New Calibration Algorithm Leads to Robust CGM Performance with Reduced Number of Calibration Measurements

Pavlo Tkachenko, Patrick Schrangl, Florian Reiterer, Luigi del Re

Institute for Design and Control of Mechatronical Systems
Johannes Kepler University Linz, Austria

Introduction

Since Continuous Glucose Monitoring (CGM) sensors tend to change their behavior (mostly sensitivity on the glucose level) over time, it is beneficial for improving the CGM system performance to calibrate the sensor from time to time using Self-Monitoring of Blood Glucose (SMBG) calibration measurements.
An ideal linear (affine) CGM sensor in the Blood Glucose (BG) domain would have the behaviour

$$I = s \cdot BG + i_0, \tag{1}$$

where I is the sensor current in nA, s the sensor sensitivity innA/(mg/dl), and i_0 the zero current in nA.
It is necessary to perform calibrations in the BG domain, since only BG calibration measurements BG_{cal} are available from the SMBG device. The goal of calibration is to estimate the parameters s and i_0 using past data of I and BG_{cal}.

Clinical data for validation

- **General description**

  In total a set of 176 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 176 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

- **Calibration**

  Most of the patients performed a first calibration measurement 3 hours after sensor insertion. The second one within two hours after the first one, and then two measurements every day (one in the morning and one in the evening) over a period of 7 days. As a result, the following number of calibration measurements has been collected:

  – 1 dataset contains 14 calibration measurements;
  – 110 datasets contain 15 calibration measurements;
  – 65 datasets contain 16 calibration measurements.

Methodology

The following strategies have been analyzed with a reduced number of calibration measurements:

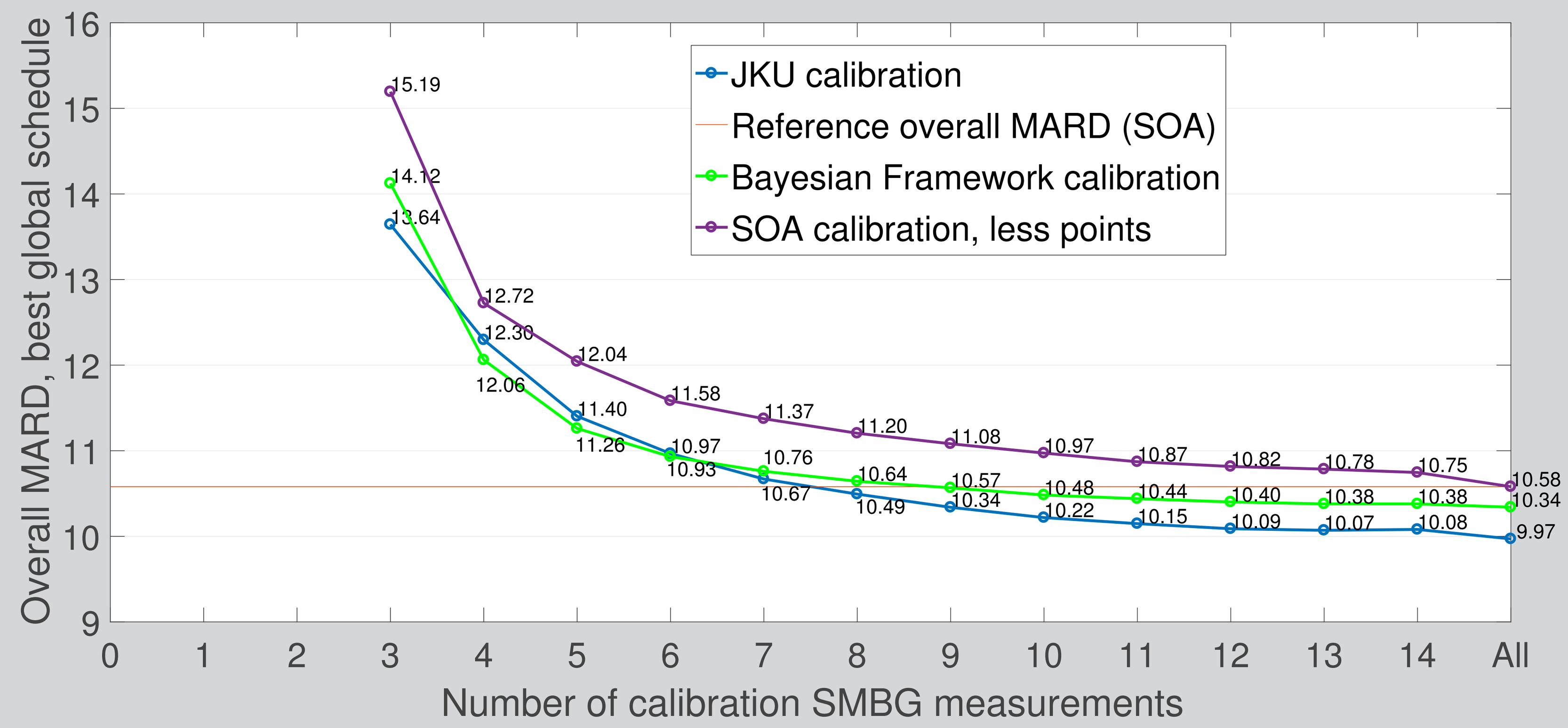
- Manufacturer's state-of-the-art (SOA) calibration algorithm;
- A calibration method based on the Bayesian Framework (BF) using the ideas from [1].
- Novel JKU calibration algorithm.

The possible times for calibration measurements were chosen identical to the ones from the original dataset. However, calibration measurements have been eliminated in order to simulate the effect of using less calibrations. As an initial point in our analysis, the first 3 calibration SMBG measurements (performed roughly 2, 5 and 17 hours after sensor insertion) are considered mandatory for each patient. Then, all possible positions of selections with cardinalities from 1 to 11 have been considered within the next 11 time slots. The calibrations with numbers 15 and 16 (if they are available) are always omitted. The following table reports the number of possible calibration schedules for each number of calibration measurements performed.

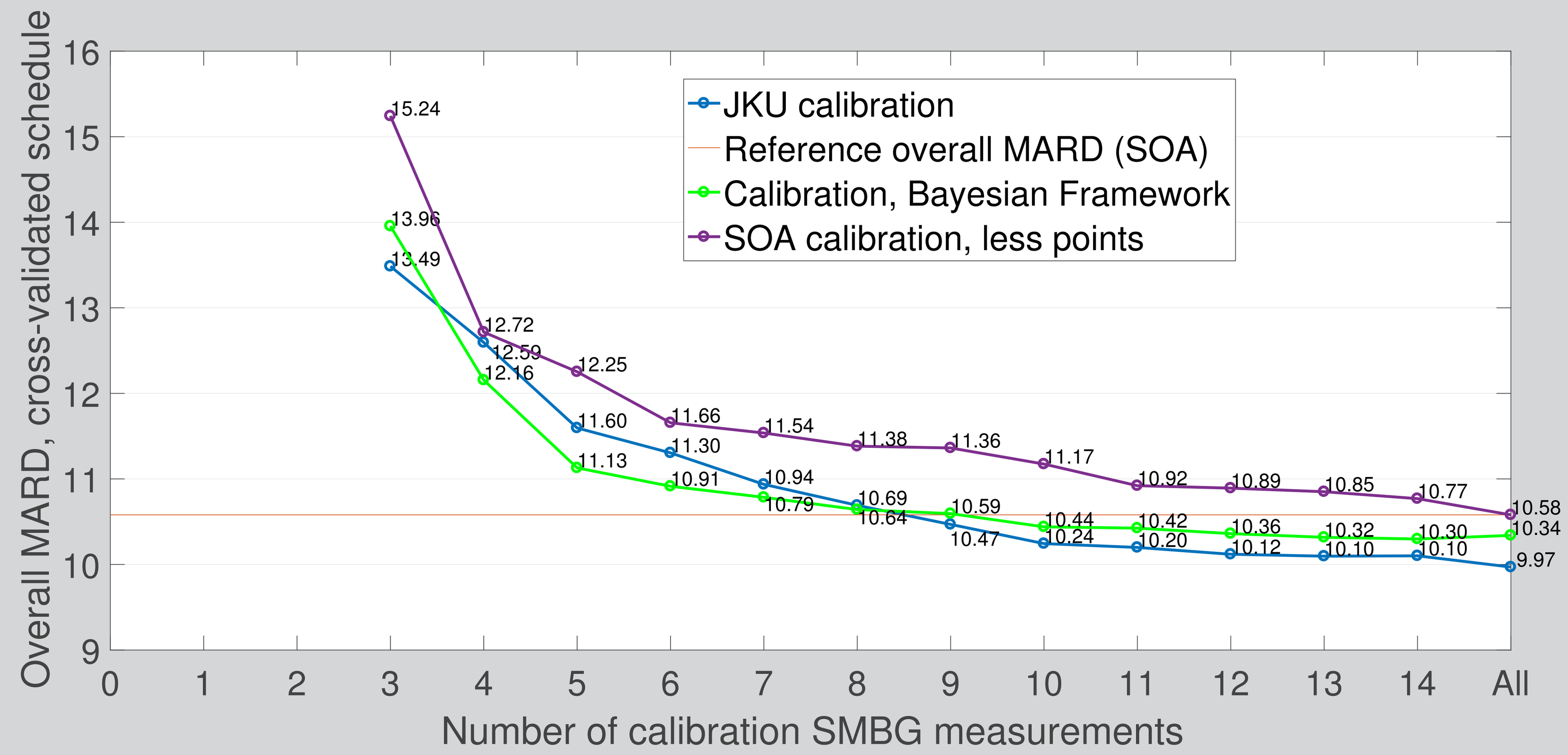
# of calibrations	3	4	5	6	7	8	9	10	11	12	13	14
# of combinations	1	11	55	165	330	462	462	330	165	55	11	1

Results

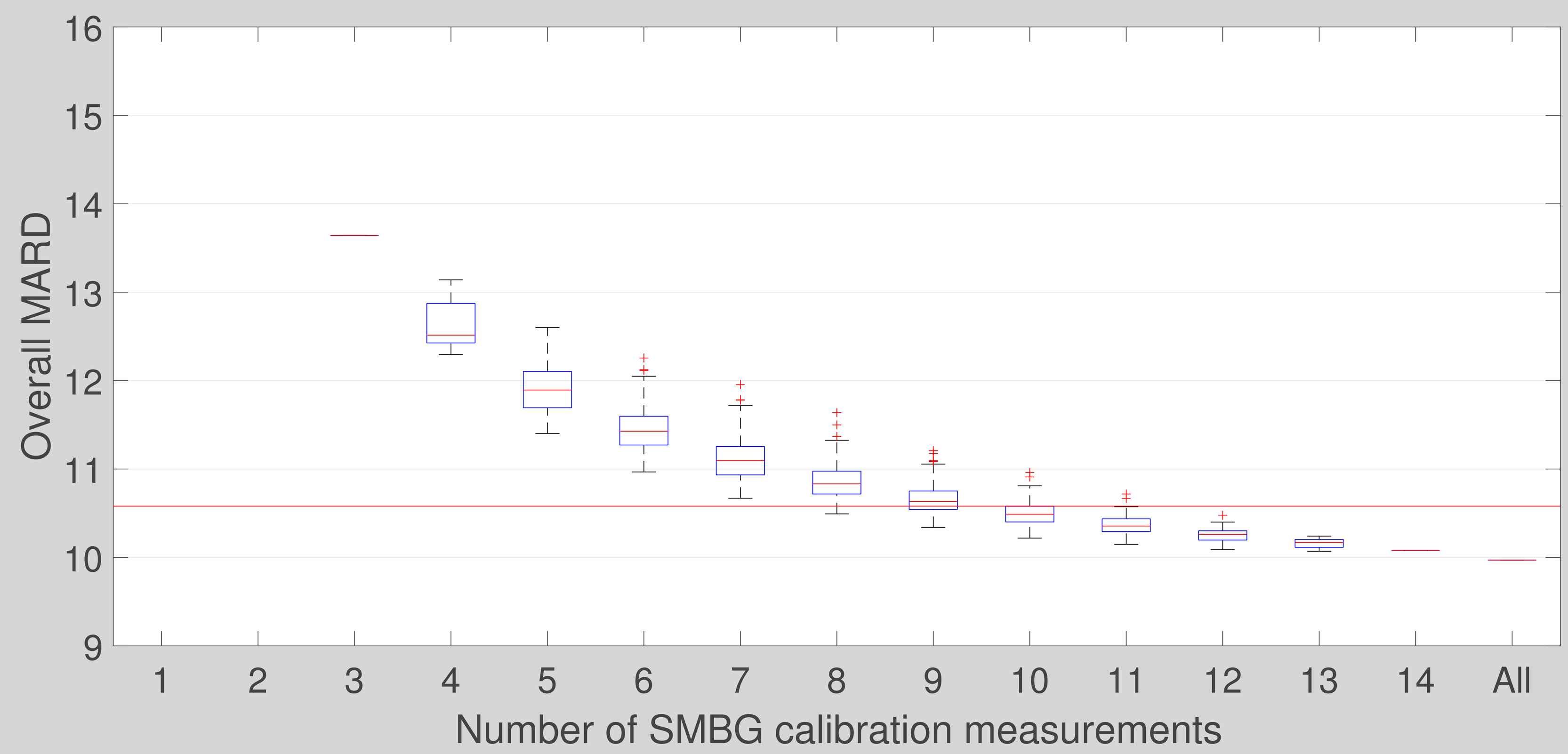
In our first experiment for the considered calibration strategies, we computed the Mean Absolute Relative Difference (MARD) for each dataset and each calibration schedule. Then, the best schedule with each number of calibration measurements as that minimizing the overall MARD was found.



In the next experiment, we made a 10-fold cross-validation analysis in order to estimate the robustness of the considered calibrations. The data was randomly partitioned into 10 almost equally sized subdatasets. Of the 10 subdatasets, a single subdataset is retained as the validation data for testing the optimal schedule for the remaining 9 subdatasets. The cross-validation process is then repeated 10 times, with each of the 10 subdatasets used exactly once as the validation data. The 10 results from the folds are then averaged to produce a single estimation.



For the JKU algorithm, we also present the MARD distribution over different schedules within the same number of calibration measurements.



Conclusion

From the results presented above one can see that the BF and JKU calibrations can be used effectively (performing better than the SOA algorithm with all points) with approximately half of the calibration SMBG measurements. The performance of the JKU algorithm is quite robust with respect to the calibration schedule as well.

References

[1] G. Acciaroli, M. Vettoretti, A. Facchinetti, G. Sparacino, and C. Cobelli. *Reduction of blood glucose measurements to calibrate subcutaneous glucose sensors: a bayesian multi-day framework.* IEEE Transactions on Biomedical Engineering, PP(99):1–1, 2017.