Short term blood glucose measurements may be severely biased

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Abstract

The values of continuous measured blood glucose have little difference when measured at short time intervals. As time increases so does the difference in average. For discretely measured values the picture is quite different: measurements made at short time intervals display a surprising higher difference than continuous measurements. We have not seen this effect reported before.

1 Introduction

Today most people with diabetes measure their blood glucose (BG) by sampling a drop of capillary blood—typically from the finger tip—and measuring with a BG-meter. Continuous measuring devices also exist like the Minimed Continuous Glucose Monitoring (CGM) that measures the BG value every 5 minutes. Here a needle has to be inserted and replaced subcutaneously every third day.

One of the main problems in the management of diabetes is to balance the dose of insulin with the near future values of the BG concentration. Being able to predict the BG level would simplify the management. Many attempts have been made to predict the value of the BG from historical data [Arita *et al.*, 1999; Hejlesen, 1998; Lehmann and Deutsch, 1998; Liszka-Hackzell, 1999; Mougiakakou and Nikita, 2002; Tresp *et al.*, 1999]. No model has shown good prediction power for more than one data set—like for instance an error rate of less than 1mM/hour. The mentioned publications involve only strip based BG measurements. Attempts to predict BG values from continuously measured BG shows a clear connection between how far into the future the prediction reaches and prediction error [Hovorka and others, 2004; Prank *et al.*, 1998]. No attempts we know of have been made to examine whether this is also true for predictions based on strip based measurements. The general assumptions seem to be that strip measurements are equal to continuous measurements, only less frequent and that the BG measurement is a sampling of the underlying reality. The present paper shows that this assumption is not sound.

2 Strip versus CGM

The accuracy of strip measurements is slightly better than continuous measurements. The accuracy is defined as the percent of measurements that are within 20% of the reference value or in the hypoglycaemic area—the zone A in the Clarke Error Grid [Clarke *et al.*, 1987].) The accuracy of measurements with a handheld meter is somewhere between 73.9% [Clarke *et al.*, 1987] and 83.5% [Alto *et al.*, 2002] and the accuracy of Minimed CGM is 70.2% [Gross *et al.*, 2000]. From these accuracies, one might think that the strip based BG measurements would be as good as CGM, just less frequent.

However, there is a very strong correlation between why people measure their BG and the actual value they measure. Consider, for example, a Modal Day plot (see Figure 1). The plot often shows low values in the small hours of the night. Is it because the BG is always low at that time? Or if the person wakes to make a measurement, is it because BG is low? In the latter case the average of the measured values have little to do with the real average.

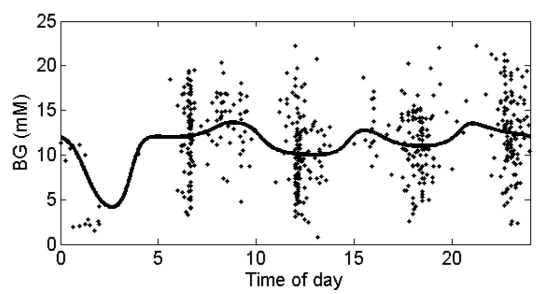

Figure 1: Modal day for data set number 20 from the AAAI 1994 Spring Symposium. The data set is one person's normal diary. Dots represent single measurements and the curve is a Gaussian smoothed average with $\sigma = 0.2$.

The Gaussian smoothed average used in the Figure is calculated by summing the value of a single BG measurement (made at time t_s) times the influence of that value at time t. The influence is calculated as $\exp\left(-\frac{(t_s-t)}{2\sigma^2}\right)\frac{1}{\sigma\sqrt{2\pi}}$.

We want to examine the degree to which BG values are related by plotting the absolute difference as a function of the time between the measured values—see Figure 2. The short term difference is high and decreases as time increases. The BG data covers 79 normal diaries including the 70 data sets from the AAAI 1994 Spring Symposium, a total of 13 615 strip measurements.

For continuously measured values the picture is quite

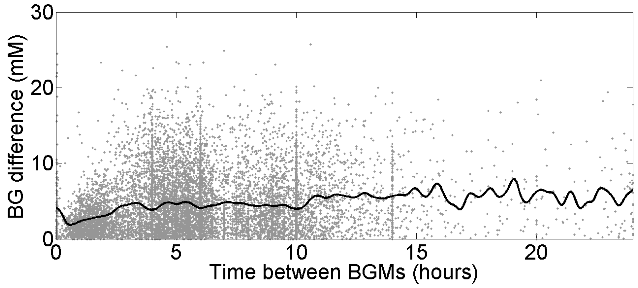

Figure 2: The dots represent the difference for single predictions and the line is a Gaussian smoothed average with $\sigma = 0.2$.

different. The deviation from one value to the next was observed at different time intervals. Summing the deviations through the complete dataset it is possible to plot the deviation as a function of the time interval—see Figure 3. Here, the deviation increases with time as would be expected.

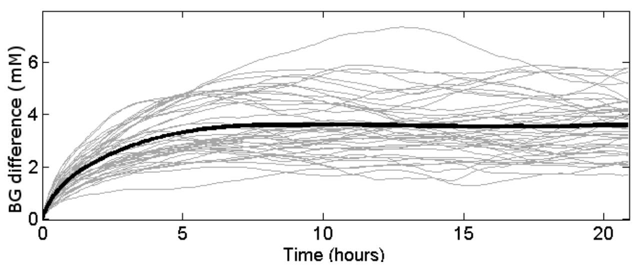

Figure 3: The grey curves show data from 42 patients in a Novo Nordisk study with 72 hours Minimed CGM measurements. The black curve is the average of the curves.

Figure 4 shows the two averages curves in the interesting area for small time intervals. The difference for small time intervals is obvious.

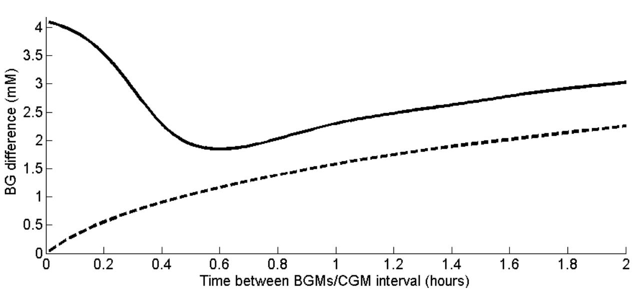

Figure 4: Strip-based (solid) and CGM-based (dashed).

Why this difference for small time intervals? Consider strip based measurements: If a person just made a measurement, why perform one more, less than half an hour later? It is likely that this occurs when there is suspicion that the first measurement was not correct, or when the person has a sensation of undergoing dramatic changes in BG. Our calculations show that these suspicions are often correct—measurements made shortly after each other are less correlated than, for instance, measurements with half an hour between them. This effect makes strip based short term prediction difficult. This is not an issue with continuously measured BG values as they are measured independently of circumstances.

3 Conclusion

We have shown that strip measurements display a strong dependence on the circumstances for measurements when made at short time intervals, making prediction of these blood glucose values relatively difficult. This is not an issue with continuously measured BG values.

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