Institute for Design and Control
of Mechatronical Systems

Diploma Thesis:

Calibration of Continuous Glucose Measurement Devices

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Abstract

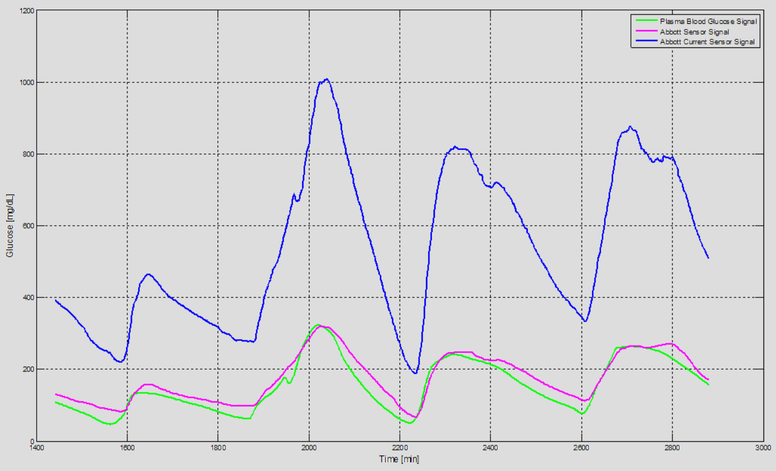
At present diabetic patients control their blood glucose level manually by measuring the concentration in blood collected from their finger tip several times a day to decide the amount of insulin dosage to be injected. The development of the continuous glucose monitor (CGM) was initiated with the hope that this new glucose measurement tool would enable significant improvements in diabetes management. This shift to minimally invasive CGM primarily involves a shift from blood glucose measurements to devices measuring subcutaneous interstitial fluid (ISF) glucose. Interstitial glucose fluctuations are related to blood glucose presumably via diffusion process. This leads to a number of issues, including distortion (which incorporates a time lag) and calibration errors, and necessitates the development of methods for their mitigation.

Different methods have been developed to describe the dynamics between ISF and blood glucose. A closer look is taken at the methods in order to change their sometimes very theoretical approach into a more practical orientated view. This includes the minimization of finger prick measurements as well as optimization for the use in patient's life. Hence, the invaluable measurements should not only be used to control the CGM device but also to improve and update its signal.

Furthermore suggestions are given for new calibration methods in order to reduce the danger current calibration methods carry with them. It is also proofed in simulation that the new methods improve sensor performance over the whole sensor life.

Introduction:

Eight patients were observed for three days in hospital and three glucose signals were obtained: the output signal shown on the display of the device (which is already calibrated), the raw current signal in NanoAmpere and the SMBG measurements. The SMBG measurements were interpolated in Matlab with the command “pchip” to get a smooth signal.



Now three methods with new approaches were applied on the raw current signal and compared to the sensor signal and the SMBG measurements. The methods are two-point calibration, deconvolution and the combination of the two methods.

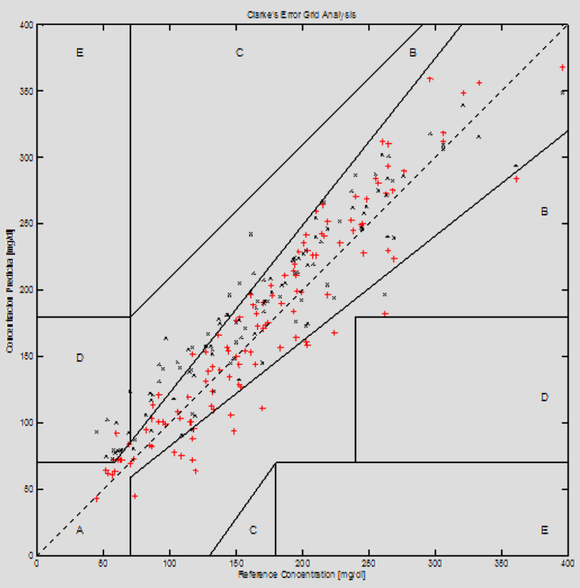
Results

Calibration

$$y_1 = mx_1 + b$$
$$y_2 = mx_2 + b$$

Estimation of sensor sensivity and y-intercept:

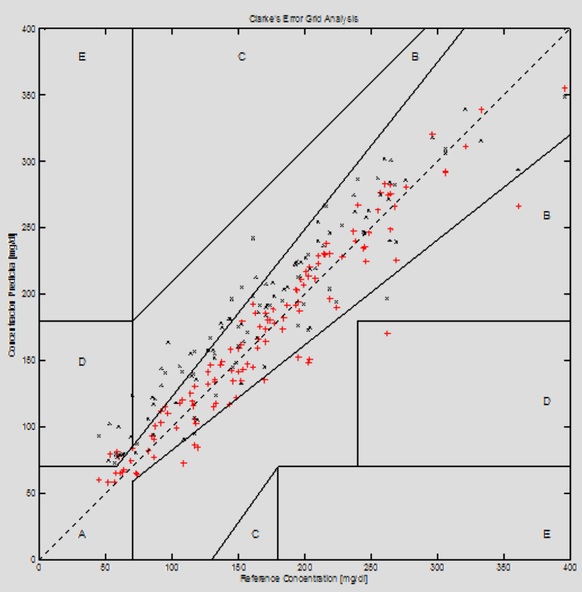
$$m = \frac{y_2 - y_1}{x_2 - x_2} \qquad b = y_2 - mx_2$$



black: sensor signal
red: raw signal calibrated

Combination

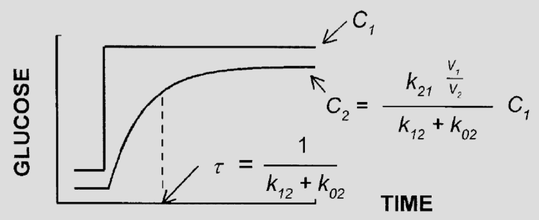
Parameter estimation and deconvolution was done on day one, the following days two-point calibration was done every 24 hours. With this combination it was possible to compensate the disadvantages of both methods.



black: sensor signal
red: raw signal calibrated

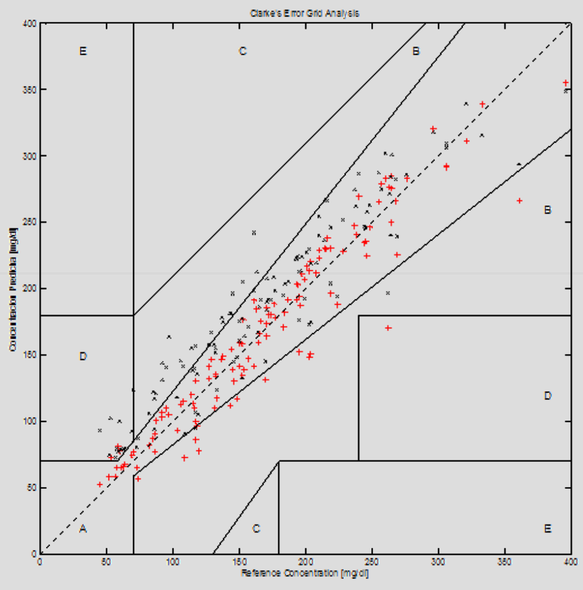
Deconvolution

Two compartment model, where ISF and plasma are seen as seperate compartments.



$$\frac{dC_2(t)}{dt} = \frac{-1}{\tau} + \frac{g}{\tau C_1(t)}$$

The parameters τ and g are estimated with 10 SMBG measurements and then the real blood glucose is estimated through deconvolution.



black: sensor signal
red: raw signal deconvoluted

Conclusions and Outlook

In this thesis the focus has been lying on trying to reduce the patients burden. Of course, the sensor performance needs to be improved in order to improve diabetes management but also the measurements in blood plasma have to be minimized and used more efficient. This means that every single measurement has to be used to improve AND control the sensor device. Since also the following days some blood plasma measurements need to be done in order to control the sensor performance these measurements were used to recalibrate the deconvoluted signal all following days of the sensor life time. In this manner the sensor performance improved - the errors could be minimized.

At this point it would be very important to implement the new methods in the sensor in order to see if they work as well in vivo. The studies should be extended to “normal life” where the patient is not only observed in hospital but also at home. It is of fundamental importance to train the patients in a proper way, because in the end they are the ones dealing with the devices and with the malignancy every day.