Institute for Design and Control
of Mechatronical Systems

Diploma Thesis:

Output Error Identification Applied to Type 1 Diabetes

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Abstract

Diabetes is the most prevalent disease in almost all countries, reaching the magnitude of an epidemic. The recent development of noninvasive sensors that provide continuous blood glucose measurements, combined with reliable prediction models, opens the possibility of predicting future glucose levels. Predicted values could be used to alert the patient of an oncoming hypo- or hyperglycemia event. For this purpose an algorithm, combining the Recursive Prediction Error Method and a MISO Output Error model structure is proposed in this work, due to the assumption that it may be more robust to varying model orders. Another rationale is the explicit use of inputs, as they are the only source of blood glucose. Two other methods, taking no inputs into consideration, the RICAM[1] predictor and a standard RLS method with exponential forgetting, were used for comparison purposes. All three methods were tested on simulated data and real data of diabetic patients.

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Introduction:

Diabetes mellitus is a group of chronic diseases that typically exhibit high blood glucose concentrations. It is one of the most prevalent chronic diseases, continually increasing in significance and numbers. The human body regulates the blood glucose using the hormones insulin and glucagon in a negative feedback. The basic effect of the disease is the impediment of glucose intake and utilization by most cells in the body, causing unnaturally high blood glucose concentrations. Concentrations above 180 mg/dL are referred to as hyperglycemia and concentrations below 70 mg/dL are referred to as hypoglycemia. At present type 1 diabetes treatment relies solely on insulin analogs. Type 2 diabetes treatment primarily relies on exercise and diet, and secondarily on oral medication and insulin analogs. Adjustment of all treatment aspects fully depends on patient daily decisions and is aimed to keep the glycemia within normal limits throughout daily activities. The recent development of minimally invasive sensors combined with the possibility of predicting future glucose levels could highly improve diabetes management. The objective of this thesis is the implementation and testing of an algorithm for model parameter estimation from blood glucose signals of diabetics obtained from simulations, patient SMBG and a CGM device. The RPEM method was used for this purpose, combined with an OE model structure. The rationale behind this choice is to take inputs explicitly into account. A comparison with methods that take no inputs into account was also performed. The results of the implemented algorithm were compared with the results of the RICAM[1] predictor and an ordinary RLS algorithm with exponential forgetting. All algorithms were given the same learning period, namely 24 hours. The validation was performed on two days that followed the learning period. Results show that in all tested categories except on the CGM signal, the RICAM[1] predictor yields best signal fits although the obtained prediction was not always favorable. RLS is tight behind, at times being able to keep up with the RICAM[1] performance. Lastly the RPEM algorithm achieved lowest performance values except in two simulated data cases.

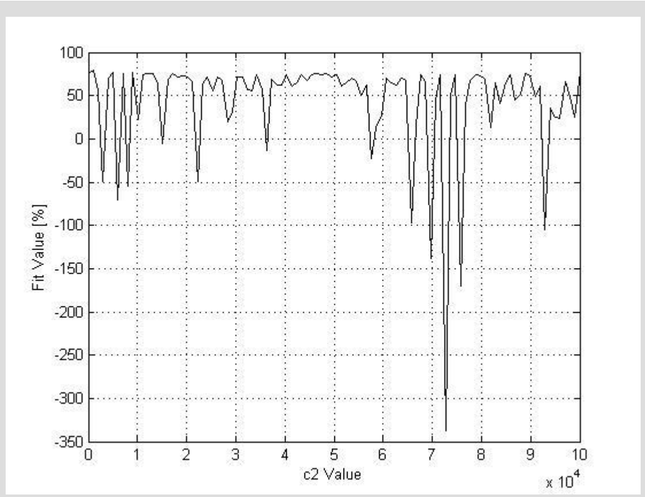
Further Topics

The MISO OE model structure was chosen due to the nature of the problem, as the measured signals contain noise from the measurement device, as well as errors arising from the approximation of a non-linear system with a linear model. The combination of method and model is assumed to provide consistent performances for variable model orders that need to be chosen prior to identification, thus requiring robustness. Another, more important rationale behind the choice is choosing a model that explicitly takes inputs into account, as they are logically the only source of blood glucose in the body.

The implementation of the chosen algorithm has initially presented instabilities making it inconsistent. The denominators become unstable by presenting poles outside the unity circle. Two methods have been additionally implemented in order to prevent this behavior. A regularization of the covariance matrix, adding a multiple of the unity matrix, has been performed. Also a pseudo parameter vector is updated and then the location of the poles proofed. If the poles remain inside the unity circle, the actual parameter vector is updated and saved for further calculations, otherwise no update is performed and the model parameters remain the same from the previous iteration.

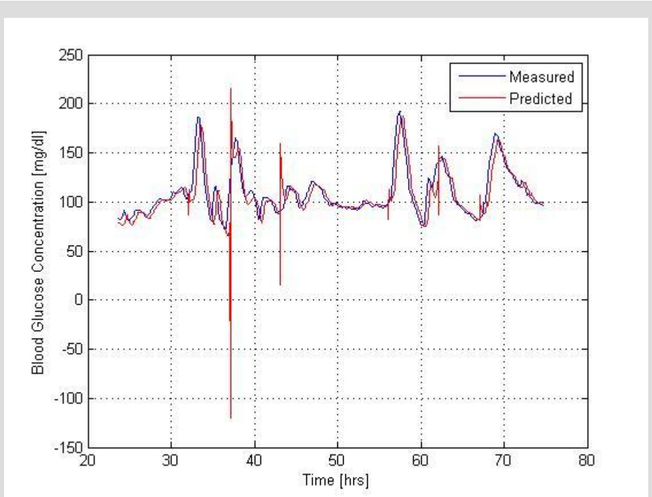
Methods were tested on data of simulated patients using the Cobelli model. Four patients were examined in this case, both with constant and variable model parameters. Tests have also been performed on recorded data of diabetics. The data from two separate trials were used, testing on two patients from each trial. The performance of the methods was estimated using different validation criteria. The Root Mean Square Error was used to evaluate the difference between the measured and predicted signal. The Fit Value (a normalized RMSE) shows how strongly the measured and predicted signal fit together in percent. Finally the Clarke Error Grid Analysis was used to provide a validation that is more clinically useful. This method indicates how the predicted values will influence the diabetes treatment of a patient and potential dangers an inaccurate glucose prediction carries.

Regularization



Searching for the best fit in estimation, an iteration over c2 values was performed, as this value highly influences the achieved performance. This is extremely time consuming as the span that has to be iterated upon is very large. The figure shows the iteration over 100 c2 values ranging between 1 and 10000, and the corresponding fit values in the case of simulated patient 4. The figure shows no particular sequence that would indicate where the maximum might lie. Also multiple maxima tend to present. This makes is almost impossible to find the maximum fit value manually by trial and error.

Instabilities



The RPEM examination of interpolated blood glucose data of patient 3 showed several spikes. Estimated parameters showed that the two parameters of the insulin nominator polynomial are both very large with opposite values, making them naturally compensating. The answer must then lie in the excitation. Inputs showed that both insulin and carbohydrates remained zero for the first 10 hours, at the beginning of the data-set. After cropping this sequence the fit value improved by approximately 9%. These findings bring the conclusion that the chosen algorithm is also sensitive to the lack of excitation.

Conclusions and Outlook

Results show that the RPEM method that considers inputs, has lower fit values than the other tested methods. The finding may appear illogical as the RICAM[1] predictor is actually an extrapolator. The RLS method used this way presents the same behavior as it only scales two past output values. Both methods use no inputs at all. This may invoke doubts considering the choices made at the beginning of this thesis, as the assumptions made were not fulfilled. The chosen method may not be appropriate for the tackled problem. The model structure might be wrong or the combination of method and model structure might be mismatched. The regularization method also has an influence on the results. Further examinations, and different choices of the testing constellation could yield detailed answers. Testing on real data of unsupervised diabetics, combined with improved measurements and more accurate sensors, provide the perfect foundation for future development.