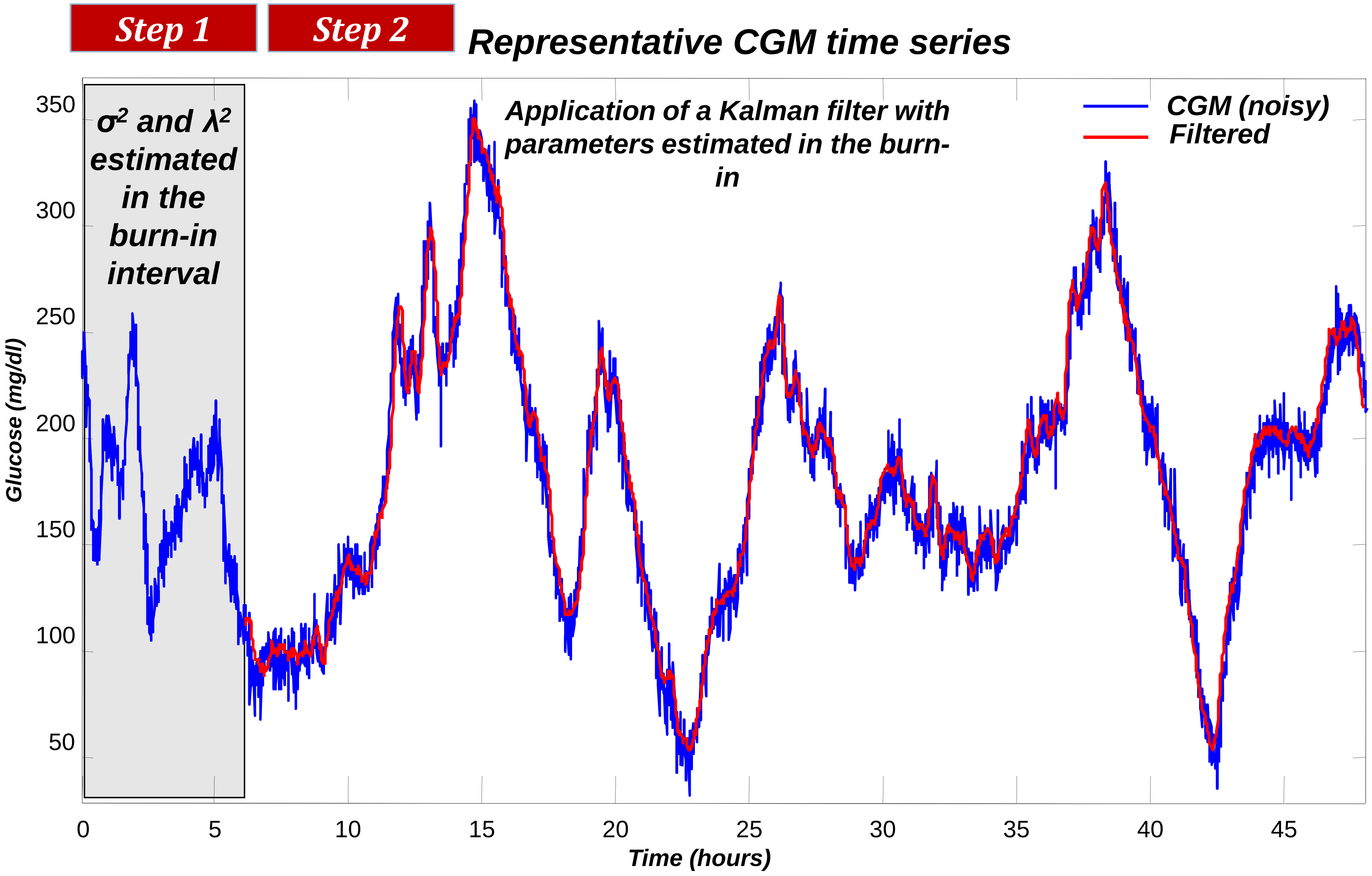
Kalman filter equations for state estimation:

$$K_t = (AP(t-1|t-1)A^T + Q)H^T(H(AP(t-1|t-1)A^T + Q)H^T + R)^{-1}$$

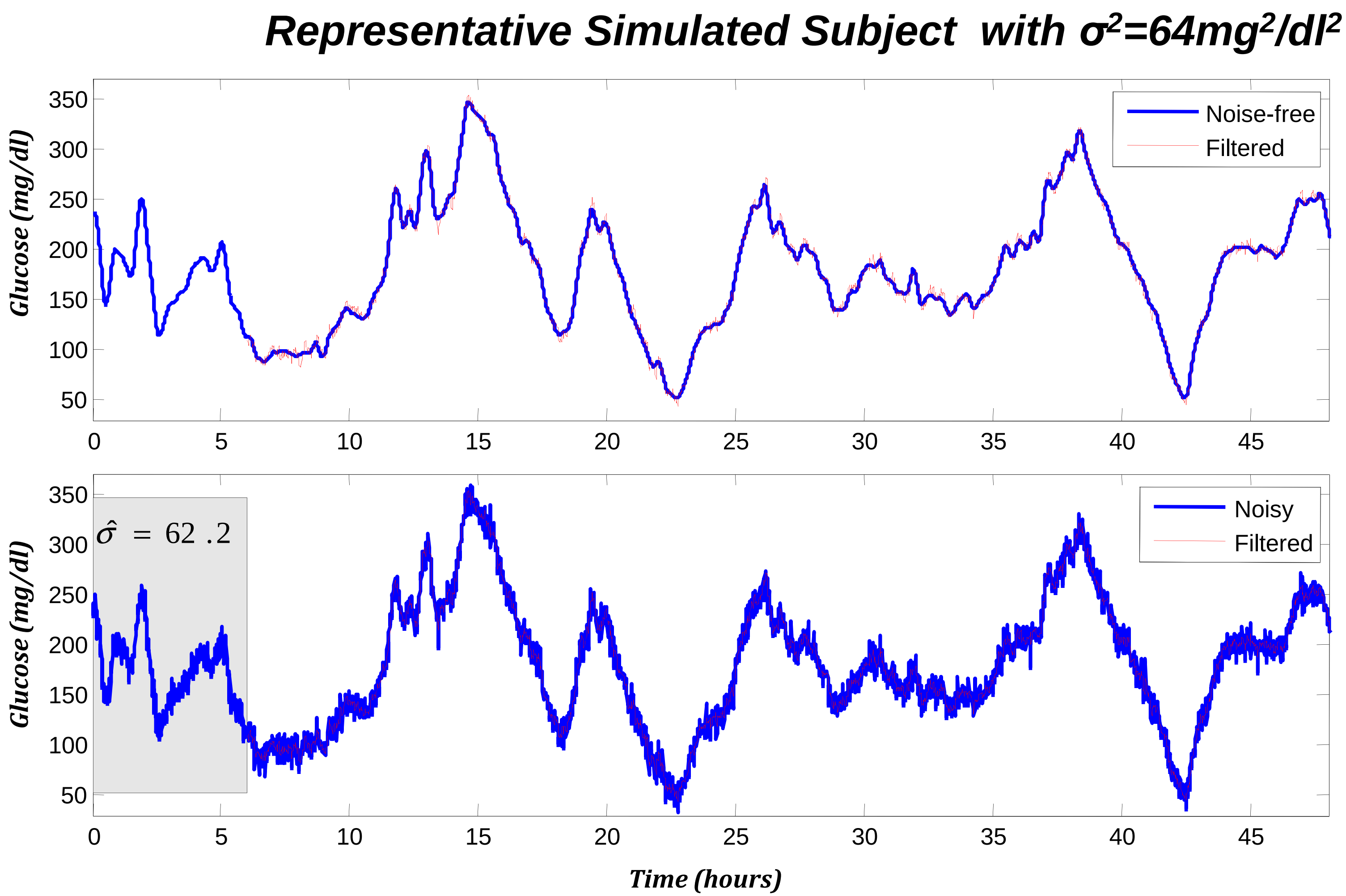
$$\hat{x}(t|t) = A\hat{x}(t-1|t-1) + K_t(y(t) - HA\hat{x}(t-1|t-1))$$

$$P(t|t) = (I - K_t H)(AP(t-1|t-1)A^T + Q)$$

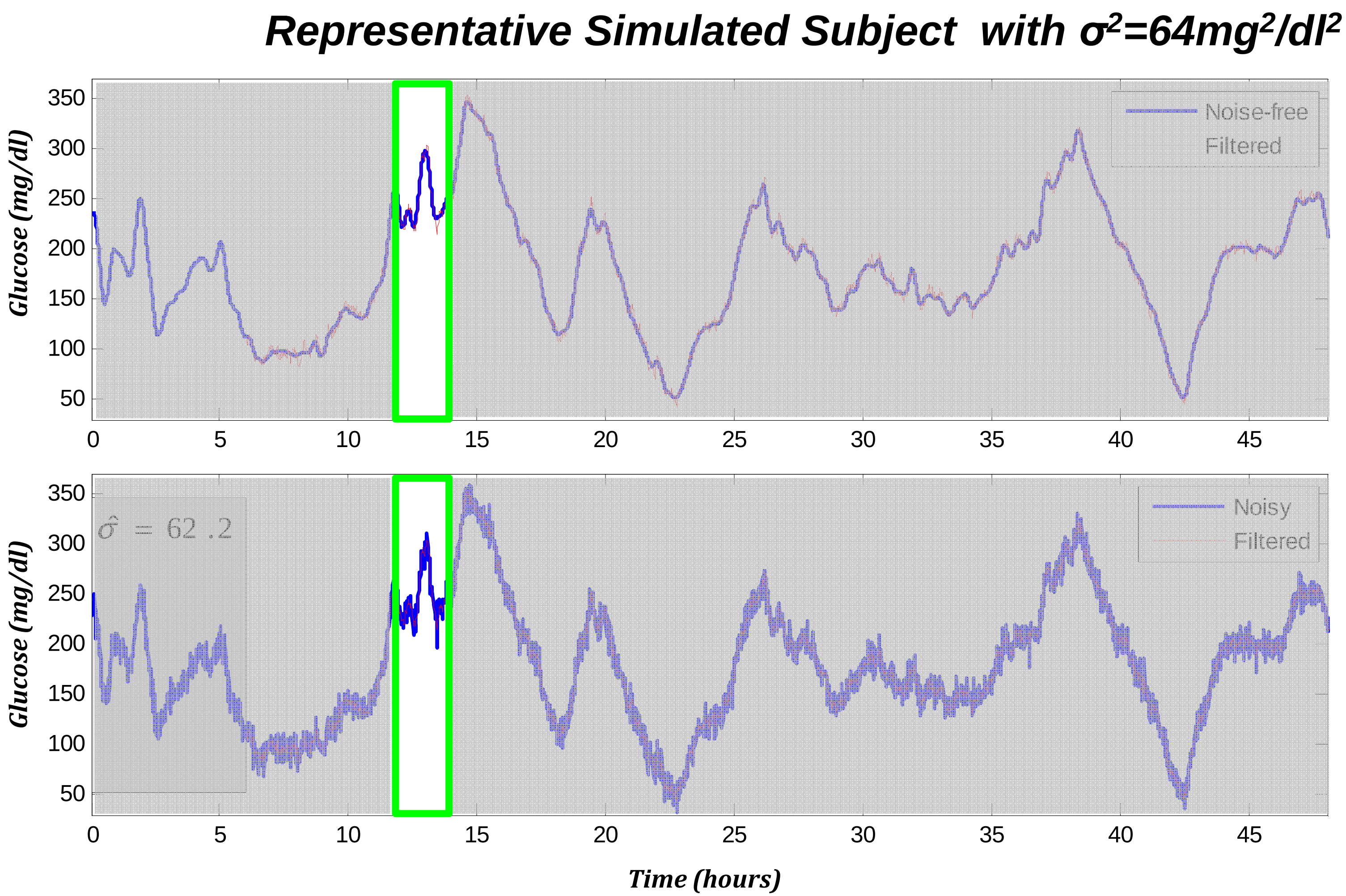
The denoising approach (overview)



Dealing with inter-individual variability of th

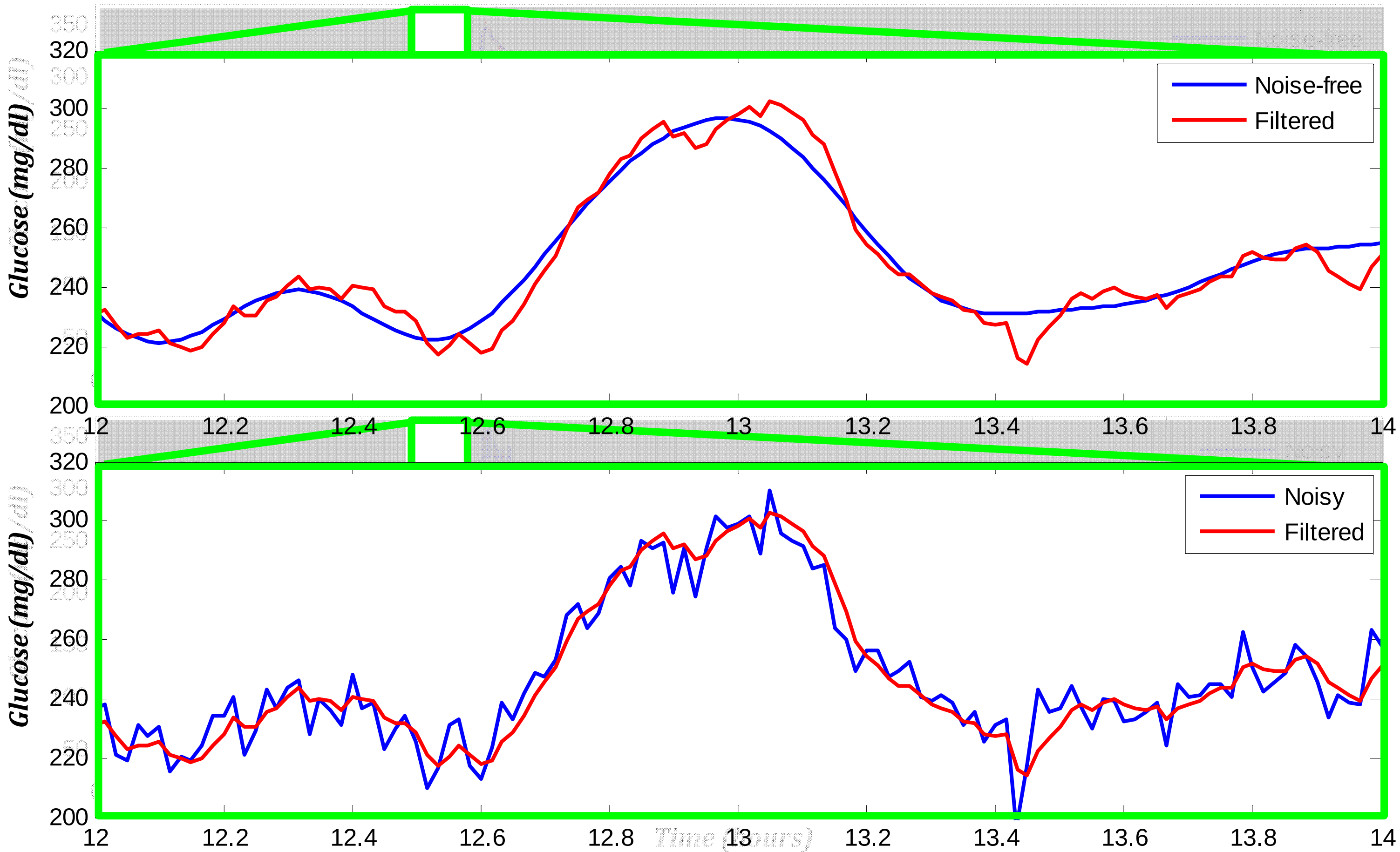


Application on a simulated dataset

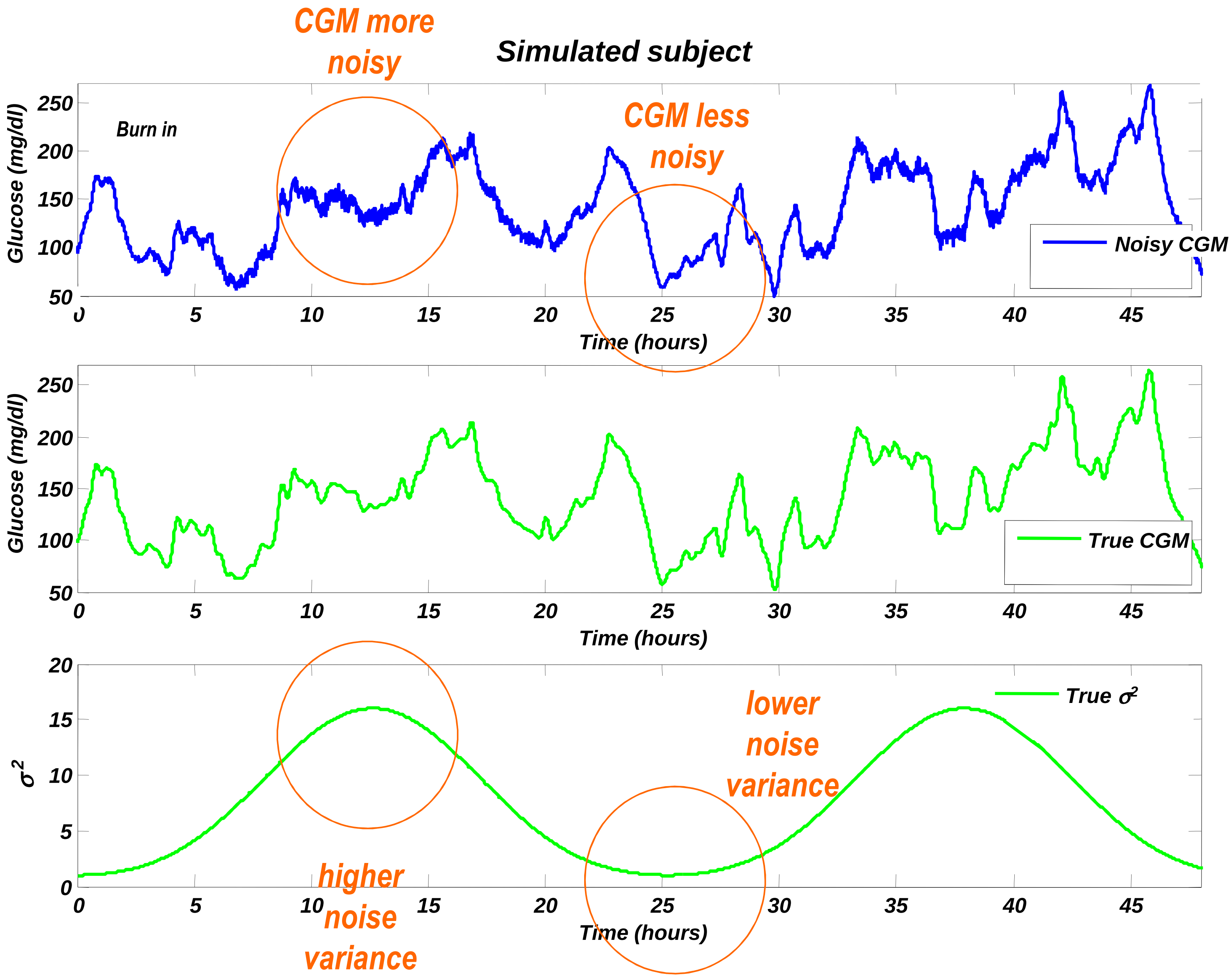


Application on a simulated dataset

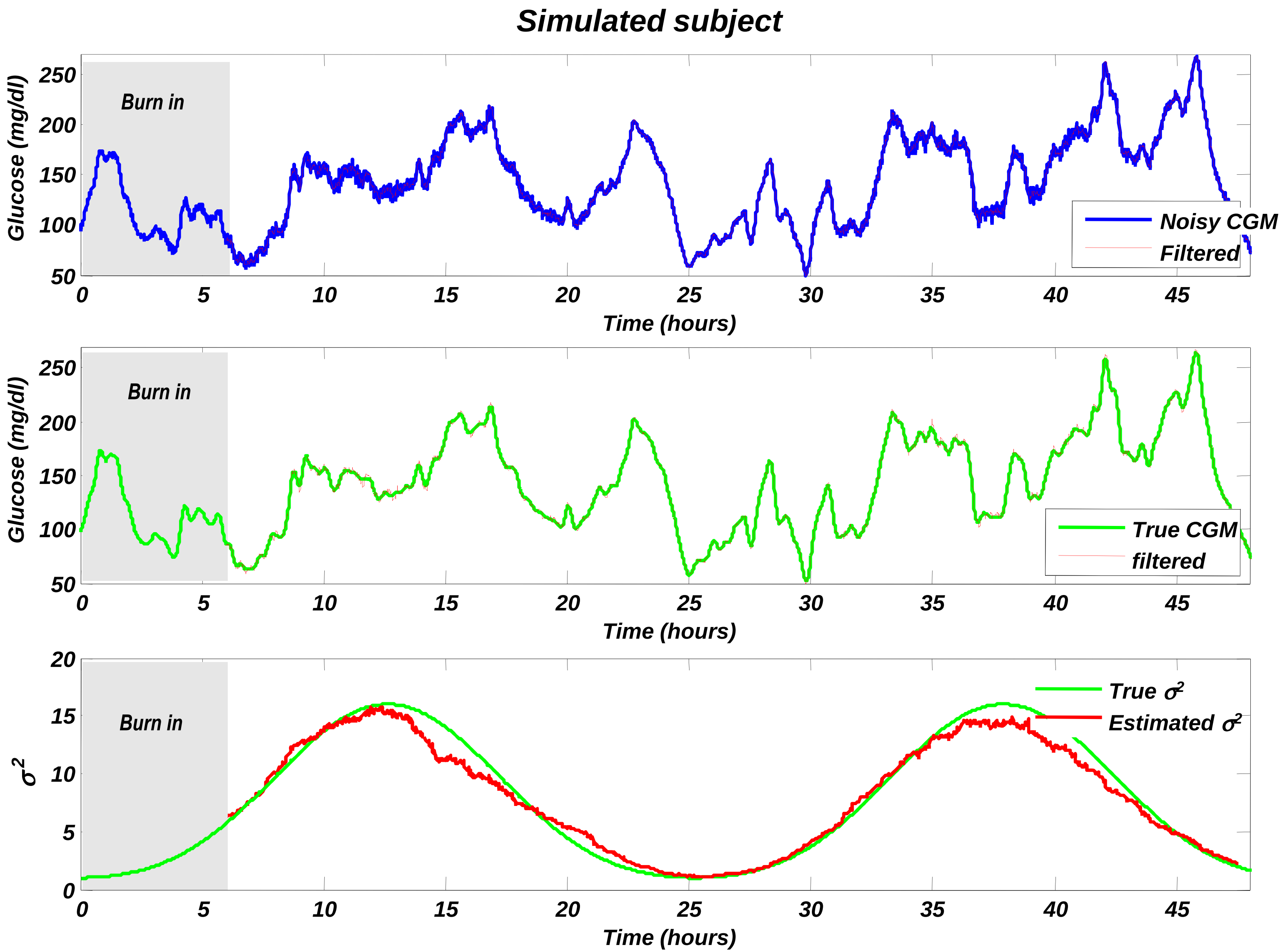
Representative Simulated Subject with $\sigma^2=64mg^2/dl^2$



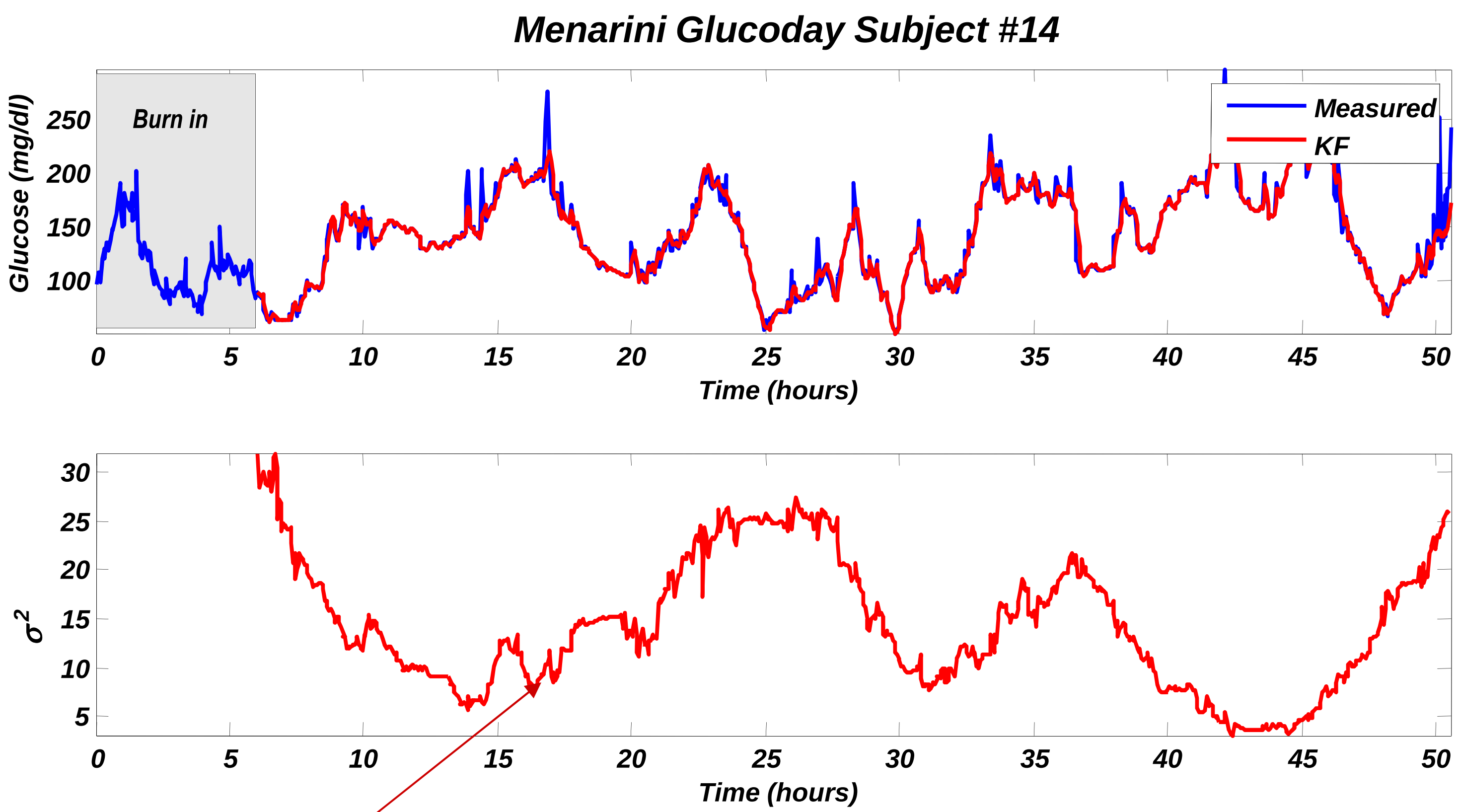
Dealing with intra-individual variability of th



Results: Simulated Data



Results: Real Data

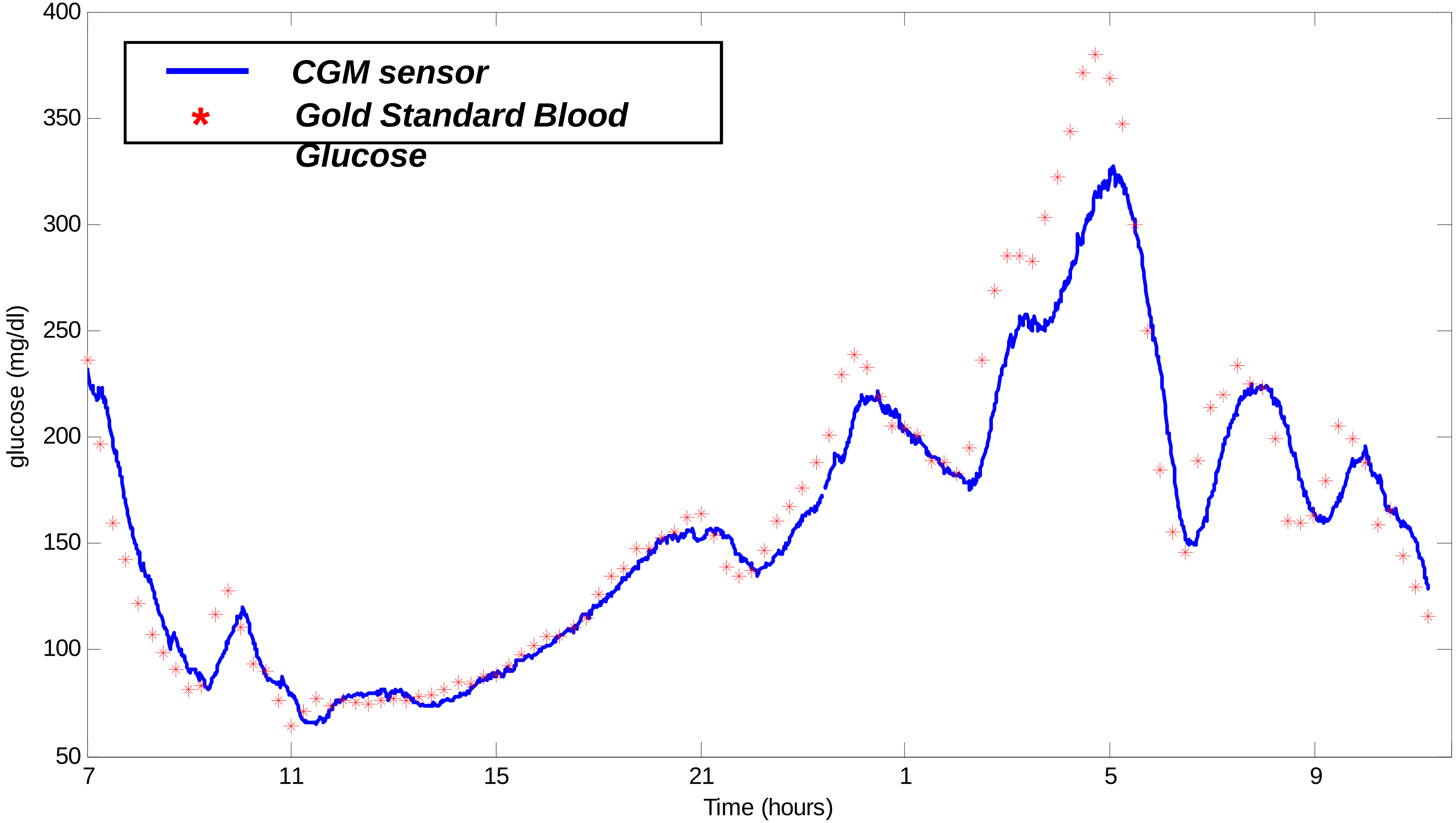


The estimated variance of the noise changes within the monitoring

(Re)-Calibration of CGM time series

Accuracy of CGM data

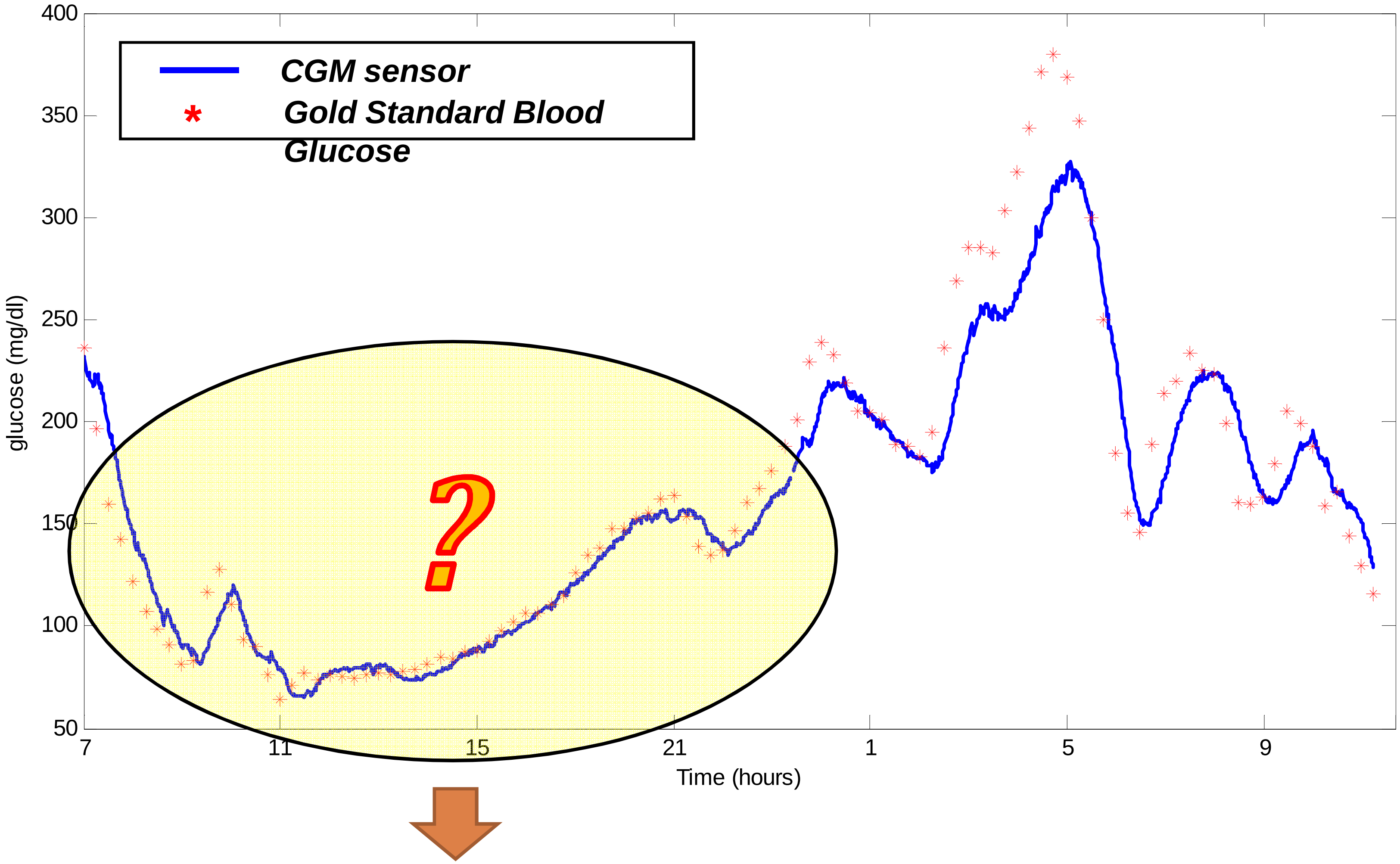
When comparing CGM data to gold standard blood glucose (BG) measurement collected in parallel, lack of accuracy of CGM sensor is visible



Lack of accuracy is:

- ***due to time-varying behavior of the sensor that makes the initial calibration suboptimal***
- ***potentially threatening (missing alert, wrong infromation given in input to the***

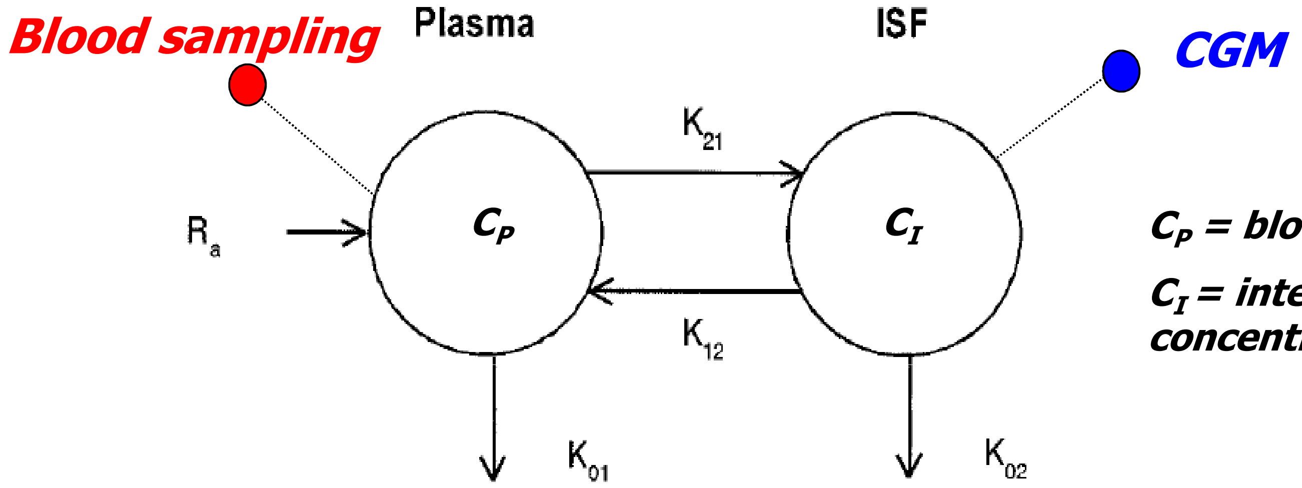
First problem: delay in the measurements



Delay of some minutes

Blood to interstitial fluid glucose physiology

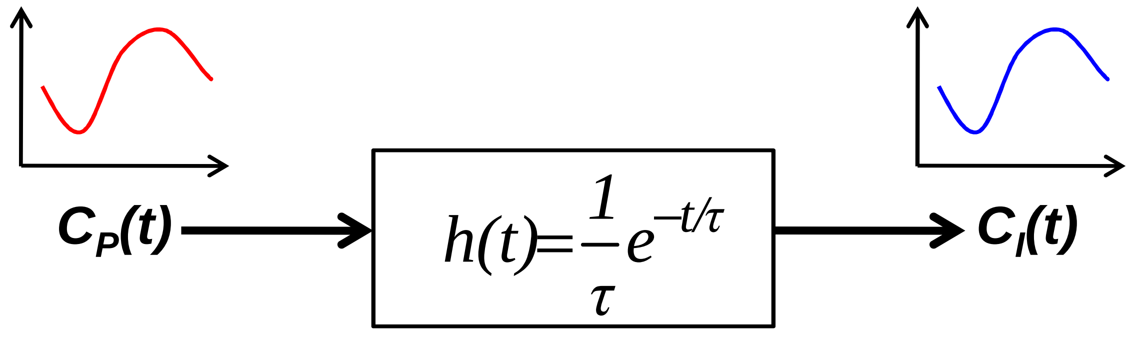
These two signals are measured in different sites → a dynamic system is present and we need to model it



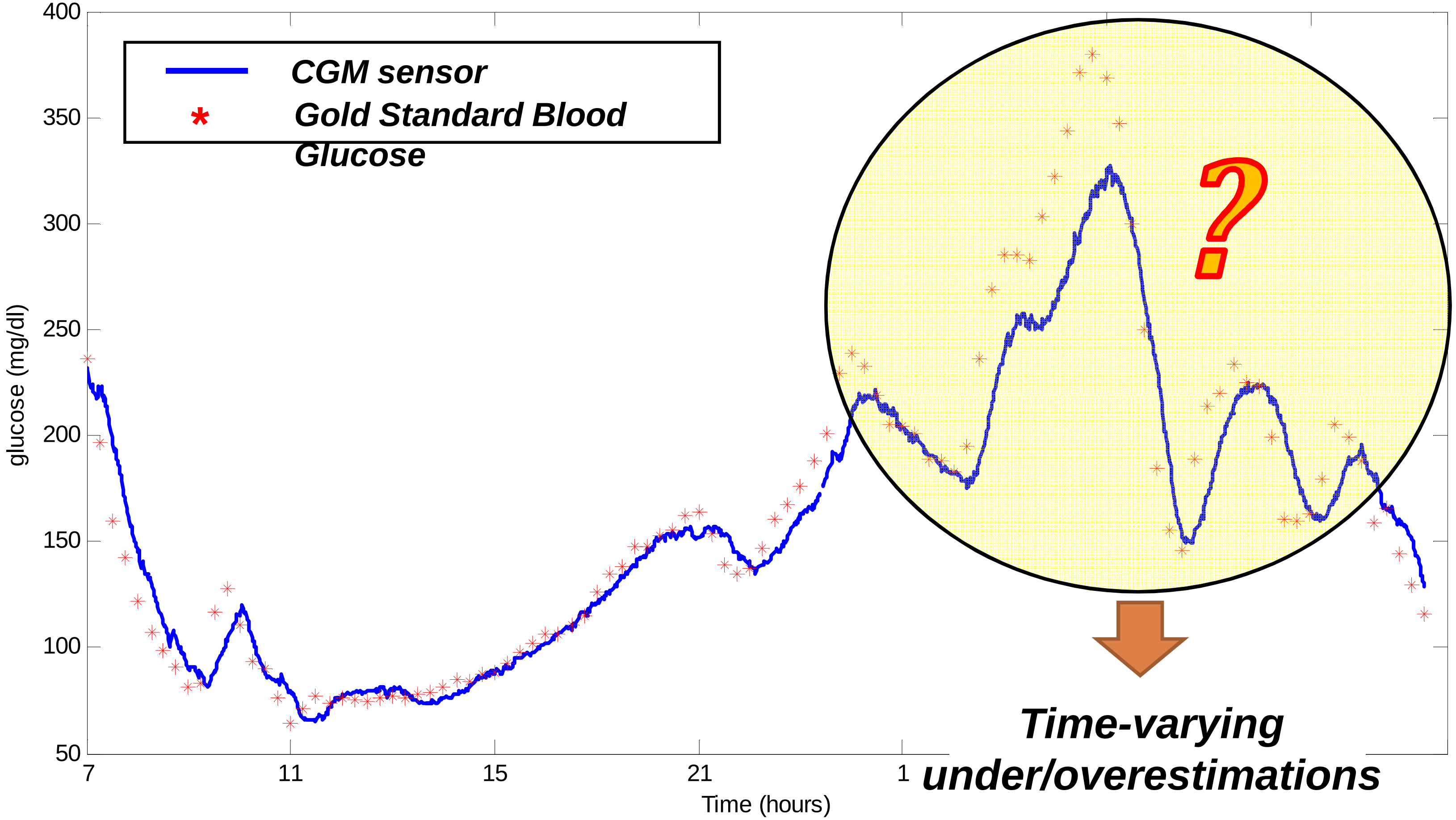
C_P = blood glucose concentration

C_I = interstitial glucose concentration

The impulse response of the system is equivalent to the action of a low-pass filter

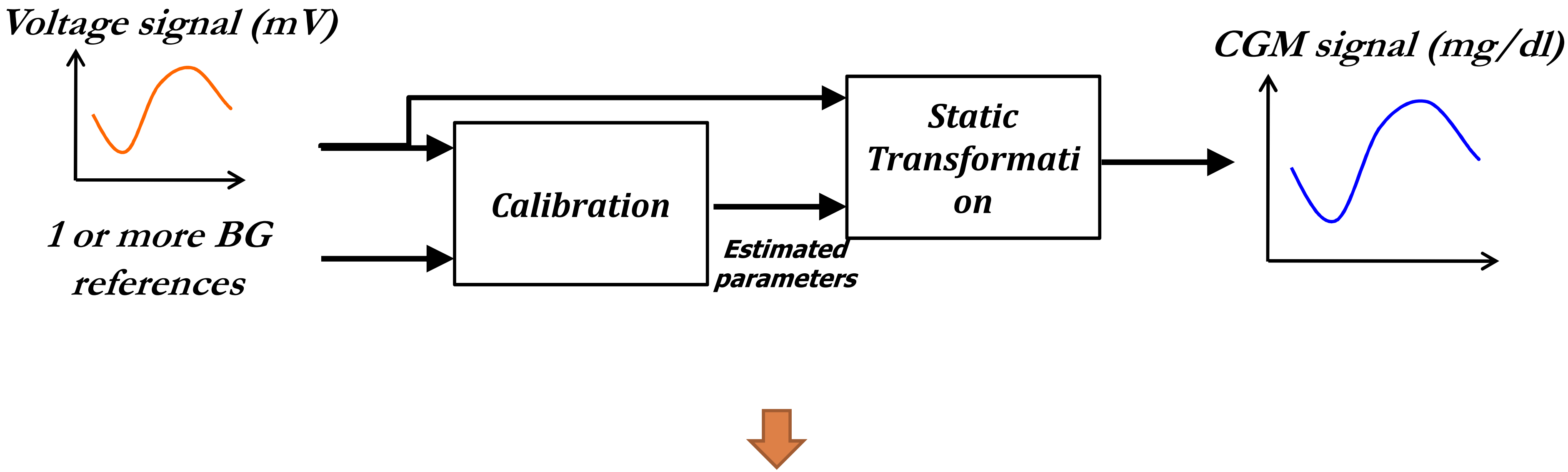


Second problem: under/overestimations



Calibration process

Calibration is the process of estimating the parameters of the static transformation that converts the electrical quantity to a glucose concentration level:



The most used static transformation is linear regression:

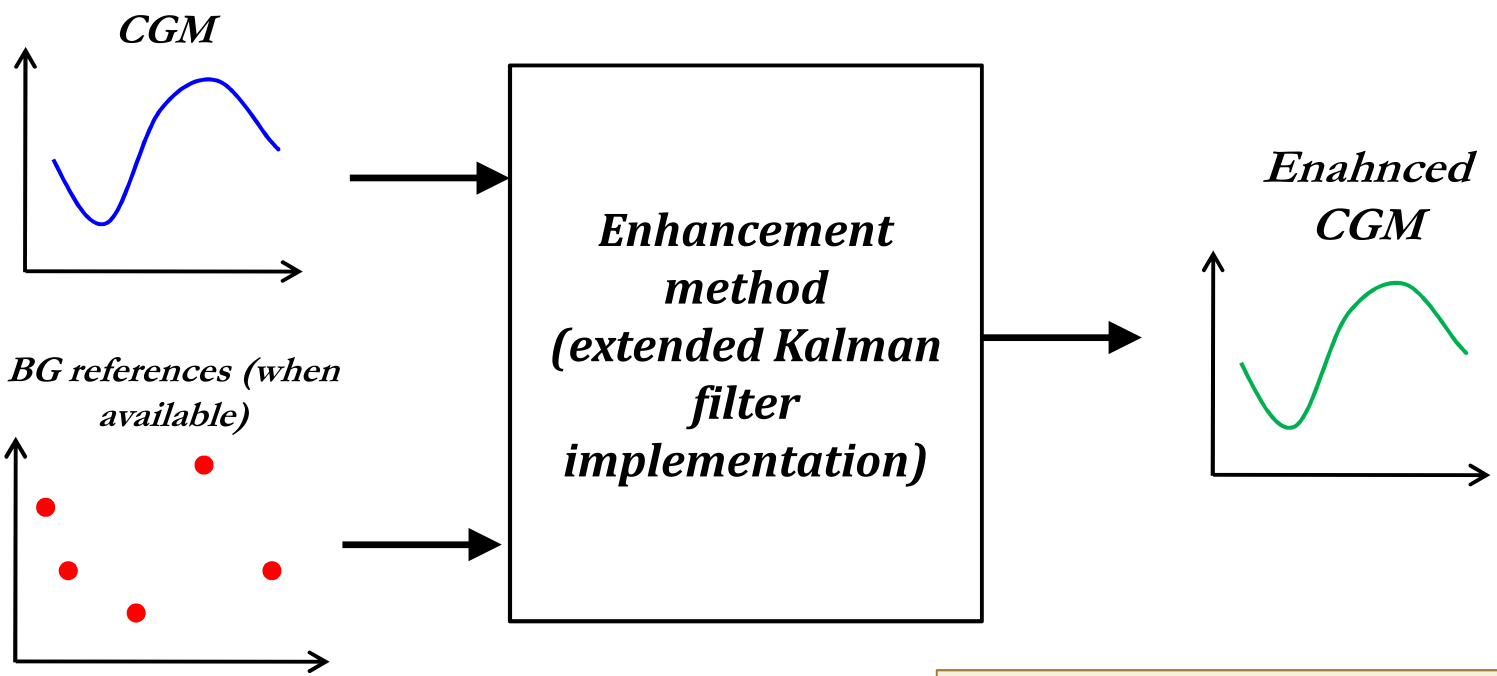
$$CGM(t) = a * current(t) + b$$

The parameter set (a,b) is estimated when at least 2 BG reference data are available

The enhancement method

IDEA: ***to develop an enhancement algorithm to recalibrate CGM data in real time in order to reduce discrepancies***

HOW? ***Every time a BG data is available, calculate the discrepancy and compensate for it***



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Models of the variables

$x_1(t) = C_P(t)$ → since the BG signal is regular, as already done in the denoising procedure, we can use an integrated random walk model:

$$\begin{bmatrix} x_1(t+1) \\ x_2(t+1) \end{bmatrix} = \begin{bmatrix} 2x_1(t) - x_2(t) + w_1(t) \\ x_1(t) \end{bmatrix}$$

$x_3(t) = C_I(t)$ → we can exploit the plasma-to-interstitial fluid kinetics model:

$$\dot{C}_I(t) = -\frac{1}{\tau(t)} C_I(t) + \frac{1}{\tau(t)} C_P(t) \quad \longrightarrow \quad x_3(t+1) = \left(1 - \frac{1}{\tau(t)}\right) x_3(t) + \frac{1}{\tau(t)} x_1(t)$$

$x_4(t) = \tau(t)$: → no information is available, thus we employ a random walk model:

$$x_4(t+1) = x_4(t) + w_4(t)$$

Measurement equations

$$y_1(t) = a(t)C_I(t) + b(t) + v_1(t)$$ ← **CGM value**

$$y_2(t) = C_P(t) + v_2(t)$$ ← **BG value**

C_I and C_P already described, we set $x_5(t) = a(t)$ and $x_6(t) = b(t)$, and we assume for both a random walk model:

$$x_5(t+1) = x_5(t) + w_5(t)$$
$$x_6(t+1) = x_6(t) + w_6(t)$$

Obtaining:

$$y_1(t) = x_5(t)x_3(t) + x_6(t) + v_1(t)$$
$$y_2(t) = x_1(t) + v_2(t)$$

State space model

- $x_1(t) = C_P(t)$ (blood glucose) — Integrated random walk
- $x_2(t)$ = additional variable — Integrated random walk
- $x_3(t) = C_I(t)$ (Interstitial glucose) — Differential equation from physiology
- $x_4(t) = \tau(t)$ — Random Walk
- $x_5(t) = a(t)$ — Random Walk
- $x_6(t) = b(t)$ — Random Walk

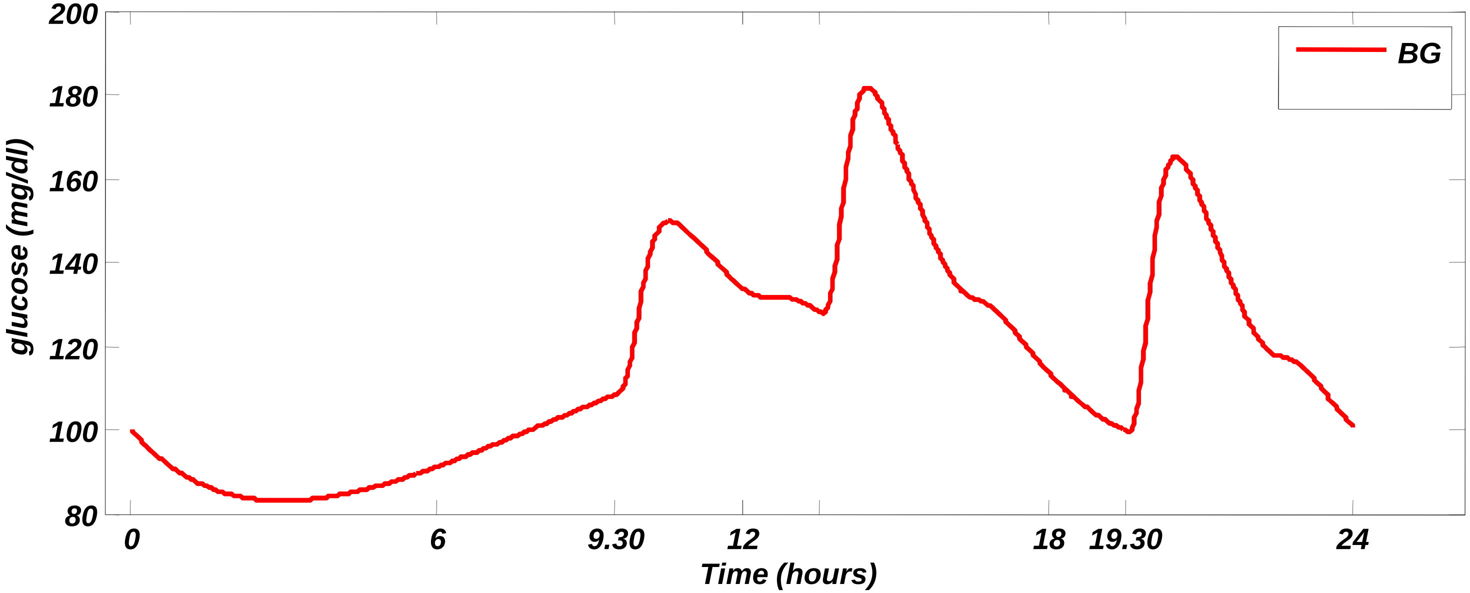
$$\begin{bmatrix} x_1(t+1) \\ x_2(t+1) \\ x_3(t+1) \\ x_4(t+1) \\ x_5(t+1) \\ x_6(t+1) \end{bmatrix} = \begin{bmatrix} 2x_1(t) - x_2(t) + w_1(t) \\ x_1(t) \\ (1 - 1/x_4(t))x_3(t) + (1/x_4(t))x_1(t) \\ x_4(t) + w_4(t) \\ x_5(t) + w_5(t) \\ x_6(t) + w_6(t) \end{bmatrix}$$

$$\begin{bmatrix} y_1(t) \\ y_2(t) \end{bmatrix} = \begin{bmatrix} x_5(t)x_3(t) + x_6(t) + v_1(t) \\ x_1(t) + v_2(t) \end{bmatrix}$$

Some equations are nonlinear in the variables $\Rightarrow$ Extended Kalman filter implementation

A simulation study to assess the EKF method

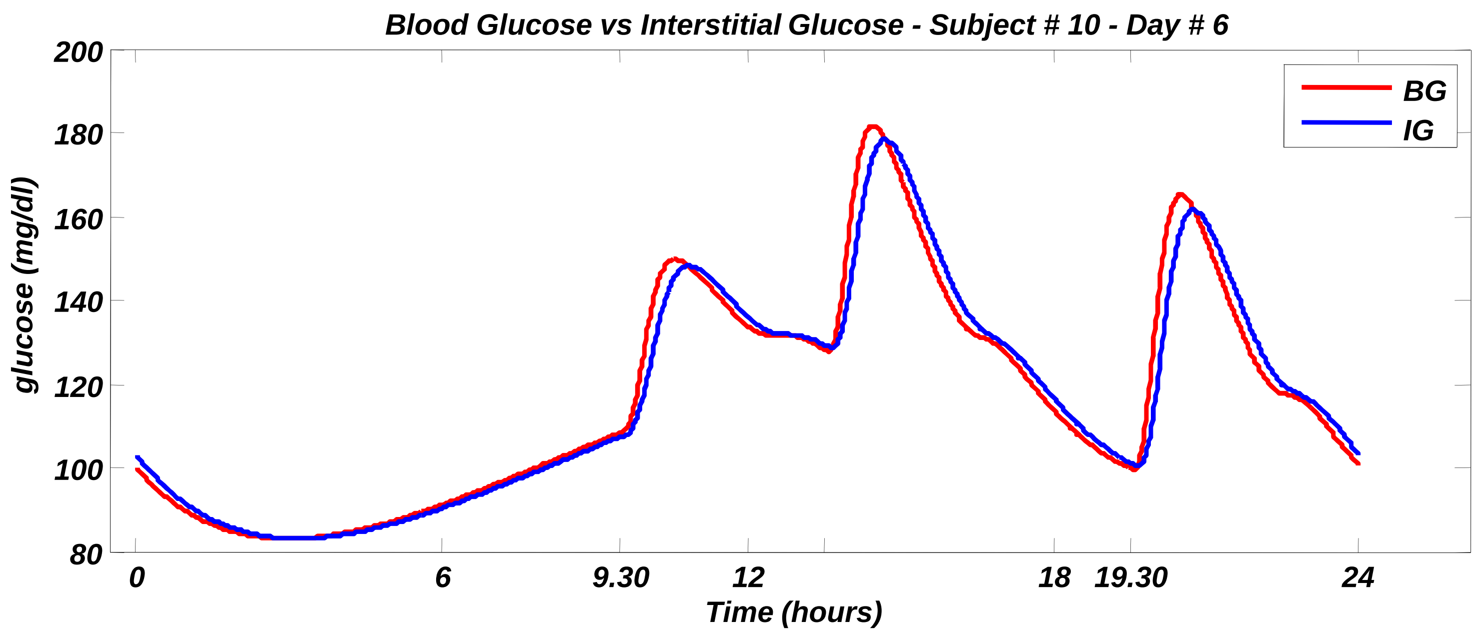
Step 1: A plasma glucose profile, BG(t), is created by the in silico simulator of (Dalla Man et al, 2007)



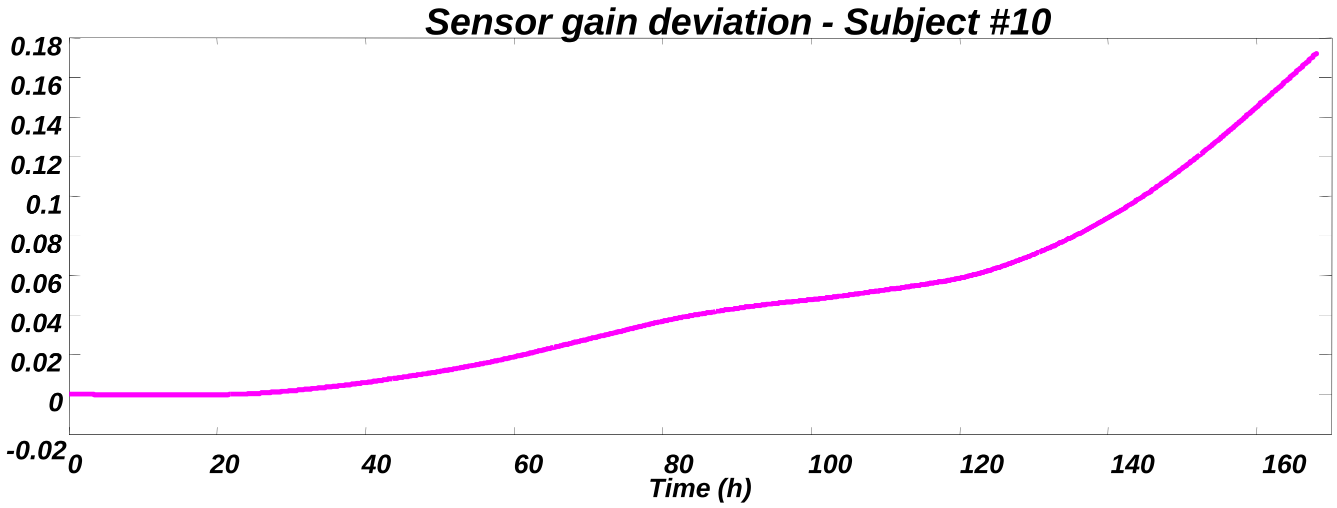
A simulation study to assess the EKF method

Step 1: A plasma glucose profile, BG(t), is created by the in silico simulator of (Dalla Man et al, 2007)

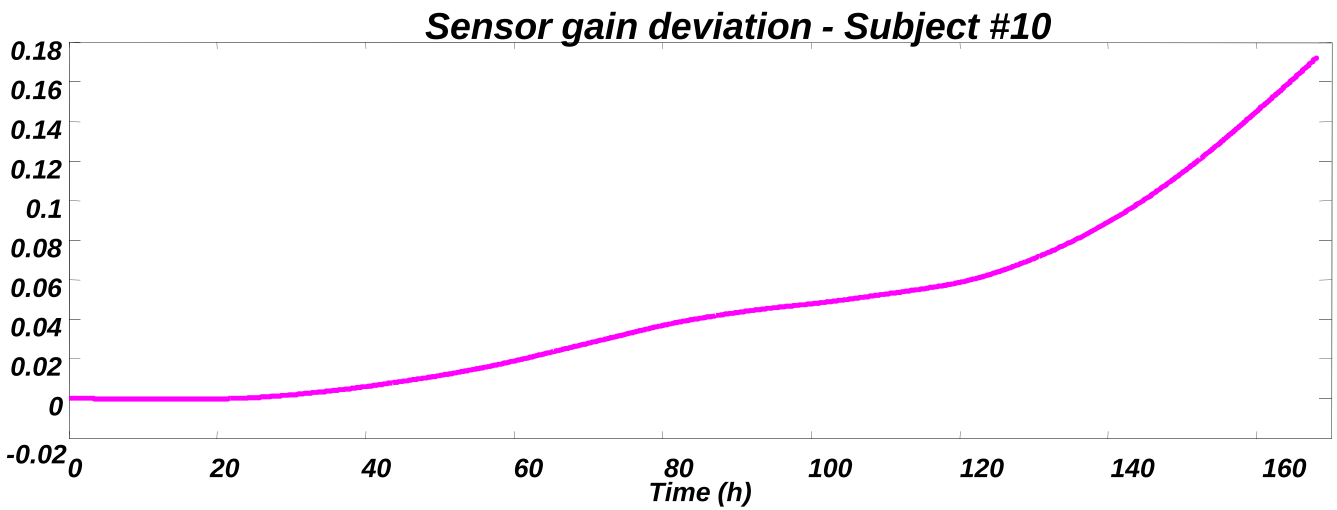
Step 2: Continuous-time interstitial glucose, IG(t) is obtained through the blood-to-interstitial fluid bicompartmental model



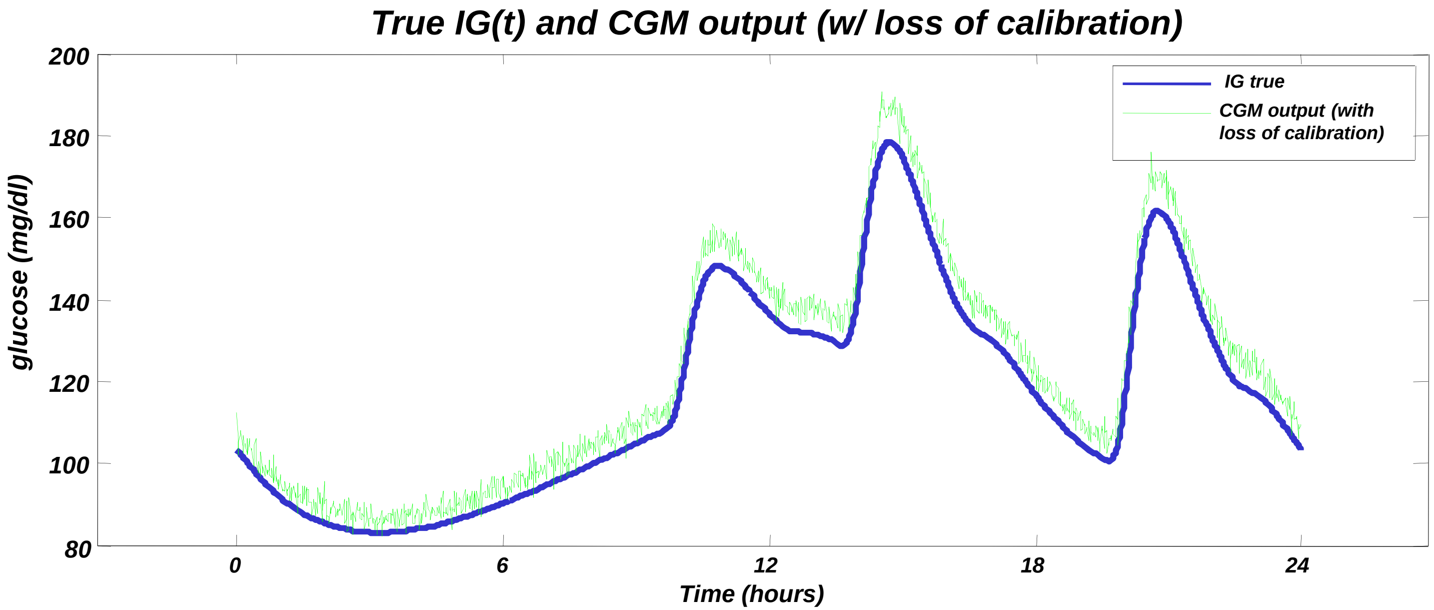
Step 3: A time-varying sensor gain error is simulated in order to describe loss of calibration



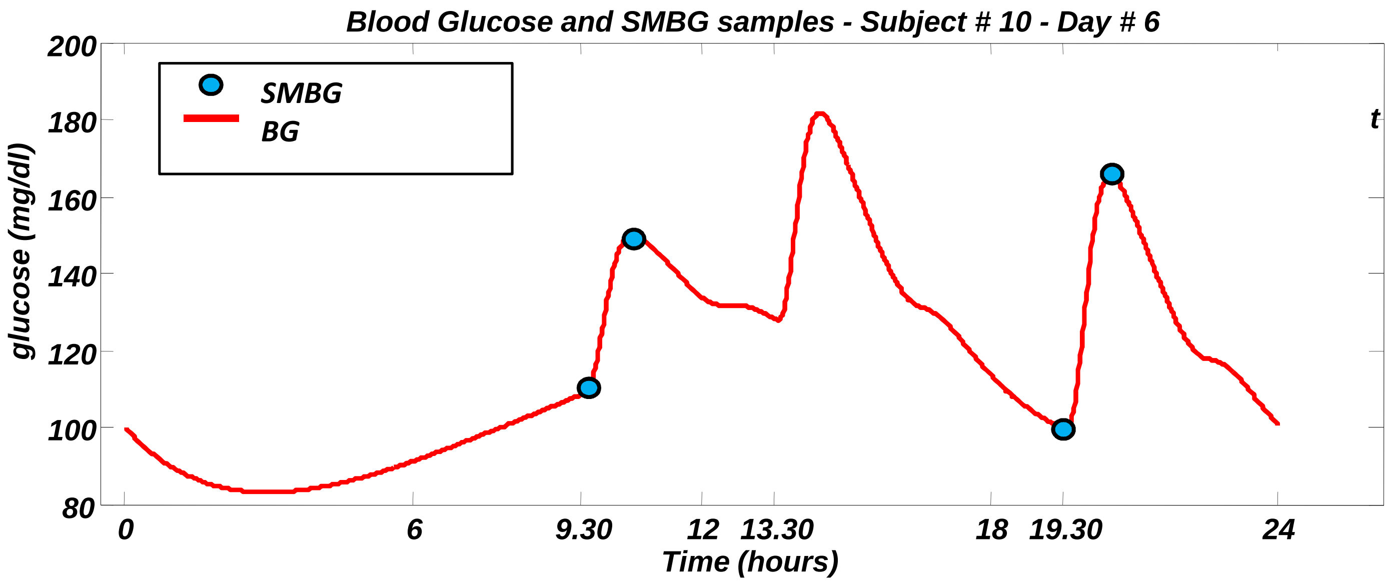
Step 3: A time-varying sensor gain error is simulated in order to describe loss of calibration



and random noise is also added to CGM data

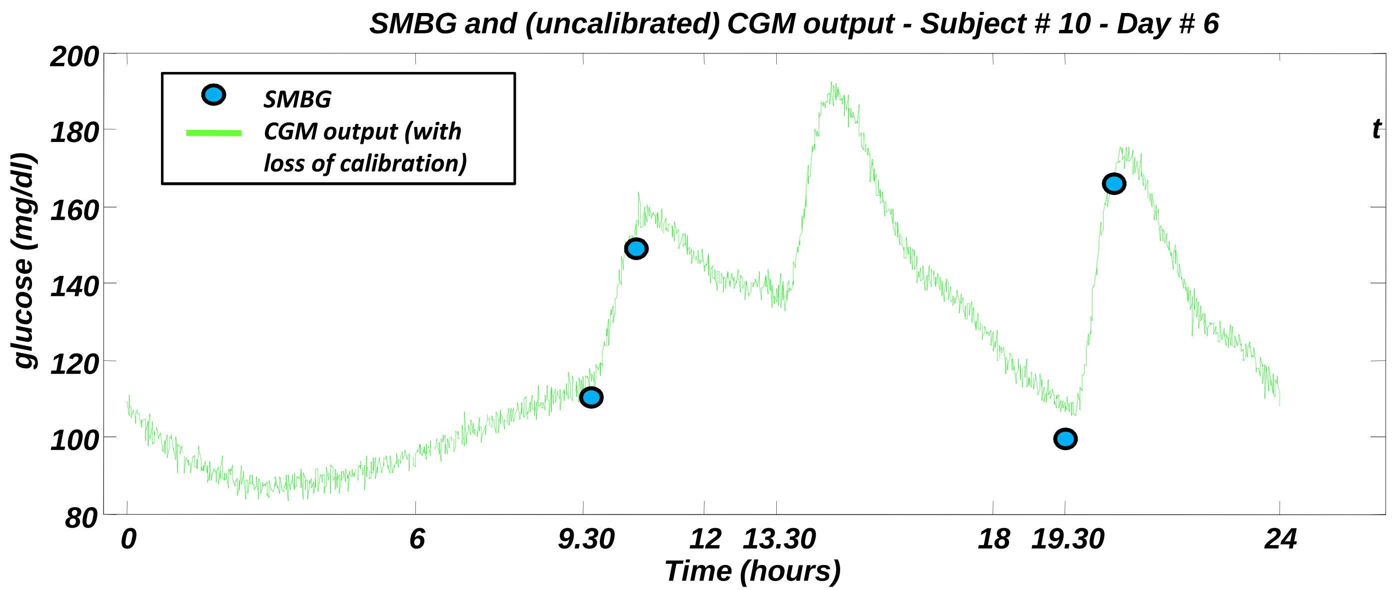


Step 5: 4 noisy BG samples per day are considered in order to simulate SM



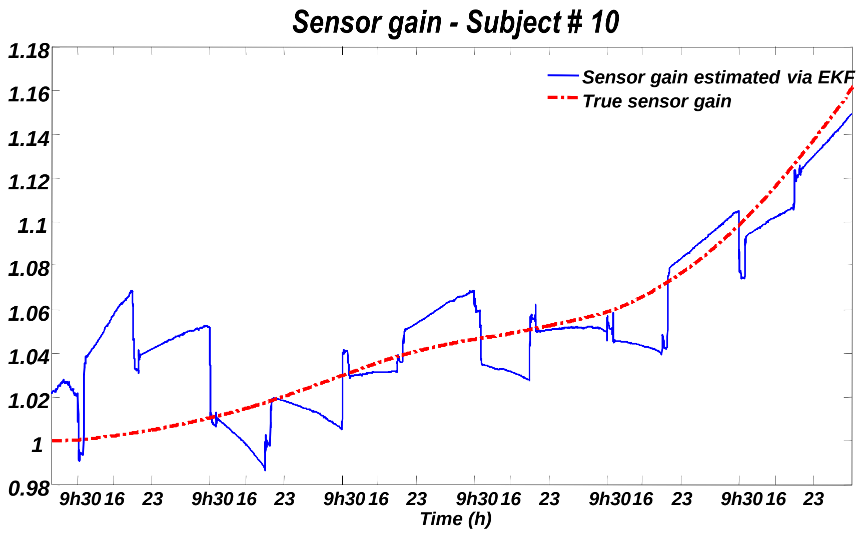
Step 6: Problem definition

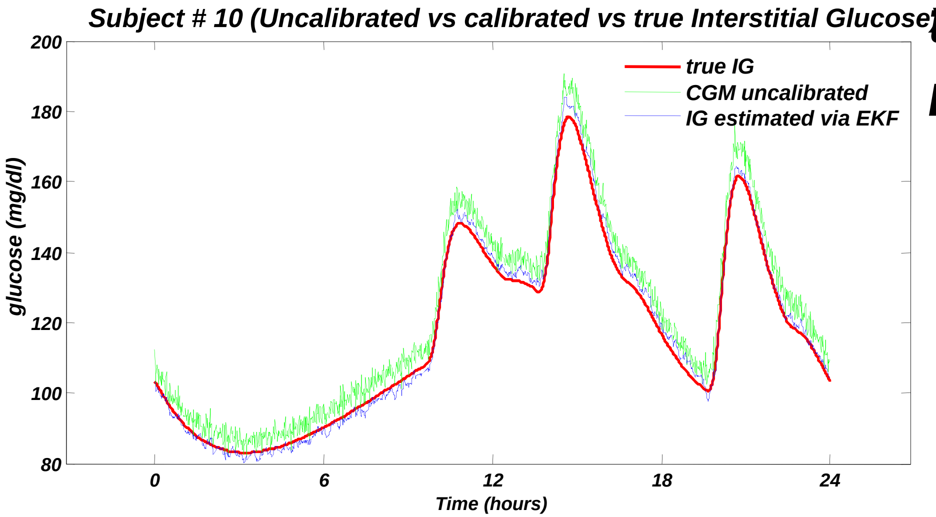
***Goal*: from the uncalibrated CGM signal and 4 SMBG samples per day .**



… the aim is to reconstruct the true IG(t)

Results (in ideal conditions): reconstruction of Sensor Gain and IG by EKF





The algorithm (via EKF) is able:

•to correctly track **the trend** in the variations of the sensor gain;

•to provide an accurate **recalibrated profile** IG(t) (significantly improves the performance of standard methods)

Assumption: a perfect model of plasma-interstitium kinetics is available (exploited within the EKF)

Comments on the EKF method

- ***Good results in simulation***
- ***On real data, setting the values of unknown covariance matrices is not trivial***
- ***We developed an hybrid approch to overcome the problem***

A 4-step recalibration algorithm

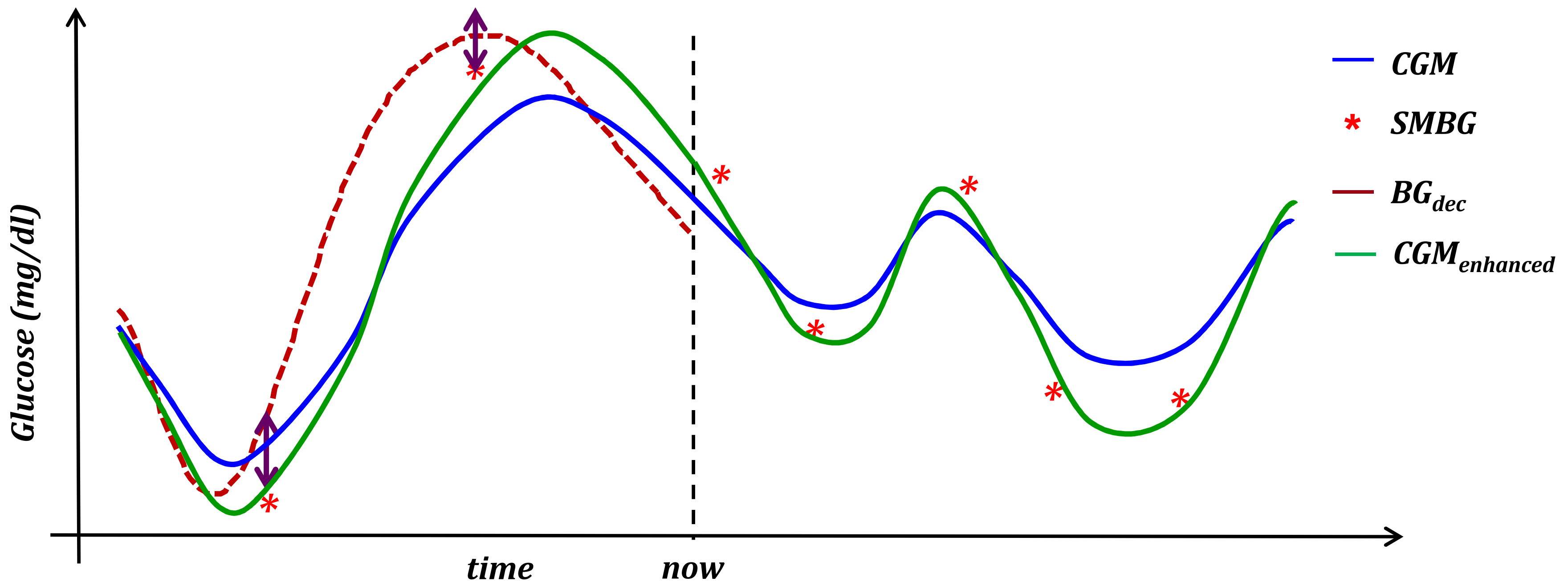
When 2 suitable fingerstick measures (SMBGs) are available:

1) ***Selection of a portion of CGM***
2) ***Reconstruction of BG concentration (BG_{dec}) via nonparametric deconvolution using a 2-compartment model of BG-to-IG kinetics***
3) ***Estimation of regression parameters of the static transformation:***

$$SMBG(t) = a\, BG_{dec}(t) + b$$

4) ***Application of the regressor:***

$$CGM_{enhanced}(t) = a\, CGM(t) + b$$



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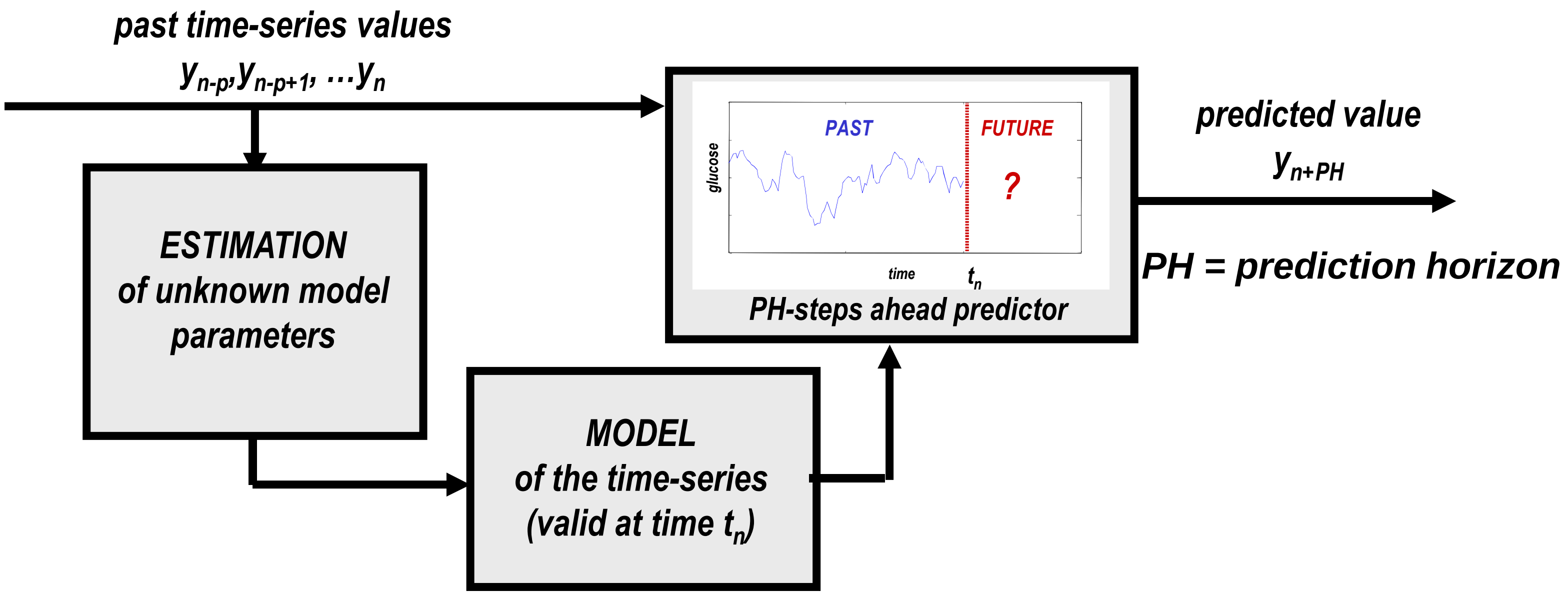
Glucose Prediction from CGM data

Prediction Algorithms



Time-varying modeling approach: at any new t, model parameters describing past CGM data are re-adjusted:

model (structure + parameter values) describes the time-series "locally"

$\Rightarrow$ *model complexity kept modest, i.e. a few parameters*

$\Rightarrow$ *model identification fast enough to allow real-time use*

The simplest prediction model

The simplest model, a 1st order polynomial:

$$u(t_i)=mt_i + q$$

At each sampling time t_i:

1) a new pair of model parameters (m, q) are identified by fitting by weighted linear least squares the past signal samples at times t_i, t_{i-1}, t_{i-2}, ….

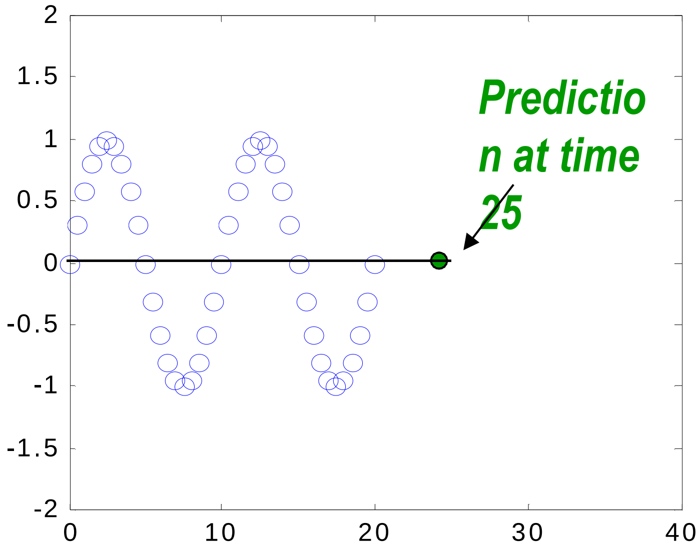
2) the model is used to predict glucose level at time t_i + PH, where PH is a tuneable prediction horizon. PH was 30 and 45 minutes.

Key: how past data are weighted in model fitting

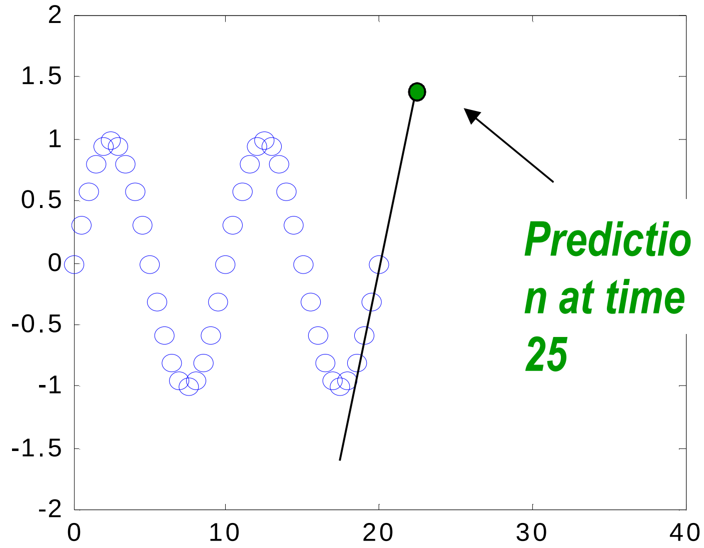
The problem of data weights

Key: *how past data are weighted in model fitting*

EXAMPLE

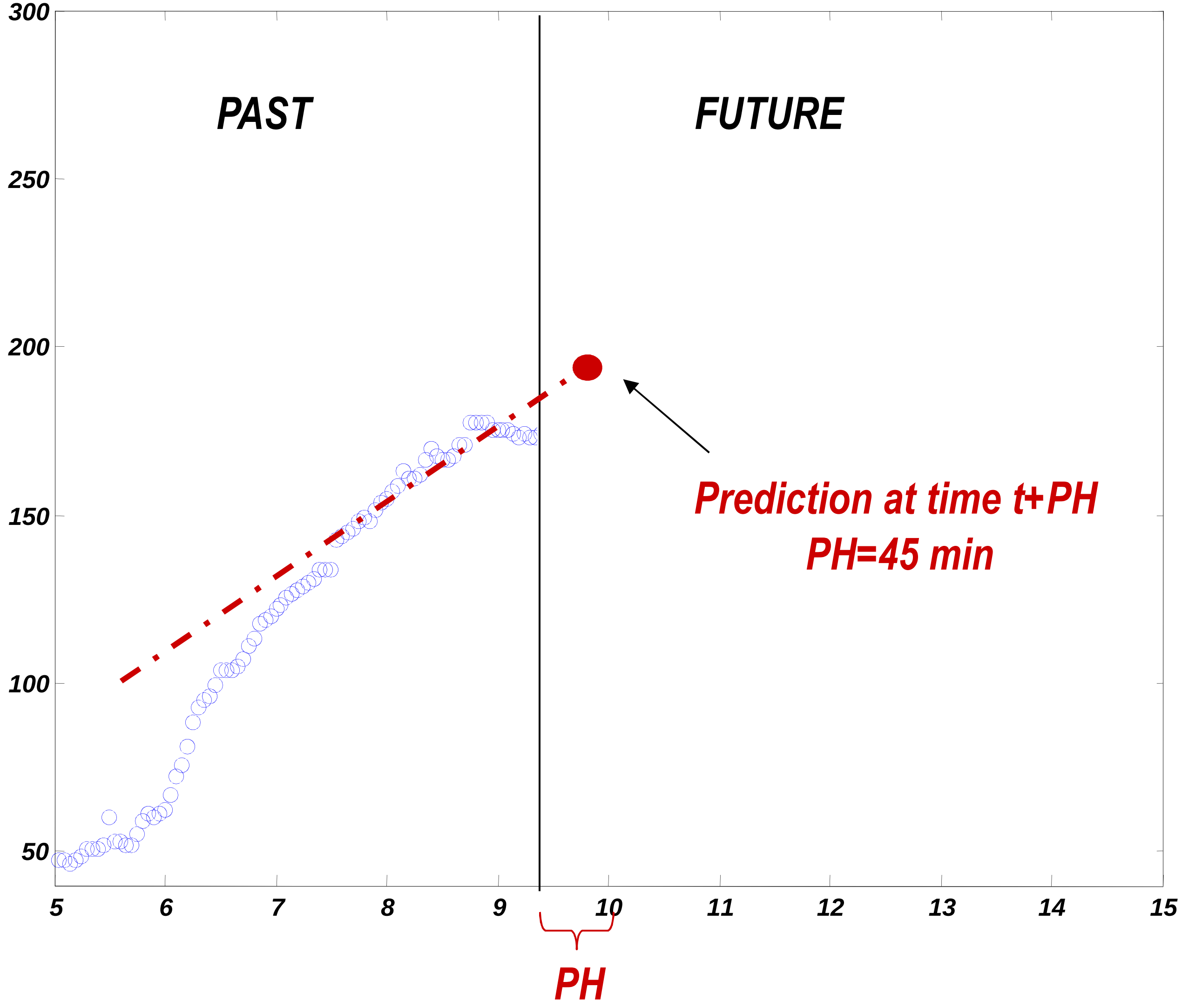


All past data
have same weight



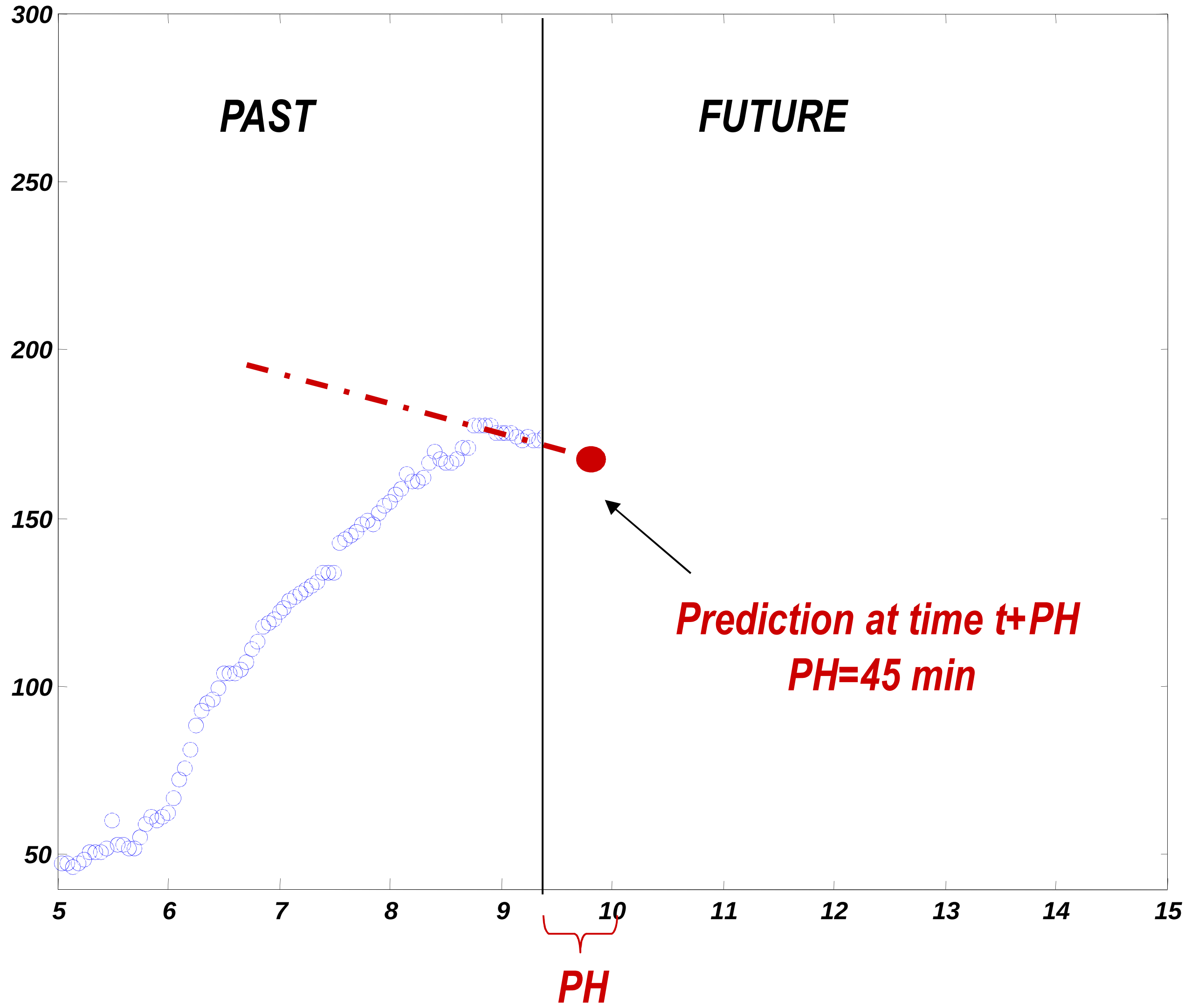
The older the sample, the lower
the weight ($\rightarrow$forgetting factor)

μ "large" (0.95)



Difficult to track changes in the trend $\Rightarrow$ the predicted profile will result consistently delayed

μ “small” (0.2)



Easier to track changes in the trend, but higher sensitivity to noise $\Rightarrow$ irregular prediction profile

Literature prediction strategies

AR/ARMA

- ***Sparacino et al., IEEE Trans Biomed Eng, 2007***
- ***Reifman et al., J Diabetes Sci Technol, 2007***
- ***Eren-Oruklu et al., Diabetes Technol Ther, 2009***
- ***Gani et al., IEEE Trans Biomed Eng, 2009***

Polynomials

- ***Sparacino et al., Diabetes Res Clin Pract, 2006***

State-space model

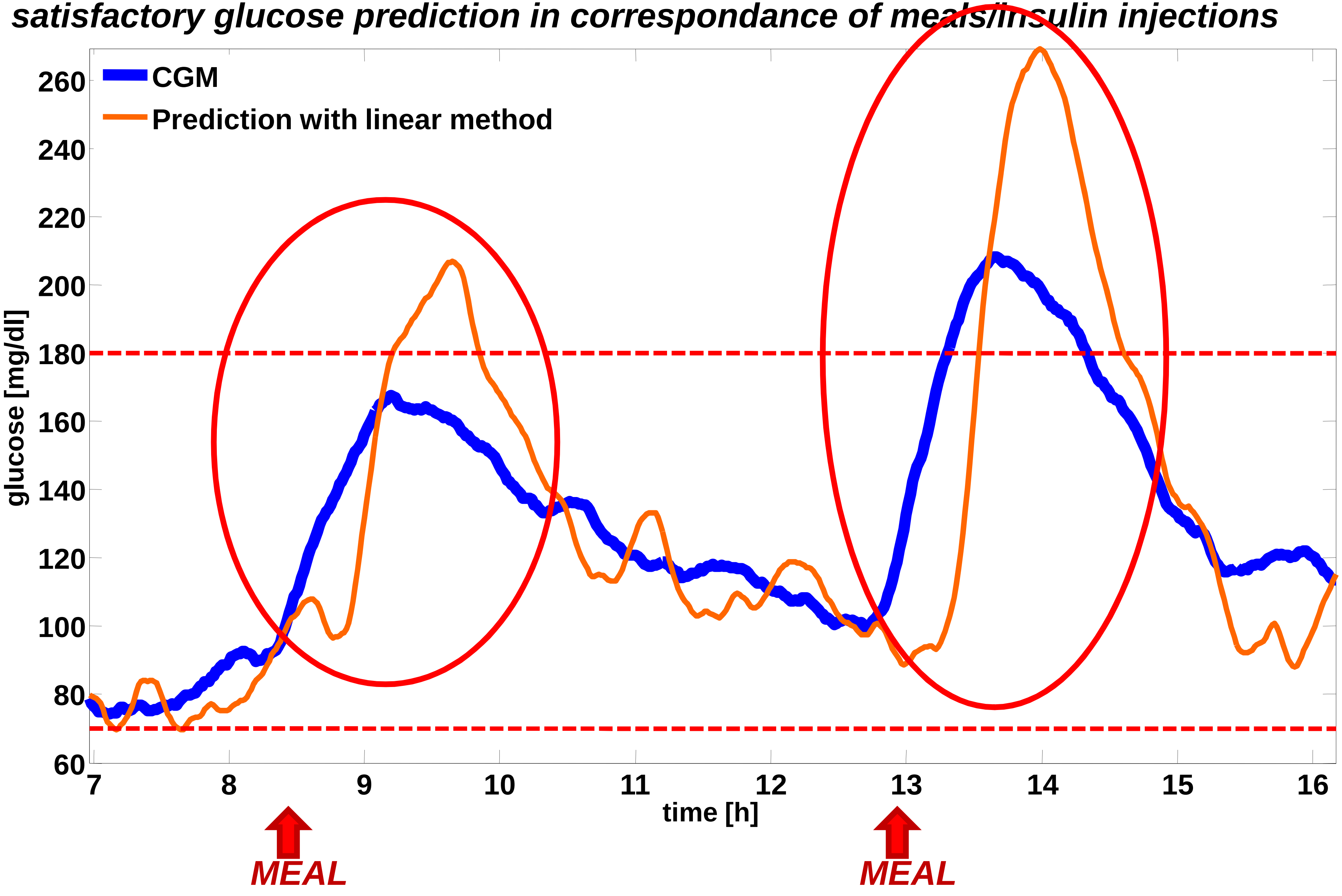
- ***Palerm et al., J Diabetes Sci Technol, 2007***

Neural Networks

- ***Pérez-Gandía et al., Diabetes Technol Ther, 2010***
- ***Pappada et al., Diabetes Technol Ther, 2011***

Literature prediction strategies

Prediction strategies based on CGM past history only are not able to perform a satisfactory glucose prediction in correspondance of meals/insulin injections



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- ***Sparacino et al., Diabetes Res Clin Pract, 2006***

State-space model

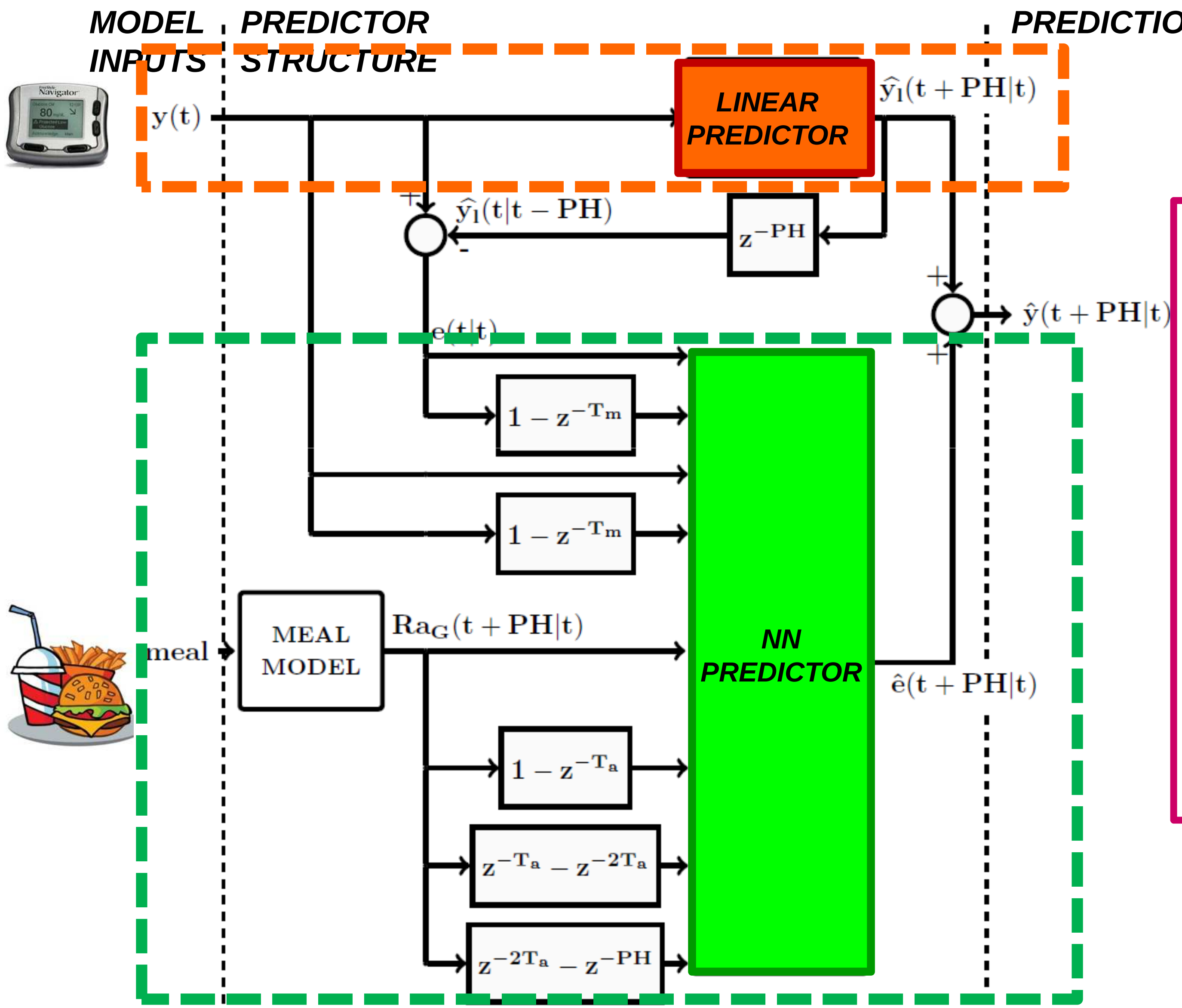
- ***Palerm et al., J Diabetes Sci Technol, 2007***

Neural Networks

- ***Pérez-Gandía et al., Diabetes Technol Ther, 2010***
- ***Pappada et al., Diabetes Technol Ther, 2011***

➡ ***Neural networks allow dealing/incorporating inputs coming from different***

Predictor structure



To better exploit NN capability of modeling nonlinearities, the NN works in parallel with a time-varying linear predictor

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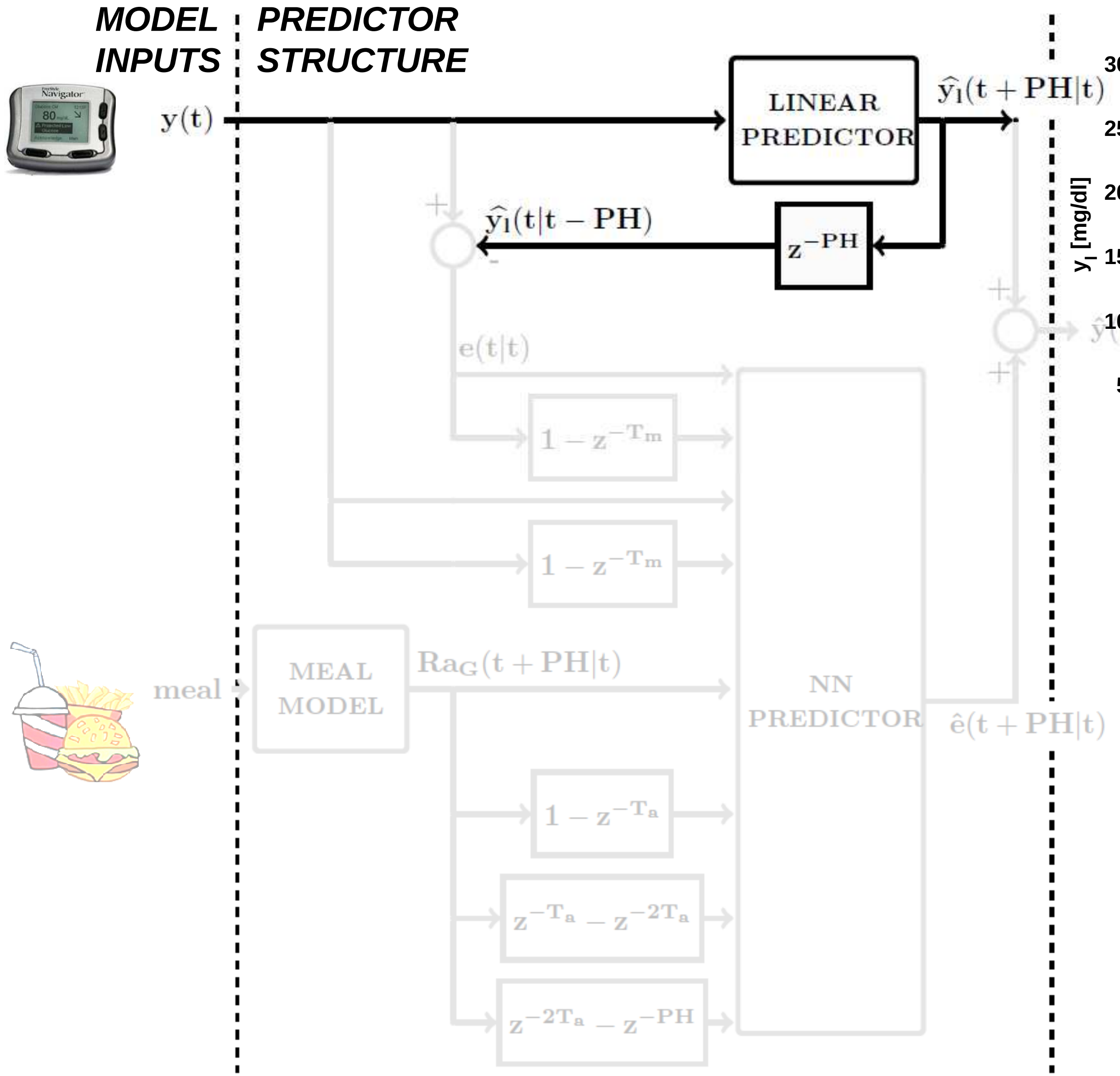
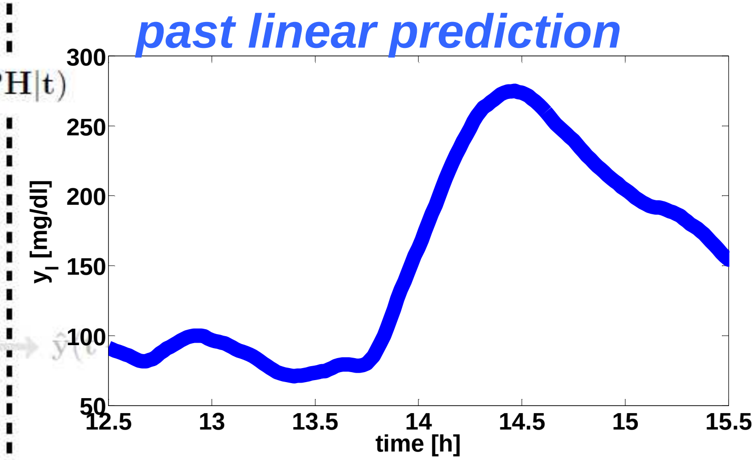
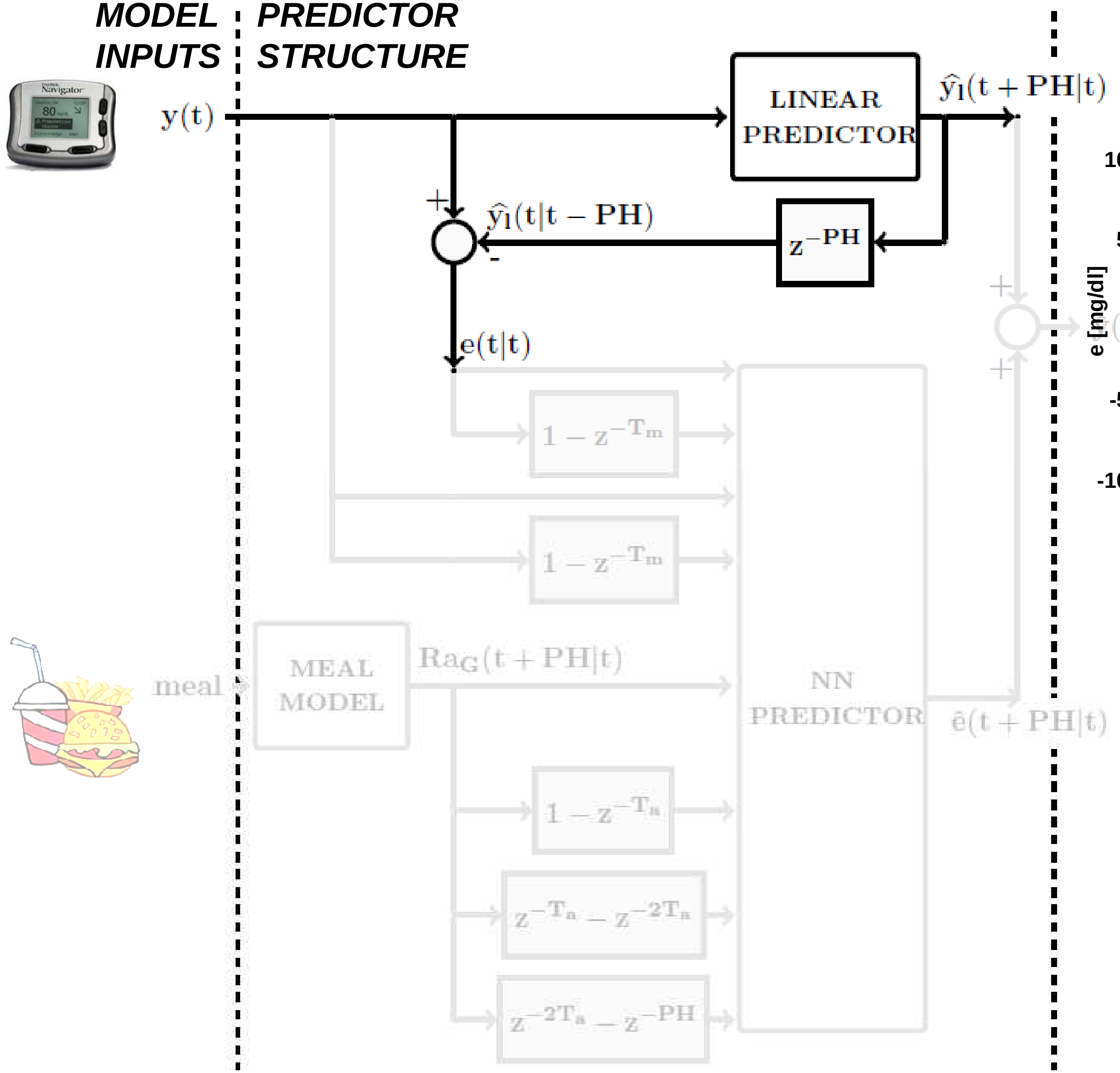
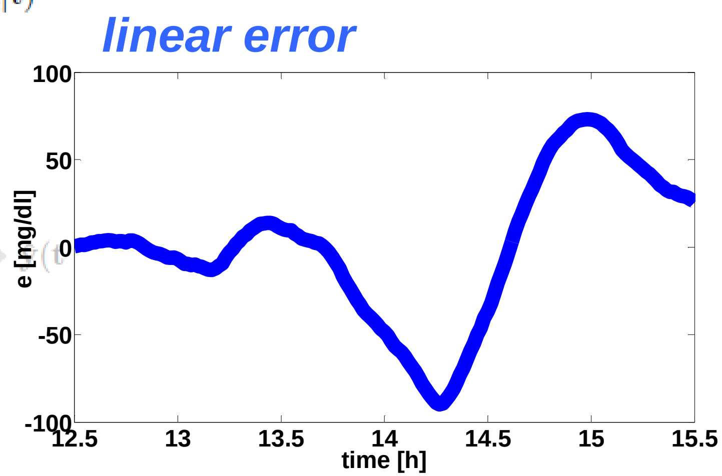
Predictor structure



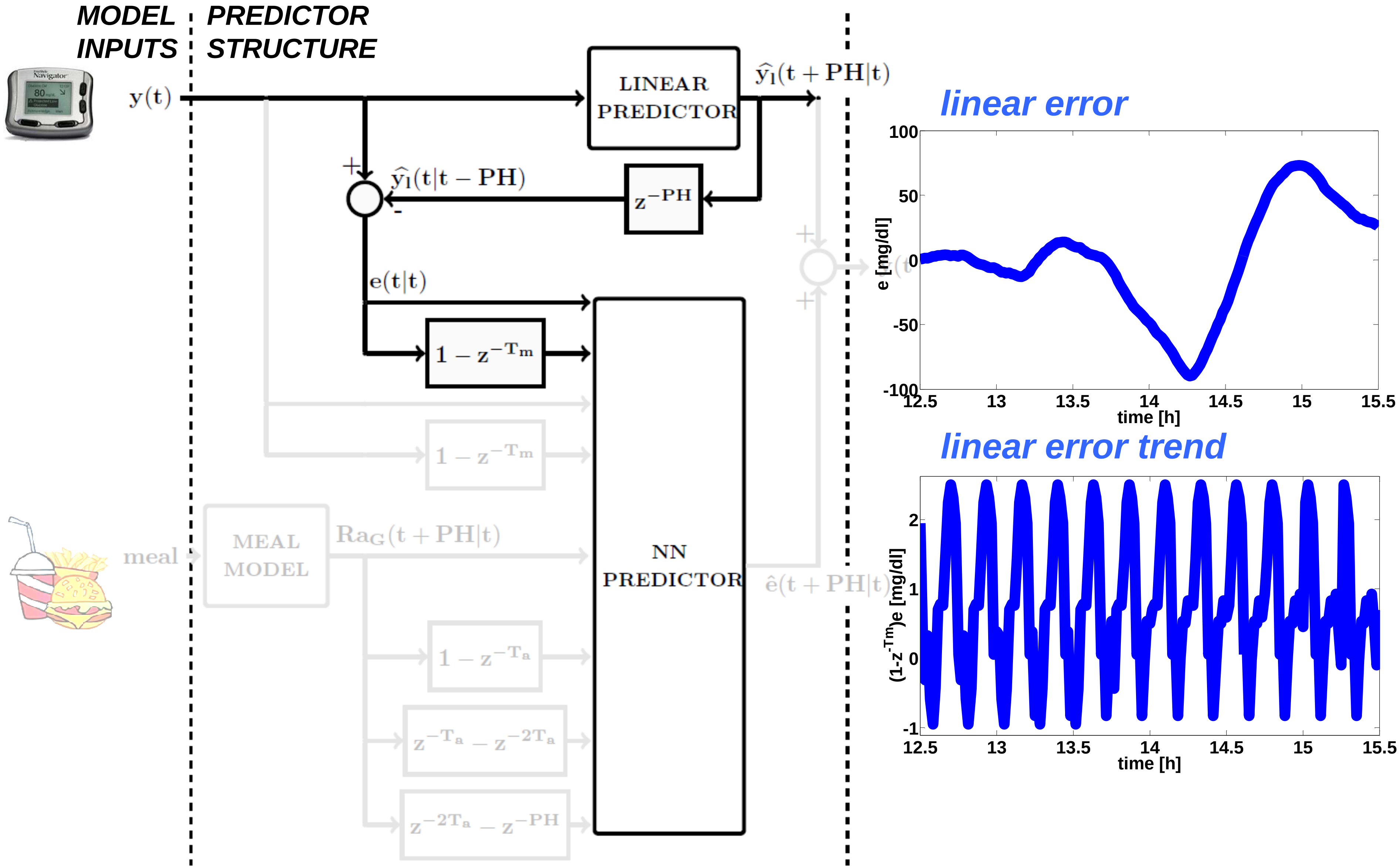


Predictor structure

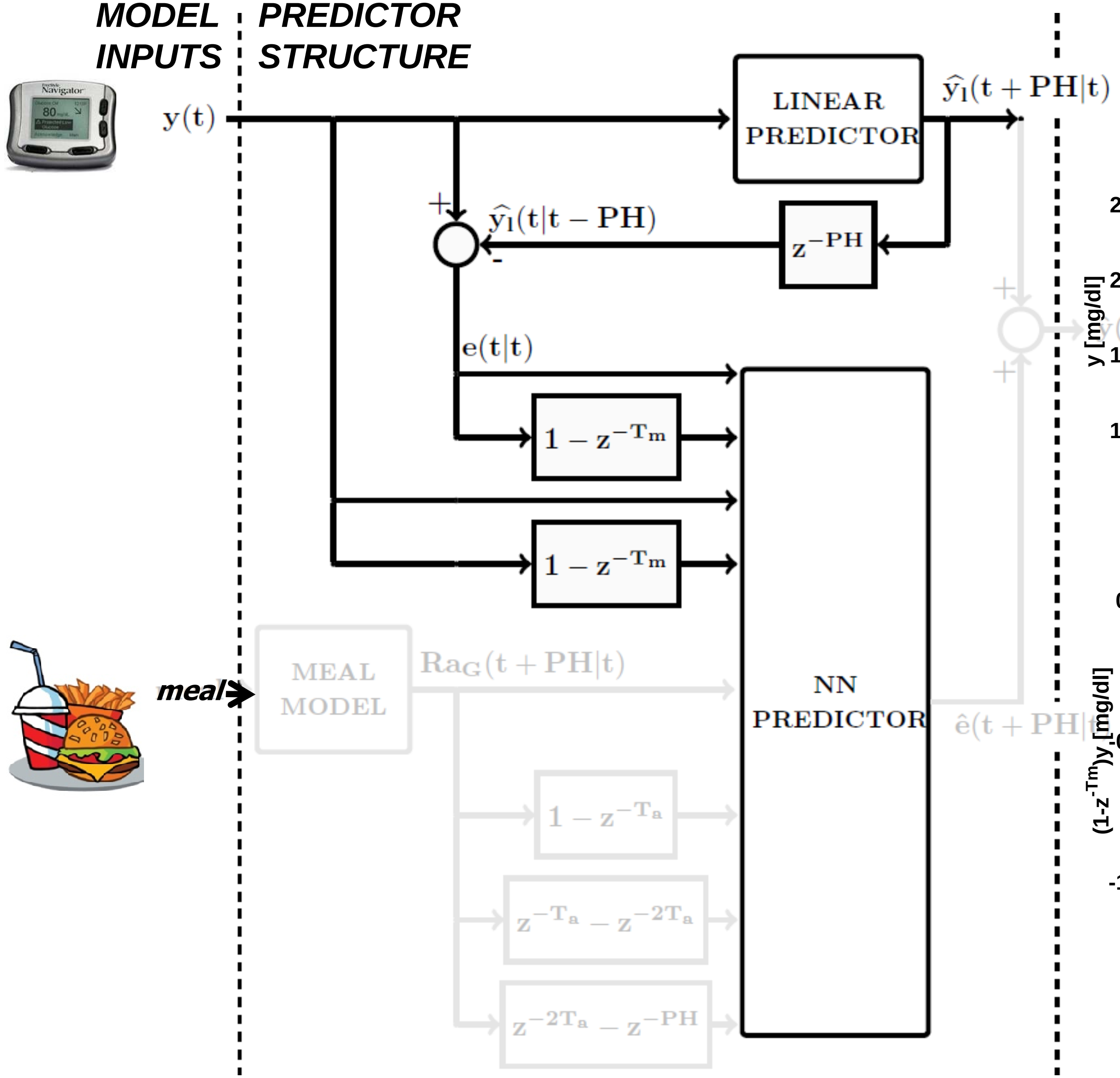


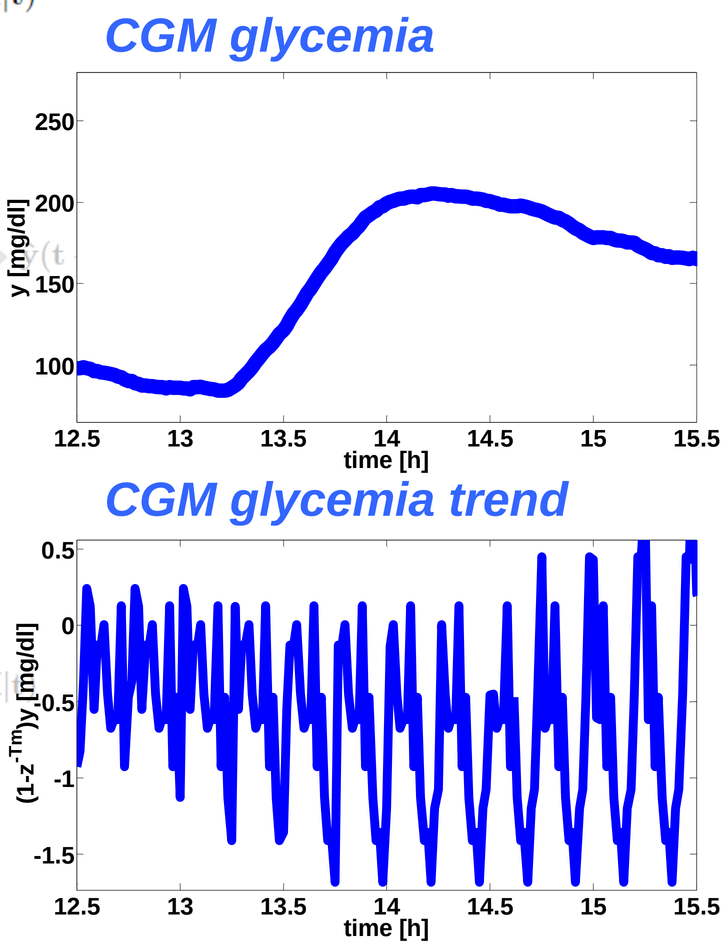


Predictor structure

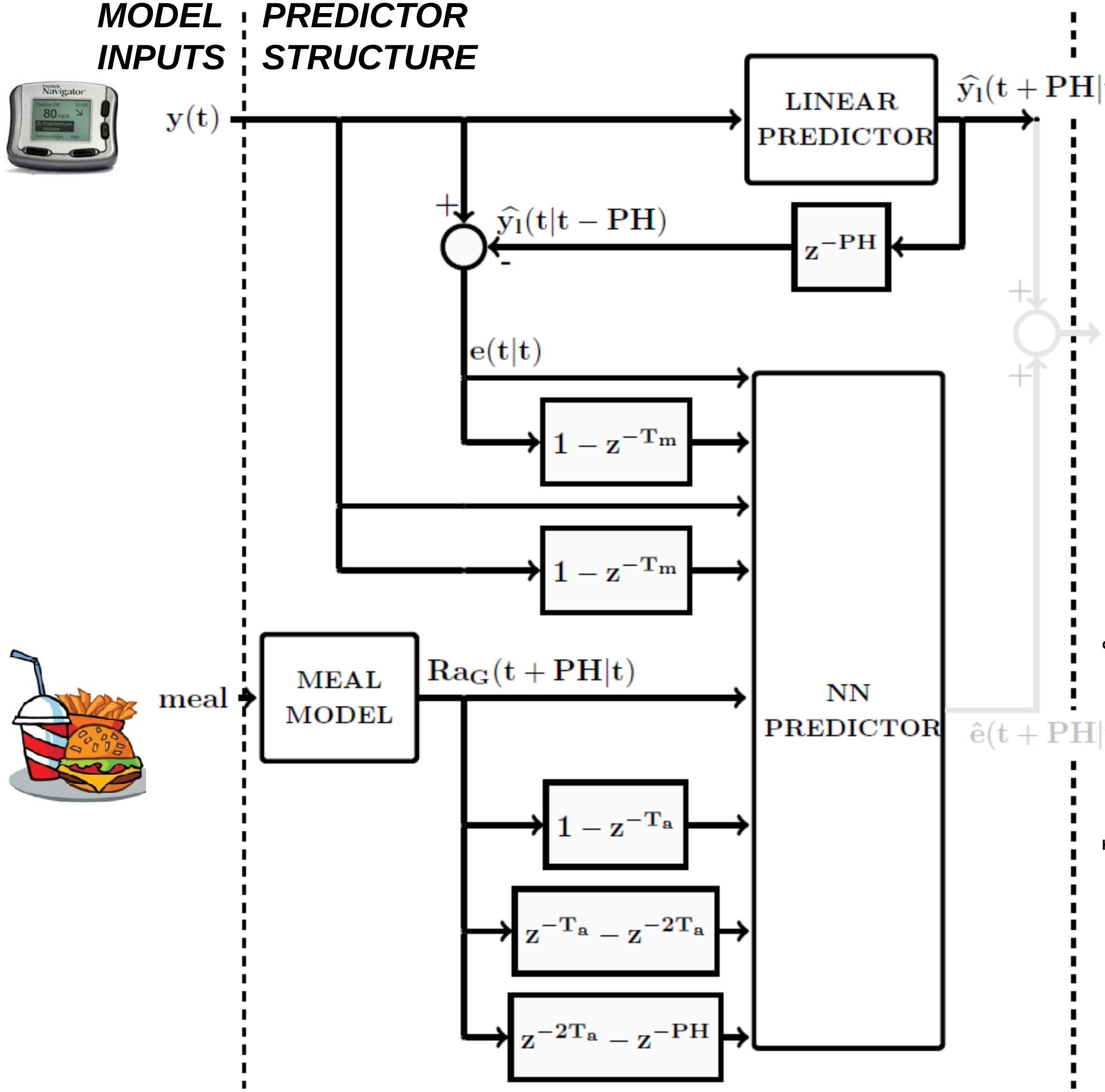


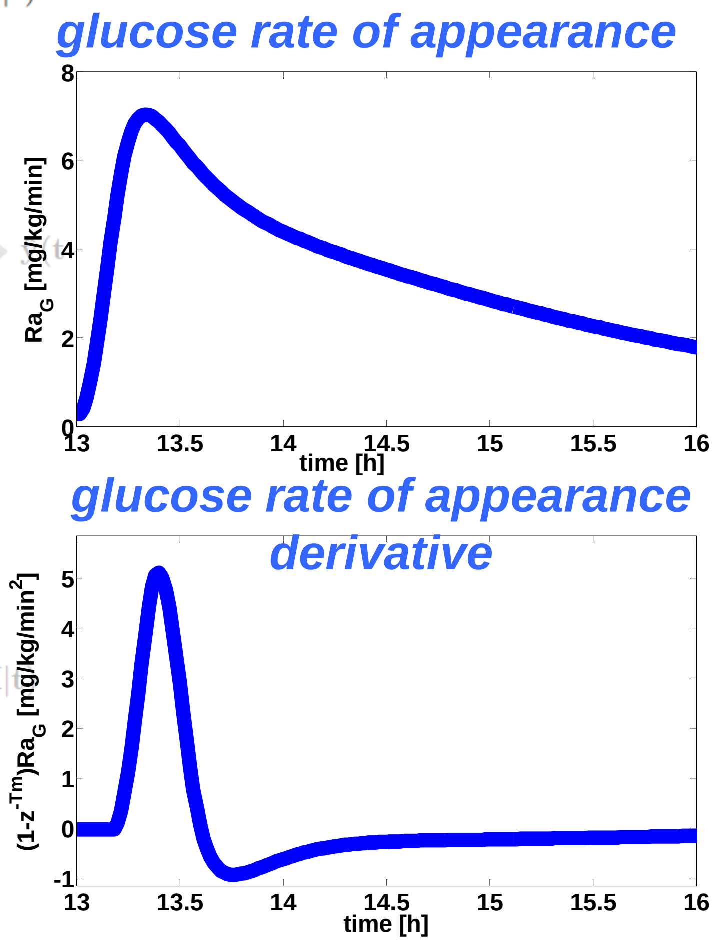
Predictor structure



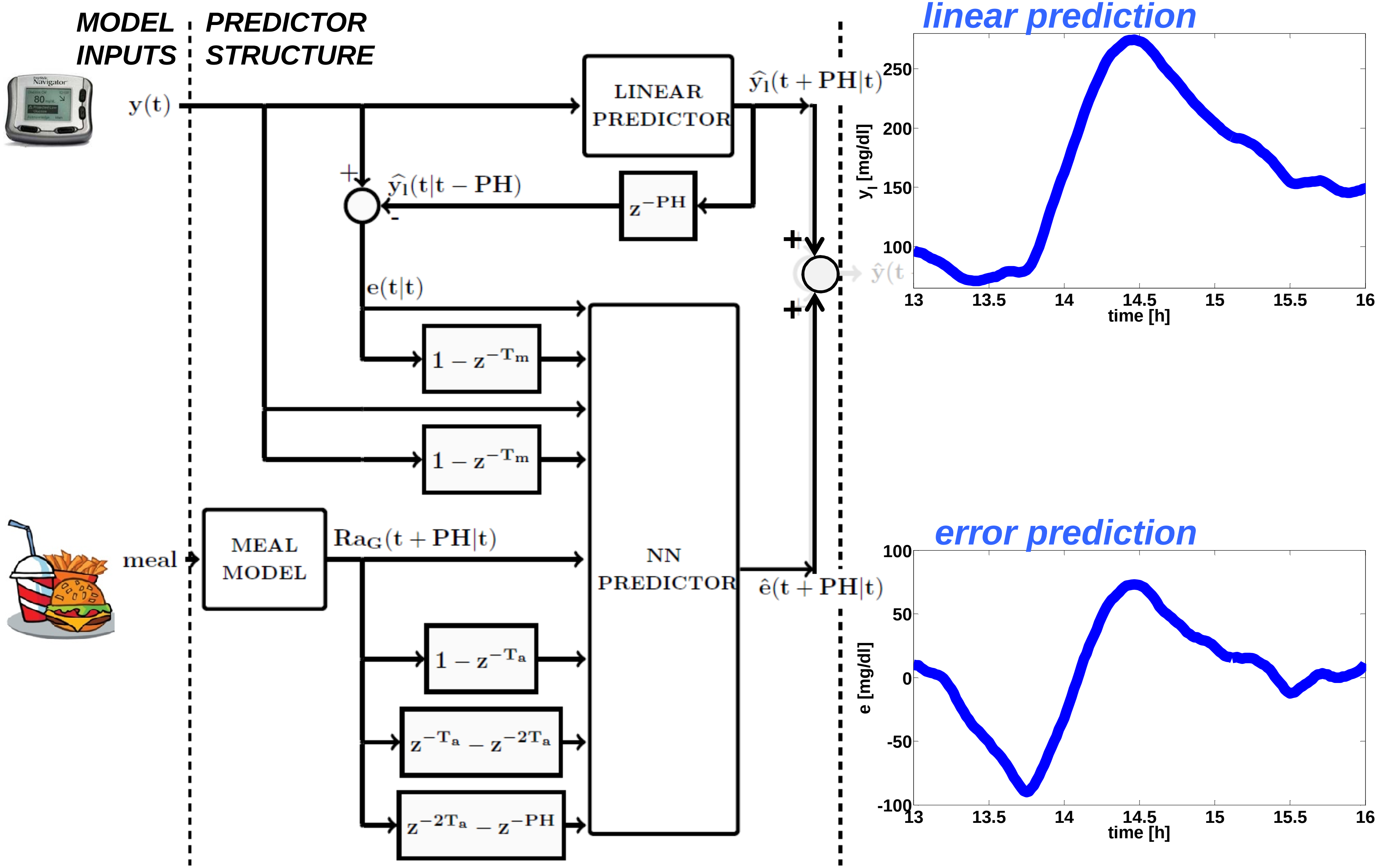


Predictor structure

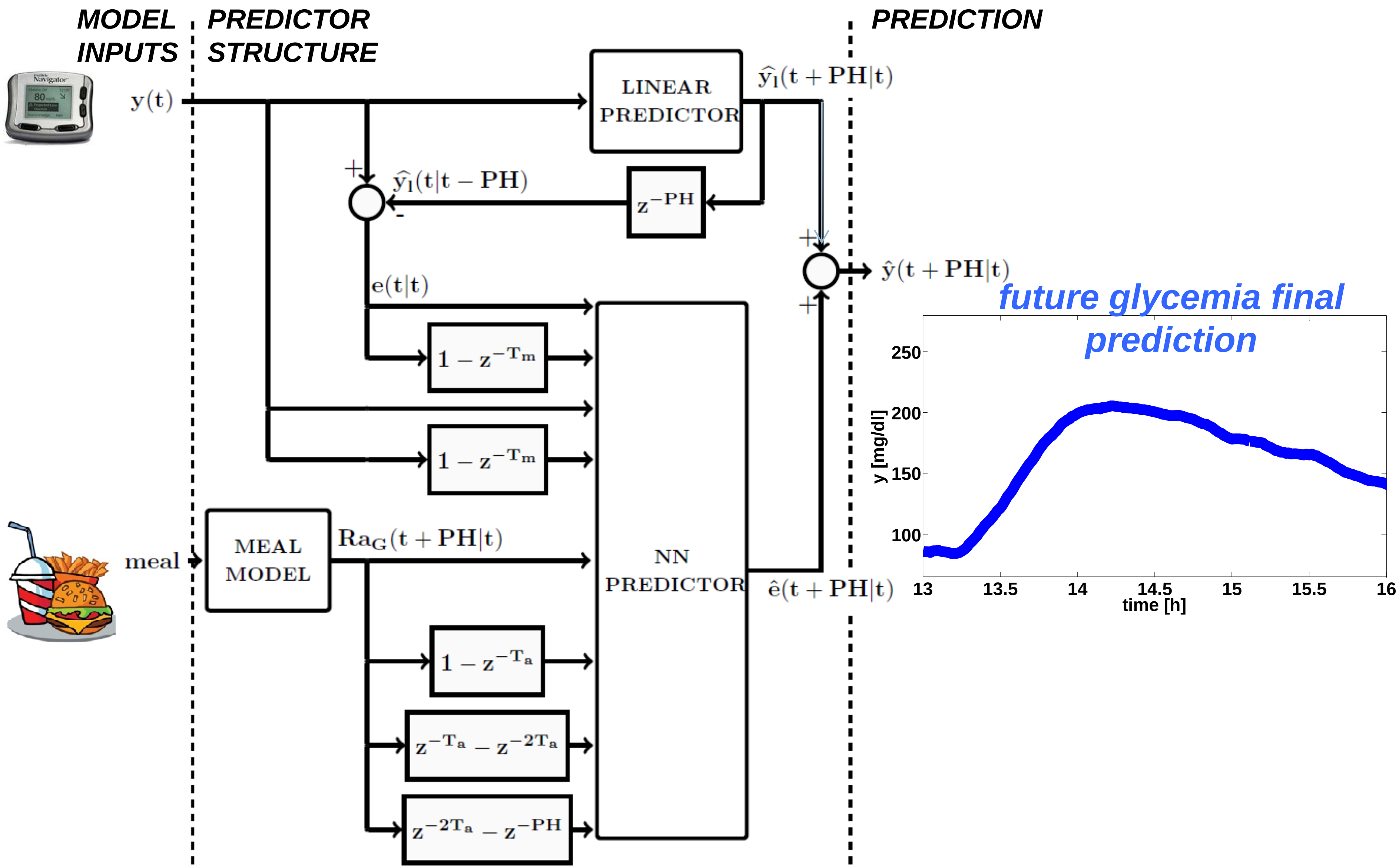




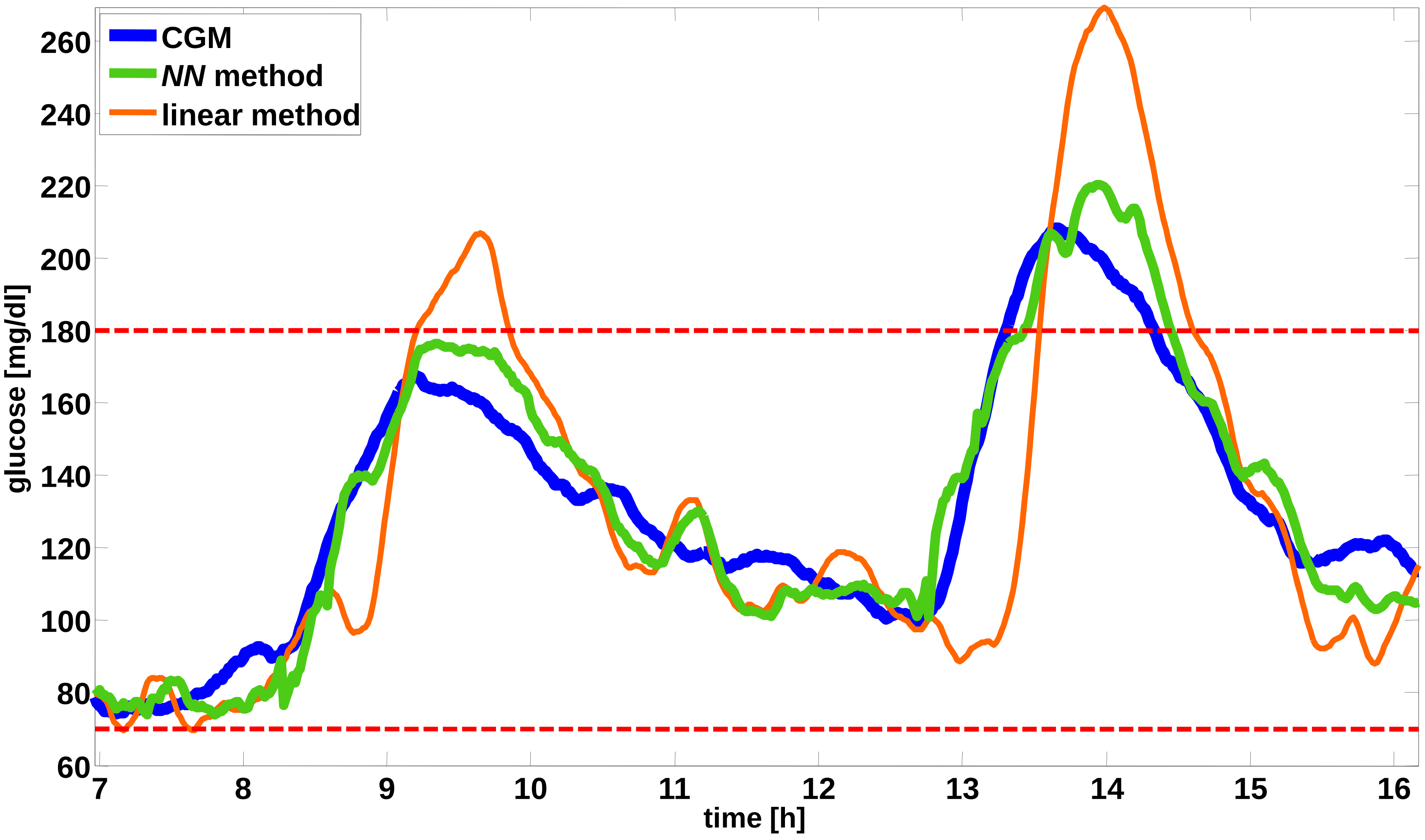
Predictor structure



Predictor structure

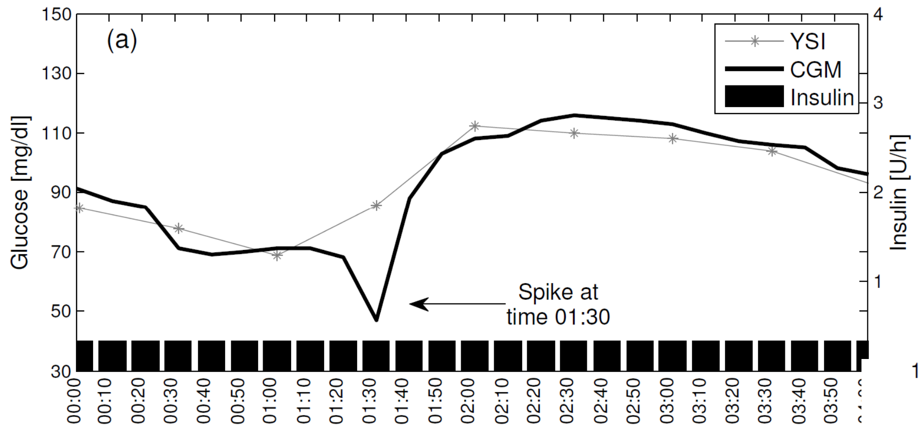


Representative dataset



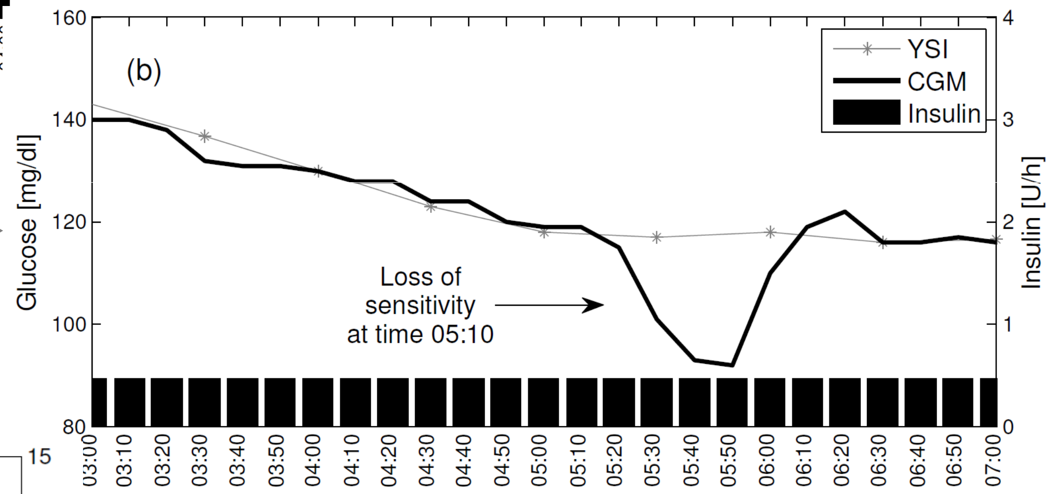
Detection of Failures of the
Glucose Sensor-Insulin Pump System

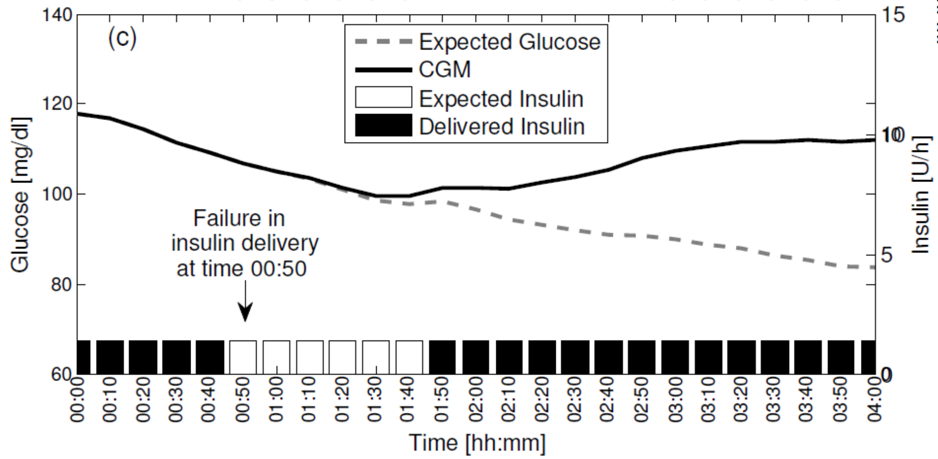
CGM-Pump Failures



Spikes

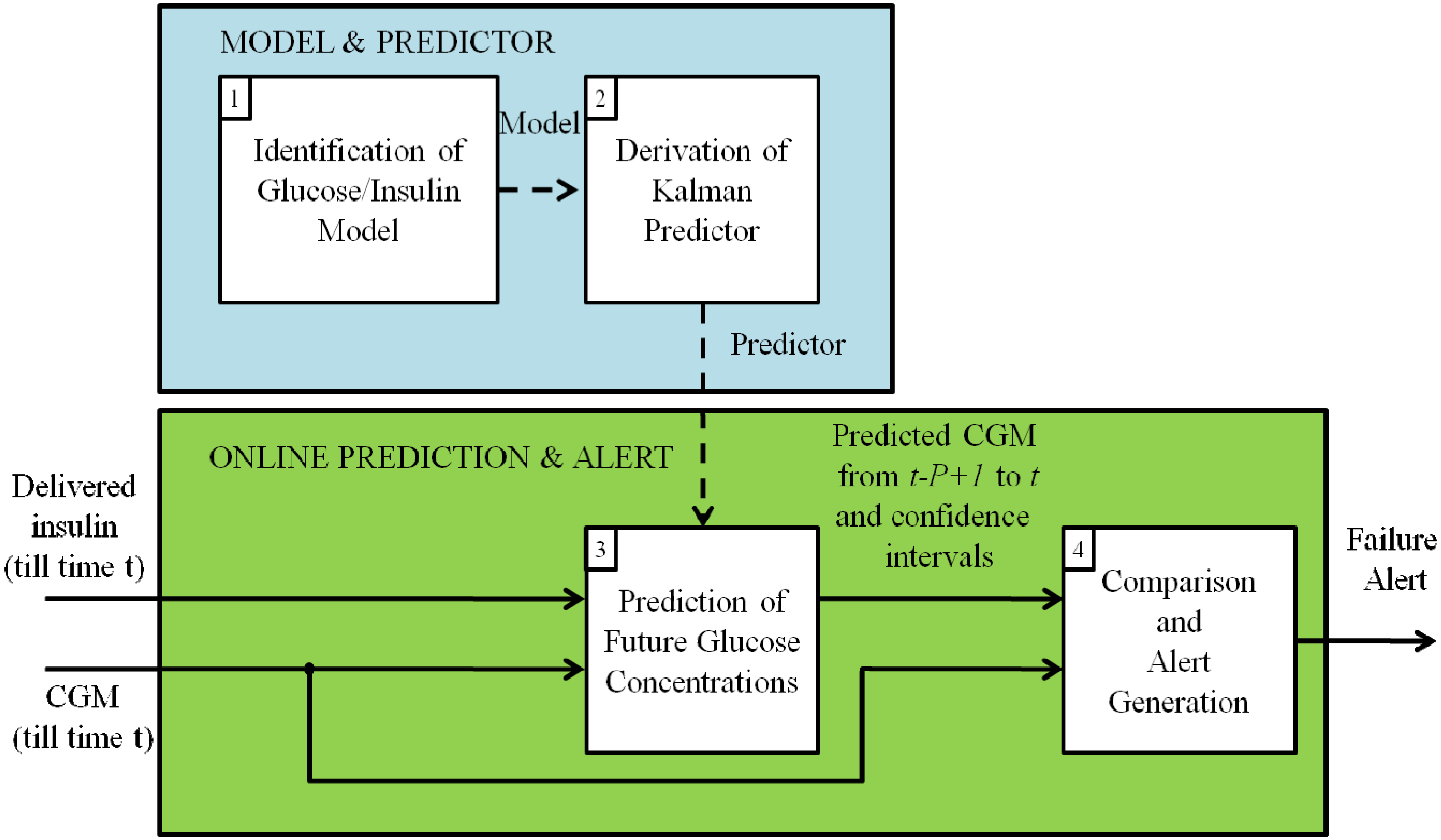
Compression Artifacts





Pump Occlusion

The Failure Detection System



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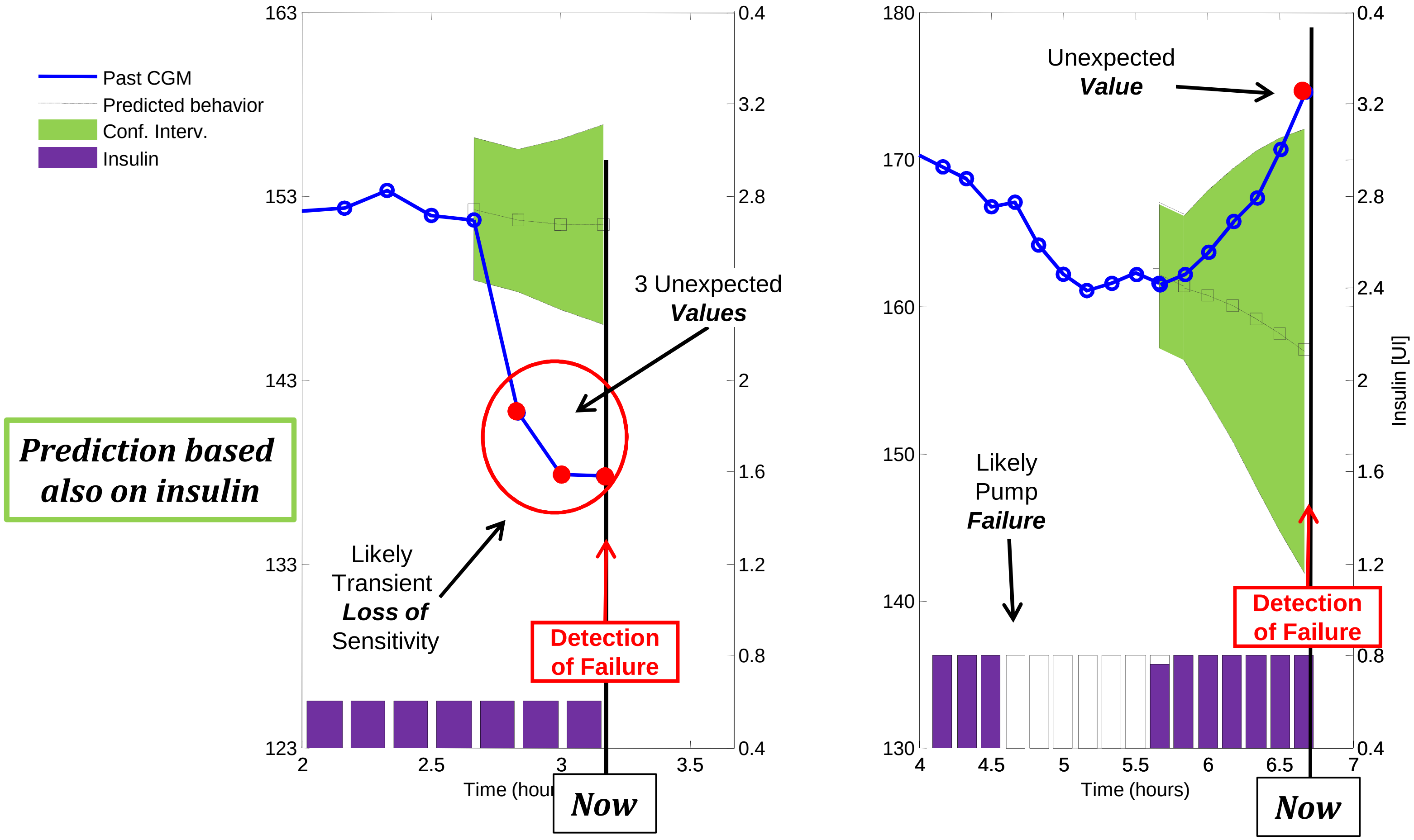
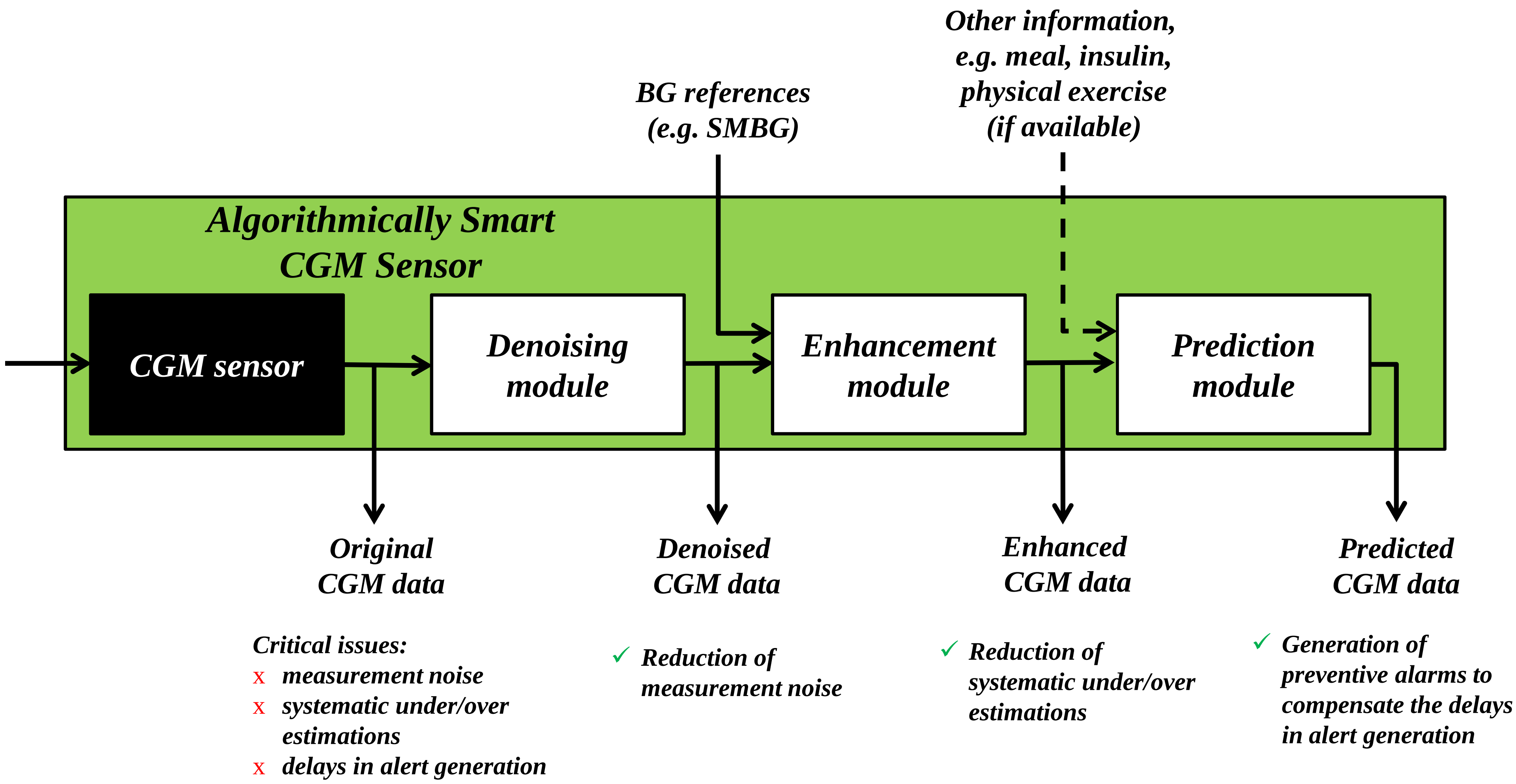
Two examples of failures



The smart sensor

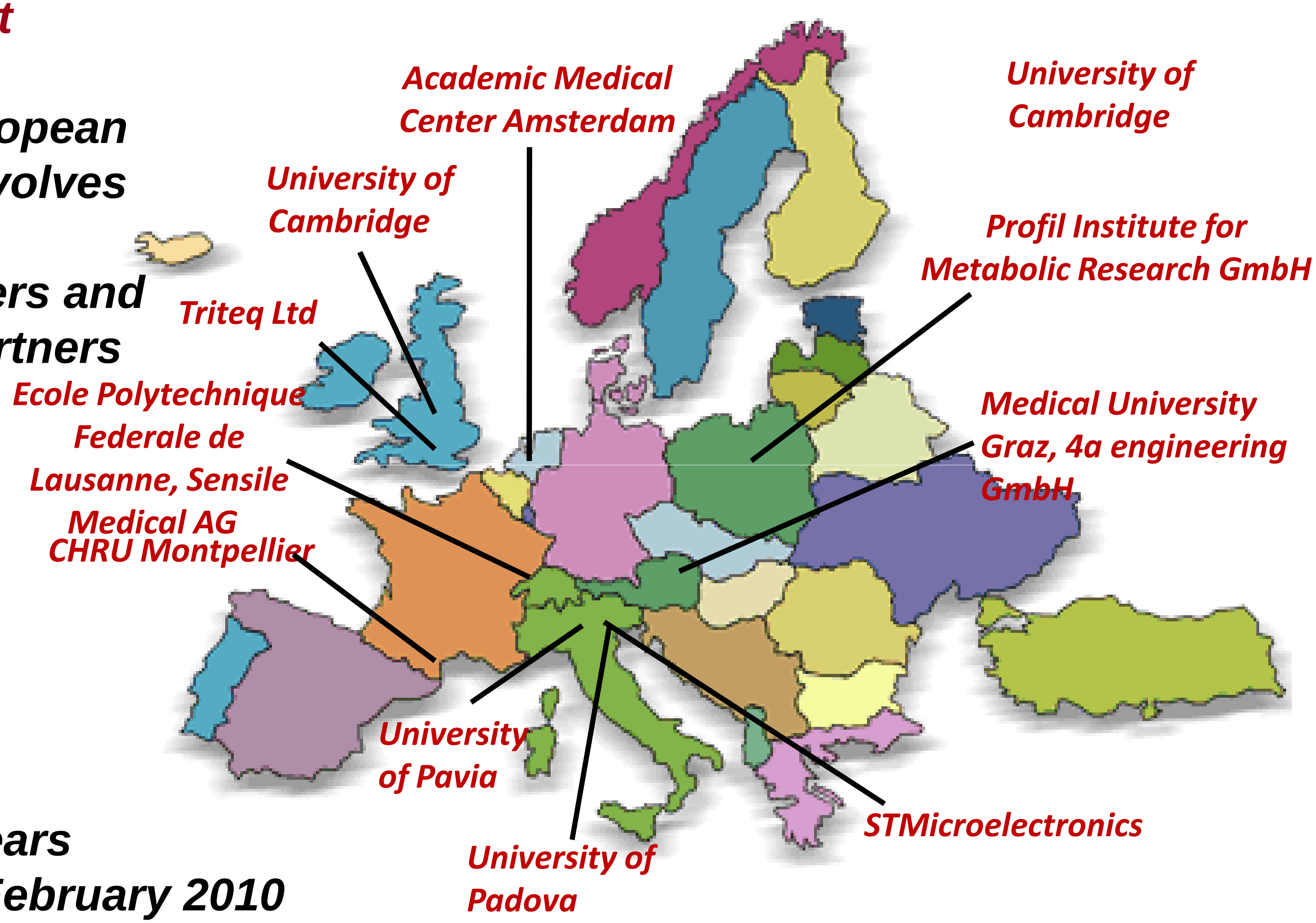
"Smart" CGM Sensor Architecture



Bringing the Artificial Pancreas @ Home

FP7-EU Project

A 10.5 M€ European project that involves 6 universities 2 clinical centers and 4 industrial partners



Duration: 4 years
Started: 1st February 2010

Impact Factor 7.735

Clinical Care/Education/Nutrition/Psychosocial Research
ORIGINAL ARTICLE

Real-Time Improvement of Continuous Glucose Monitoring Accuracy

The smart sensor concept

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ON BEHALF OF THE AP@HOME CONSORTIUM

with a system for real-time generation of alerts when the measured glucose value crosses hypoglycemic (e.g., 70 mg/dL) or hyperglycemic (e.g., 180 mg/dL) thresholds (7). Another possible use is within systems that combine a CGM and a continuous subcutaneous insulin infusion pump in a single unit, the so-called sen-

RESULTS—The denoising module improves the smoothness of the CGM time series by an average of ~57%, the enhancement module reduces the mean absolute relative difference from 15.1 to 10.3%, increases by 12.6% the pairs of values falling in the A-zone of the Clarke error grid, and finally, the prediction module forecasts hypo- and hyperglycemic events an average of 14 min ahead of time.

Final Remarks
(Giovanni Sparacino)

Technology Transfer

Data:
venerdì 06.07.2012

il mattino di Padova

Estratto da Pagi

L'INTROITO SARÀ DI 180 MILA EURO

Il Bo vende i suoi studi a San Diego

Farà fruttare la ricerca sul monitoraggio dei pazienti diabetici

Il Bo si butta sul mercato internazionale e punta a far fruttare la ricerca che viene svolta dentro le mura dell'Università. E' stato siglato un patto tra Padova e San Diego attraverso cui l'ateneo monetizzerà gli studi di Ingegneria medica realizzati nell'ultimo anno: Padova ha inventato un nuovo metodo per monitorare i pazienti diabetici.

Per l'ateneo il contratto di opzione e le eventuali cessioni dei brevetti alla DexCom comporteranno un introito minimo di almeno 180 mila euro. Gli inventori sono i professori Claudio Cobelli, Giovanni Sparacino e l'ingegner Andrea Facchinetti, che operano nel gruppo di ricerca del dipartimento di Ingegneria dell'Informazione.

I brevetti riguardano il monitoraggio del glucosio, la prevenzione dell'ipoglicemia e un sensore dell'insulina. La decisione di aprirsi nuovamente al mercato internazionale è stata assunta ieri pomeriggio nel corso della seduta del consiglio di amministrazione: sono state approvate una sfilza di delibere prima della pausa estiva.

Il consiglio di amministrazione ha deciso di aumentare l'offerta formativa post lauream per l'anno accademico 2012-2013. Saranno attivati, infatti, settanta corsi di Master: 51 sono rinnovi mentre 19 sono prime attivazioni. Si va dalla pianificazione e gestione del prodotto turistico alla conservazione della fauna selvatica; dall'esercizio fisico nella cura delle malattie croniche alle tecnologie per l'energia solare nei paesi africani.

Il cda ha anche aderito al Progetto Venetonight 2012 per la promozione della Ricerca. Nell'occasione, come l'anno scorso, l'ateneo padovano aprirà le proprie porte per far conoscere alla città la propria attività in un settore vitale per l'economia come quello della ricerca.

Fabiana Pesci

Conclusions (1 of 2)

- Diabetes is a **socio-health emergency** of the 3rd millenium

- A better management of diabetes can have a great impact in **quality of life** of diabetic subjects and **economic costs** for national health systems

- (Minimally-invasive) **sensors for CGM** are key in several open-loop and closed-loop applications

- Several issues are **open** (patient's discomfort, biocompatibility, stability, duration, miniaturization, …) and some of them concern **algorithms**

Conclusions (2 of 2)

•DEI developed several on-line algorithms for improving **reliability** and **usability** of CGM sensors

•Some of these algorithms raised the interest of one of the major CGM sensors **manufacturers** (DexCom Inc)

•Padova-DexCom collaboration is promising and will hopefully become a nice example of how academic research can meet industry needs without loosing **independency** and **scientific objectives**