Analysis of Enhanced Prediction Algorithms for Time Lag Compensation in CGM Systems

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Introduction

Continuous glucose monitoring (CGM) sensors measure the glucose concentration in the interstitial fluid (IG), whereas the user is interested in the glucose level in the blood (BG). It is well known that there is a time delay between the BG level and the measured CGM signal. To counterbalance this effect, a model that describes this time delay is needed.
The dynamics between BG and IG can be described by a first order filter model as

$$\tau \frac{dIG(t)}{dt} = -IG(t) + BG(t) \tag{1}$$

where τ is the time constant for diffusion.
In our analysis we compared performance of different prediction algorithms for the compensation of the CGM time lag.

Methodology

The following linear and nonlinear prediction models have been considered in this analysis:

- **Linear autoregressive models (ARX)**

  An autoregressive (AR) model is a representation of a random process; the notation $AR(n)$ indicates an autoregressive model of order n, defined as

  $$IG_{est}(t_k) = \sum_{i=1}^{n} a_i \cdot IG_{est}(t_{k-i}) + \epsilon_k$$

  where $a_1, \ldots, a_n$ are the parameters of the model and ϵ_k is white noise.

  The used **ARX structure** with h steps ahead prediction has the form

  $$IG_{est}(t_{k+h}) = \sum_{i=0}^{n} a_i \cdot IG_{est}(t_{k-i}) + b_0 \cdot \frac{dIG_{est}}{dt}(t_k) + \epsilon_k,$$

  where the derivative $\frac{dIG_{est}}{dt}(t_k)$ being the exogenous input is estimated using a Kalman filter [1].

  Two main classes of ARX models have been implemented:

  - a **global ARX model**, trained on the global training set (abbreviated as GARx in the results table);
  - a **patient-specific ARX model**, with specific parameters for each patient (abbreviated as PSARx in the results table).

- **Nonlinear autoregressive models (NARX)**

  For h steps ahead prediction, a NARX model with polynomial regressors has the form

  $$IG_{est}(t_{k+h}) = f_p(IG_{est}(t_{k-1}), \ldots, IG_{est}(t_{k-n_a}), \frac{dIG_{est}}{dt}(t_k), \ldots, \frac{dIG_{est}}{dt}(t_{k-n_b+1})) \cdot \theta + \epsilon_k$$

  f_p is a function that spans all polynomial combinations of its arguments up to a degree p, θ is the model's parameter vector. The model orders are n_a and n_b. We fixed $n_b = 1$.

  In the comparison table these models are denoted GNARx$_p(n_a)$ and PNARx$_p(n_a)$, where G stands for global models and P stands for patient-specific models, respectively.

- **CWT-based differentiation method**

  Additionally, we analyzed the same first order filter model (1), but with the derivative calculated based on continuous wavelet transform (CWT) originally published in [2].

Clinical data for validation

- **Description of the dataset**

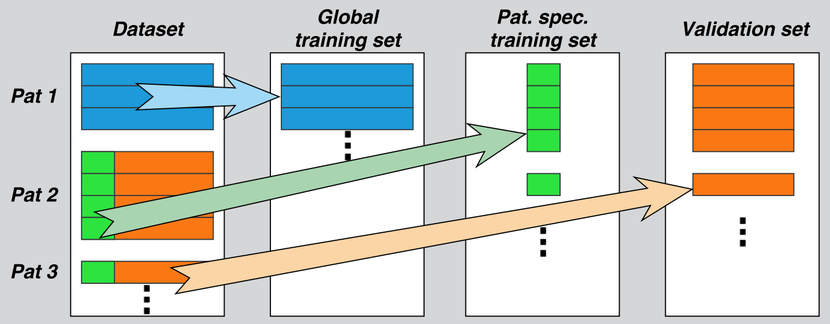
  In total a set of 177 records (experiments) was used. Each record contains data of one patient measured over a period of 7 days. The records contain data of 77 different patients in total. Each of the 177 records among others contains the following data:

  - sensor signals and corresponding time stamps (one current value every minute)
  - SMBG reference measurements available about every hour and their time stamps

- **Splitting the data**

  Since the behavior of global and patient-specific prediction algorithms has to be evaluated and compared, it has been chosen to split the whole dataset into three different sets:

  - a **global training set**, consisting of the entire data sequences of 120 experiments taken on randomly selected patients;
  - a **patient-specific training set**, consisting of the first day of data taken from the rest of patients;
  - a **validation set**, consisting of the latter six days of data taken from the same patients as the patient-specific training set.



The sensor sensitivities have been estimated beforehand from the SMBG and the current data by means of an off-line calibration algorithms [3].

Results

The column "PH" (in min) represents the prediction horizon h for a specific prediction model that leads to the minimum average MARD. Note that h was varied and the minimum average Mean Absolute Relative Difference (MARD) on the training set was found. This value of h was then fixed for each specific model and average MARD on the validation set was evaluated (column "MARD").

Model	MARD	PH h
No prediction	9.09	0.00
Model (1)	7.80	8.00
CWT	7.69	8.00
GARx(2)	7.69	12.00
GARx(4)	7.70	12.00
GARx(11)	7.70	12.00
GNARx$_2$(2)	7.86	10.00
GNARx$_2$(4)	7.86	10.00
PSARx(2)	7.72	16.00
PSARx(4)	7.88	19.00
PNARx$_2$(2)	8.29	15.00
PNARx$_2$(4)	8.61	15.00

Conclusion

It can be concluded that the global ARX model of order 2, GARx(2), and the CWT-based two-compartment model perform best in terms of MARD. The higher order linear as well as the nonlinear models do not bring any significant performance improvements when evaluated on the validation set, due to the possibility of overfitting the estimation data, they even perform worse on the validation data than the simpler (and more robust) models. The same reasoning applies for the patient-specific models. In general, using prediction is beneficial compared to no prediction, but the gain of advanced algorithms is relatively low compared to the SOA model (1).

References

[1] Bequette, B. Wayne. *Continuous Glucose Monitoring: Real-Time Algorithms for Calibration, Filtering, and Alarms*. Journal of Diabetes Science and Technology 4.2 (2010): 404–418.
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[3] Reiterer F., Polterauer P., Freckmann G., del Re L. *Identification of CGM Time Delays and Implications for BG Control in T1DM*. In: Kyriacou E., Christofides S., Pattichis C. (eds) XIV Mediterranean Conference on Medical and Biological Engineering and Computing 2016. IFMBE Proceedings, vol 57. Springer, Cham