Neural Network Based Filter for Continuous Glucose Monitoring : Online Tuning with Extended Kalman Filter Algorithm

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Abstract: - This paper deals with removal of errors due to various noise distributions in continuous glucose monitoring (CGM) sensor data. A feed forward neural network is trained with Extended Kalman Filter (EKF) algorithm to nullify the effects of white Gaussian, exponential and Laplace noise distributions in CGM time series. The process and measurement noise covariance values incoming signal. This approach answers for the inter person and intra person variability of blood glucose profiles. The neural network updates its parameters in accordance with signal to noise ratio of the incoming signal. The methodology is being tested in simulated data with Monte Carlo and 20 real patient data set. The performance of the proposed system is analyzed with root mean square(RMSE) as metric and has been compared with previous approaches in terms of time lag and smoothness relative gain(SRG). The new mechanism shows promising results which enables the application of CGM signal further to systems like Hypo Glycemic alert generation and input to artificial pancreas.

Key-words:- Continuous Glucose Monitoring, Denoising, Extended Kalman Filtering, Laplace noise, Neural network, RMSE.

1 Introduction

Diabetes becomes an alarming threat to public health. World Health Organization (WHO) has estimated that 285 million people are affected with diabetes around the world and this number is expected to increase up to 438 million by year 2030. Diabetes Mellitus is a chronic device due to the failure of pancreatic beta cells in secreting sufficient insulin. Insulin is the hormone required for the uptake of glucose from the blood stream to body cells. The glucose concentration in blood fluctuates in response to food intake, hormonal cycles or behavioral factors. The Diabetes Control and Complications Trial group (DCCT) has proved that if the blood glucose variations are maintained the range of 70 to 120 mg/dL, the complications of the disease can be avoided. The daily management of diabetes can be improved by regular monitoring of blood glucose and proper drug administration.

1.1 Continuous Glucose Monitoring

The CGM devices use minimal invasive electro chemical sensors placed subcutaneously.[1] The CGM devices assist the diabetes people in analyzing the fluctuations of blood glucose and their variation trend. Evaluation of accuracy of CGM monitors is complex for two primary reasons. 1. CGMs assess BG fluctuations indirectly by measuring the concentration of interstitial Glucose but are calibrated via self monitoring to approximate BG. 2. CGM data reflect an underlying process in time and consist of ordered-in-time highly interdependent data points.[2][3] Apart from the physiological time lag, improper calibration, random noise and errors due to sensor physics and chemistry affects the accuracy of CGM data. This deteriorates the performance of CGM signals in Hypoglycemic alert generation and control input to Artificial pancreas.

The CGM standards report [4] has provided consensus guidelines on how the data should be used and presented in CGM devices. Varied types of CGM devices are available now a days. The Food and Drug Administration (FDA) of US government has approved Glucowatch® and CGMS® with alert generation. The CGM manufacturers have not opened out the full details of their filtering. Some of their information can be known from the patents.[5][6] The studies have shown that the percentage of false alarm and missing alarm is of 50. This might be due to the insufficient filtering. Therefore more advanced technique should be adopted in the preprocessing of CGM sensor data before using it in further applications.

1.2 Review on Filtering of CGM sensor data

The signal processing in continuous glucose monitoring can be explained with the equation,

$$y_k = u_k + v_k \qquad \text{----(1)}$$

where y_k is the received CGM signal, u_k is the unknown glucose value at time 'k' and v_k is the additive noise which results for the measurement error. Given the expected spectral characteristics of noise, low pass filtering represents the most natural candidate to denoise CGM signals. One major problem with low pass filtering is that, since signal and noise spectra normally overlap, removal of noise v_k, will introduce distortion in the true signal u_k. This distortion results in a delay affecting the estimate of true signal. Understanding how denoising is done inside commercial CGM devices is often difficult, but some of the informations can be obtained from the registered patents which are given below. Medtronic Minimed has patented the use of moving average filter.[7] Dexcom suggests the use of IIR filters.[8] Panteleon and colleagues cited the use of a 7'th order FIR filter[9]. Keenan and associates have studied the delays in CGMS Gold and GuardianRT devices.[10] Chase et al., developed an integral based fitting and filtering algorithm for CGM signal, but it requires the knowledge of Insulin dosages.[11] Knobbe and Buckingham used a Kalman filter for the reconstruction of CGM data.[12] Palerm et al., used the optimal estimation theory of Kalman filter algorithm for the prediction of glucose profile and detection of hypoglycemic events.[13][14] Kuure-Kinse worked with a dual rate Kalman filter for the continuous glucose monitoring.[15] Fachinetti et al., adopted the real time estimation of parameters of Kalman filter for online denoising of random noise errors in CGM data..[16] The same group have tried the extended Kalman filter algorithm for calibration errors.[17] Facchinetti et al., arrived an online denoising method to handle intraindividual variability of signal to noise ratio(SNR) in CGM monitoring, implemented with a kalman filter by continuously updating their filter parameters with a Bayesian smoothing criterion[18]. Earlier they worked with tuning of filter parameter only in the burning interval to assess the interindividual SNR variation. Since the CGM time series observed with different sampling rates must be processed by filters with different parameters, it is clear that optimization made on order and weights of the filters cannot be directly transferred one sensor to another. Moreover, filter parameters should be tuned according to the SNR of the time series, e.g., the higher SNR, the flatter the filtering. Precise tuning of filter parameters in an automatic manner is a difficult problem for the basic filters. So far the filtering approaches have been tested with a consideration of white Gaussian noise alone in CGM sensor data. Xuesong chen identified the presence of double exponential or Laplace noise in CGM time series in his work for impact of continuous glucose monitoring system on model based glucose control.[19] Inspite of these tremendous works by various research groups, achievement of 100% accurate prediction is still a tough task. This shows the need of more smart filtering algorithms.

For reliable real time monitoring of blood glucose, the filtering algorithm should account for:

1. Short term errors due to motion artifacts.
2. Random Noise and other noise models.
3. Errors due to imperfect calibration.
4. Long term errors due to performance deterioration of sensor, bio fouling, inflammatory complications etc..
5. Uncertainty in physiological parameters.

Filtering of short term errors and random errors for the linear case is simple. To account for errors due to imperfect calibration and sensor electronics we go for non linear modeling which could be achieved with Extended Kalman Filter(EKF). But to track the uncertainties in physiological parameters, some artificial intelligent modeling technique is needed. An artificial neural network which does information processing as per the way of biological neurons would be the best choice. The processing time of neural network will be of no concern with today's high performance processors.

Therefore the proposed method Hybrid Filtering Technology (HFT) comprises of a Feed forward neural network with Back propagation algorithm trained with EKF algorithm. Training of feed forward neural network can be seen as state estimation for non linear process. The EKF method gives excellent convergence performance compared to traditional gradient descent optimization technique. Our proposed system has been tested with WGN, Exponential noise and Double Laplace noise. The remaining part of the paper is organized as follows. Section 2 describes the materials and methods, section 3 explains the hybrid filtering technique, section 4 deals with the experimental actions and results, section 5 gives the related discussion and section 6 is the conclusion.

2 Materials and Methods

2.1 Data

The data used in this paper comes from two data sets. The first set is through simulation with Monte Carlo. The second one is the real patient data set obtained through the diabetes resource [22].
In the first phase we obtained the continuous glucose profile data from the meal simulation model of Dalla Man.[20][21] 25 data sets have been generated from the simulation with different parameters of diabetic patient. Each data set is applied with Monte Carlo 20 times so as to have 20*25 = 500 sets of data. The data are added with both WGN and Double Laplace noise with varying variances of noise distributions.[23] One of the representative glucose profile is shown in figure 1. Blood glucose profiles were created with 5 minutes sampling interval.

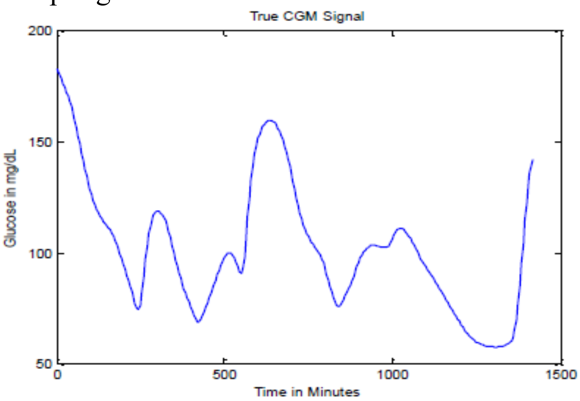

Fig.1: A Representative simulated Noise free CGM profile

2.2 Noise Distributions

Breton et al., modeled the sensor error based on a diffusion model of blood to interstitial fluid glucose transport which accounts for the time delay and a time series approach, which includes auto regressive moving average noise to account the interdependence of consecutive sensor errors. He had given a histogram of sensor error with fitted normal distribution(green) and fitted Johnson distribution(Red) which is reproduced here in figure2.

They have pointed out that the discrepancy between sensor and reference glucose differ from random noise by having substantial time-lag dependence and other non independent identically distributed (iid) characteristics.(i.e., the error is independent of previous errors and drawn from the same time independent probability distribution). But they have omitted high frequency errors(period of 1 to 15 minutes) in their modeling due to the need of fine samples.[24]

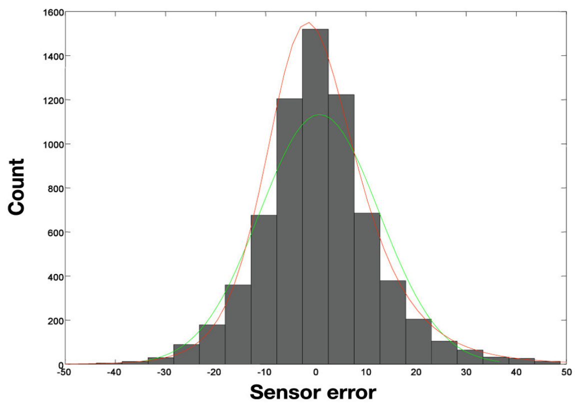

Fig 2: Histogram of of sensor error with fitted normal distribution(green) and fitted Johnson distribution(Red)

Specifically no study has reported a histogram of CGM values versus gold standard measures[25]. However an approximate model can be created using the available literature and data. The error profile can be simply and approximately modeled using a normal distribution with 17% standard deviation. This standard deviation and distribution allows 78% of the measurements to be within 20% matching the reported values in [26]. A maximum of 40% (2.5 standard deviation) can be applied. A sample model of normal distributed random noise added to a simulated glucose profile is shown in figure 3.

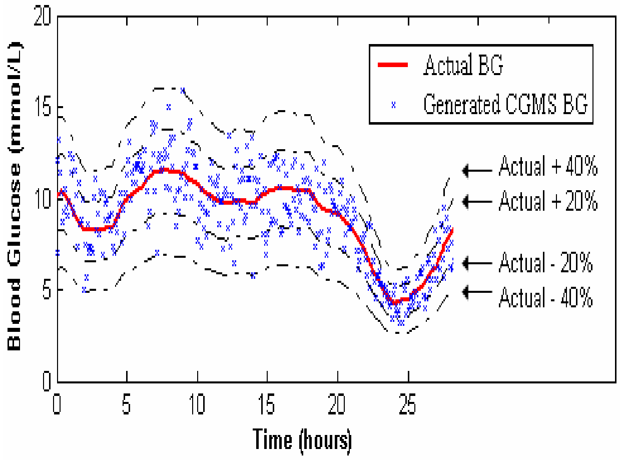

Fig 3: Example of approximated CGMS error to a simulated glucose profile. Dashed lines show 20% and 40% bounds to estimate the magnitude of any error[11]

The Laplace distribution is also called as double exponential distribution. It is a distribution of differences between two independent variates with identical exponential distribution. The probability density function of the distribution is given by

$$f((x) / \mu,b) = (1/ 2b) \exp (- (|x-\mu| / b)) \quad \text{---- (2)}$$

where 'µ' is location parameter and 'b' is a scale parameter. The Laplace distribution sets more values closer to zero. Hence it may represent the CGM sensor noise reported in the literature. The double Laplace Distribution noise is generated separately with two different pairs of standard deviation and mean. The inlier of the distribution is defined using the data reported in to lie within ± 20% range and the region from ± 20% to ±40% is defined as outliers. These two different processes are completely isolated from each other. [23]

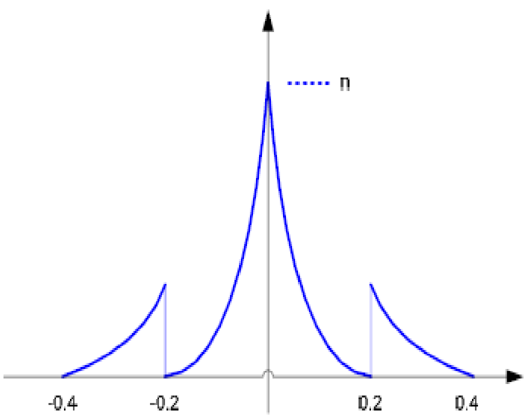

Fig. 4: Approximated Double Laplace Distribution

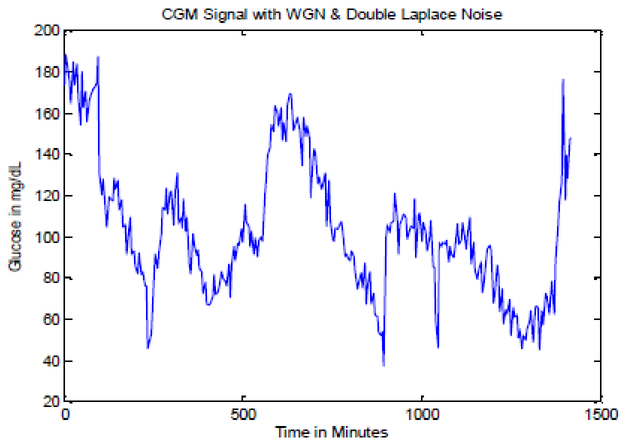

Fig. 5: A Noisy CGM Time Series

2.3 Overview of the Proposed System

BG fluctuations are continuous process in time BG(t). Each point of that process is characterized by its location, speed and direction of change. Thus, at any point in time BG(t) is a vector. CGM sensors allow the monitoring of the process in short (e.g 3 to 10 minutes) increments, producing a discrete time series that approximates BG(t). Clarke's Error Grid Analysis is used to judge the precision of the CGM sensors in terms of both accuracy of BG readings and accuracy of evaluation of BG change[2]. The data sets obtained with a simulation and with Monte Carlo are used first for training and testing the new methodology. The WGN of different variance values and the double Laplace noise distributions of different location and scale parameters are added to the generated glucose profiles. The noisy CGM data are applied to an artificial neural network that is being trained with Extended Kalman Filter (EKF) algorithm. The new filtering approach with the combination of neural network and EKF algorithm is named as Hybrid Filtering Technique (HFT). First 20% data of noisy CGM is used to train the neural network in the HFT with EKF algorithm. The remaining data is applied for filtering through HFT. The root mean square error (RMSE) between the actual value and the filtered value are computed to analyze the performance of the proposed mechanism. In our previous work, we tried this methodology with variability of signal to noise ratio (SNR) from one person to another(interperson variability).[34] This paper analyses the applicability of HFT to SNR variation in a single person(intraindividual variability).

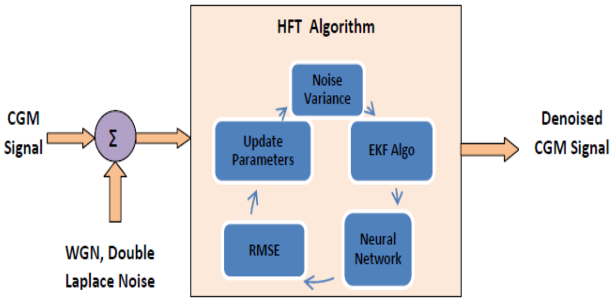

Fig.6 : Overview of Proposed System

3 Hybrid Filtering Technique

The transport of glucose from blood to ISF is represented as a diffusion model [27] given by

$$d(IG(k))/dk = -\frac{1}{\tau} IG(k) + \frac{g}{\tau} BG(k) \qquad \text{---- (3)}$$

Where $d(IG(k))/dk$ is the rate of change of ISF glucose, 'τ' is the time constant that defines the dynamic relationship between BG and IG and 'g' is the static gain that is equal to '1' under steady state conditions.

The ISF glucose is related to CGM reading with a deviation. Let ' □ ' be the time varying deviation of sensor gain from unitary value. The variation in unknown signals can be described by random walk models of order 2 which is common in physiological process. The model order is decided by Akaike Information Criteria. [28]

$$BG(k+1) = a1 * BG(k) + a2 * BG(k-1) + w1(k) \qquad \text{---- (4)}$$

$$IG(k+1) = \left(1 - \frac{1}{\tau}\right) IG(k) + \left(\frac{1}{\tau}\right) BG(k) \qquad \text{---- (5)}$$

$$\square(k+1) = c1 * \acute{\alpha}(k) + c2 * \acute{\alpha}(k-1) + w2(k) \qquad \text{---- (6)}$$

where w1(k) and w2(k) are assumed to be zero mean noise distributions with variances '$\square_1^2$' and '$\square_2^2$'.

3.1 State Space Modeling

To obtain a state space dynamic model, let x1 = BG(k), x2 = BG(k-1), x3 = IG(k), x4 = IG(k-1), x5 = □(k) and x6 = □(k-1).

Then the state equations for the process can be written as follows.

$$\left.\begin{aligned}
&x1(k+1) = a1*x1(k) + a2*x2(k) + w1(k);\\
&x2(k+1) = x1(k);\\
&x3(k+1) = \left(1 - \frac{1}{\tau}\right)x3(k) + \left(\frac{1}{\tau}\right)*x1(k);\\
&x4(k+1) = x3(k);\\
&x5(k+1) = c1*x5(k) + c2*x6(k) + w2(k);\\
&x6(k+1) = x5(k);
\end{aligned}\right\} \quad (7)$$

The measurement model is given by

$$Y(k) = x3(k)*x5(k) + v(k); \qquad \text{---- (8)}$$

Where y(k) is the CGM signal obtained with IG(k) with multiplicative sensor gain deviation □(k) and v(k) is the zero mean noise distribution with variance '$\square_3^2$'. This nonlinear measurement model is linearized with Extended Kalman Filter algorithm. [29]

3.2 Extended Kalman Filter Algorithm

The minimum variance estimate of state vector of a dynamic discrete time process is governed by a non linear stochastic difference equation

$$X(k+1) = f(X(k),w(k)) \qquad \text{--- (9)}$$

With a measurement vector,

$$Y(k) = h(X(k),v(k)) \qquad \text{---- (10)}$$

Where f and h are non linear vectorial functions. W_k and V_k are the vectors of process and measurement noises respectively. w(k) and v(k) are assumed to be zero mean white noise processes with covariance matrices Q_k and R_k respectively. 'f' is the non linear function that relates the state at previous time step 'k-1' to the state at time step 'k'. 'h' is the non linear function that relates the state and measurement vector. Estimation of state vector X is done similar to linear case.[24] The time update equations are given as follows.

Estimate of state vector :

$$\hat{x}(k+1/k) = f(\hat{x}(k/k), 0) \qquad \text{---- (11)}$$

Estimate of Covariance matrix at k'th sampling time :

$$P(k+1/k) = A_k P(k/k) A_k^T + W_k Q_k W_k^T. \qquad \text{---- (12)}$$

The measurement update equations are :

$$K_k = P(k+1/k) H_k^T (H_k P(k+1/k) H_k^T + V_k R_k V_k^T)^{-1} \qquad \text{---- (13)}$$

$$\hat{x}(k+1/k+1) = \hat{x}(k+1/k) + K_k(y(k+1) - (\hat{x}(k+1/k),0)) \qquad \text{---- (14)}$$

$$P(k+1/k+1) = (I - K_k H_k) P(k+1/k, 0) \qquad \text{---- (15)}$$

Where A_k and H_k are the Jacobian matrices of the partial derivatives of f and h with respect to X, whereas W_k and V_k are the Jacobian matrices of partial derivatives of f and h with respect to w_k and v_k respectively. K_k is the Kalman gain matrix at the k'th sample and I is the identity matrix with size as that of X.

The State transition matrix A_k obtained from the process model and the vector H_k from measurement model are applied to the neural network as initial weights.

3.3 Neural Network

The two main forms of system representation in modeling control processes are state space and input-output. Identification of nonlinear dynamic systems represented by state space difference equations can be performed by recurrent neural networks. Since the interactions between the factors for glucose metabolism are complex, multidimensional, highly nonlinear, stochastically and time variant time series, the neural network model seems to be a more suitable predictor. It has been proven that inclusion of past measurements increases the prediction accuracy of the neural network considerably.[33] The neural network can model the input-output behavior of the glucose metabolism and with the assistance of EKF , it is applied for denoising of errors in glucose dynamics.

The architecture of HFT filter is shown in figure 7. It is a multi layer feed forward back propagation neural network with an input, hidden and an output layer. The output and hidden units have bias. The input layer is connected to hidden layer and hidden layer is connected to output layer through interconnection weights. These weights are decided by extended Kalman filter algorithm. The non linearity in the glucose time series can very well be estimated and corrected by EKF. The EKF provides minimum variance estimates in system applications where the dynamic process and measurement models contain non linear relationships. Since the HFT comprises of only one hidden layer the computational complexity is less in this network.

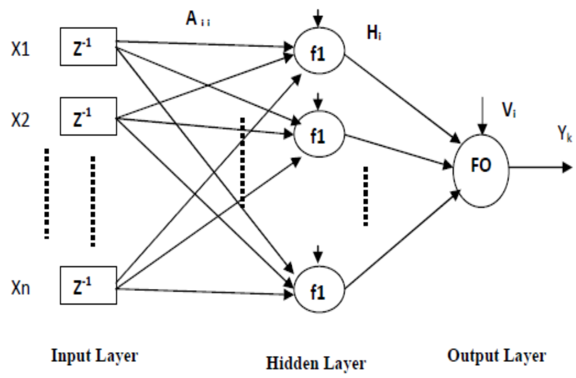

Fig 7: HFT Neural Network.

The training of back propagation network involves four stages, viz

1. Initialization of weights.
2. Feed forward.
3. Back propagation of errors.
4. Updation of weights and biases.

During first stage which is the initialization of weights, some small random values are assigned. During feed forward stage each input unit (X_i) receives an input signal and transmits this signal with a weightage to each of the hidden units $Z_1, Z_2, \ldots\ldots Z_p$. Each hidden unit summarizes the inputs and its bias (H_j),then calculates the activation function(f1) and sends its signal Z_i to each output unit. The output unit calculates the activation function(F0) with bias (V) to form the response of the net for the given input pattern.[30]

During the back propagation of errors, each output unit compares its computed activation Y_k with its target value 't_k' to determine the error. Based on the RMSE, the factor 'δ_k' (k = 1,2,….m) is computed and used to distribute the error at the output unit 'Y_k' back to all units in the hidden layer. Similarly the factor 'δ_j' is computed for each hidden unit Z_j. For efficient operation of back propagation network, appropriate parameters should be assigned for training.[31]

4 Experiments and Results

The proposed mechanism was implemented in the working platform of MATLAB (R2010a) to denoise the CGM data. The glucose profiles have been obtained from a type 1 diabetes simulator.[20][21] The anthropological parameters of the diabetes patient model such as age, weight, body mass index, disease duration etc.. for the simulator are chosen with heuristic approach so as to get different types of CGM profiles. The continuous glucose time series data were generated in varied ranges with ages between 10 to 75 and weight between 30 to 87 kg. The calories intake and insulin dosages are chosen in such a way to have hypo and hyper glycemic occurrences. 25 data sets were obtained through the simulator. Each in turn were simulated n=20 times with Monte Carlo method. Thus, there are 25x20 = 500 CGM time series in total where each is different due to the addition of noise with random parameters. Monte Carlo simulation has been used to have statistical analysis of the results. The noise sequences with variance values in the span of 5 to 25 mg^2/dL^2, and different scaling and location parameters are applied to the reference glucose profiles. The time lag for the glucose to traverse from blood to interstitial fluid is taken to be average of 6 minutes. [32]

With the aid of the simulator generated data set and real patient data obtained through the diabetes resource[22], our proposed work HFT filter comprising of neural network and extended Kalman filter has been evaluated with Monte Carlo method and validated with Root Mean Square Error (RMSE). The process and measurement noise variance are initialized with q= 0.1 and r = 0.1 mg^2/dL^2 respectively. Initially, the inputs to the neural network are applied as vectors of size 6 x 1. The state vector is of size 6 x 6. The IG values from the sensor are given to the network's input layer. At hidden layer neural nodes, the weighted inputs are applied to activation similar to tansigmoidal function. This function introduces a non linearity in the model. The nodes at output layer are applied with linear activation function. The output of the network depends upon the weights '$A^{n}_{i,j}$ ' of the neurons that are determined by the EKF state estimation and correction approach. 'n' represents n'th layer and the suffices i,j denotes the traversal of input from i'th node in first layer to j'th node in next layer. i = 1,2….N_i and j = 1,2,….N_j. In each iteration, the updated variance values are analyzed. If the rate of change is more , then the input vector size is expanded automatically to capture the intra individual variability of SNR. If the vector size is small, less number of data points are needed which usually gives a good approximate representation of the true values. Higher vector size requires more number of data points, which offers a good description of the trend in glucose profile.

The State matrix 'A' and measurement vector 'H' used in the experiment as per the above discussion in section 3.1 are given below.

A =

$$\begin{bmatrix} a1 & a2 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1/\tau & 0 & 1-(1/\tau) & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & c1 & c2 \\ 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix};$$

H = [0 0 1 0 1 0] ;

4.1 Qualitative Analysis

The noisy CGM signals are applied to both Hybrid Filtering Technique and online denoising by KF method[18]. The resultant output is compared with the actual noise free CGM time series. RMSE between the filtered signal and the true glucose signal is calculated as the performance metric. The proposed HFT mechanism has been compared with the online Kalman filter (KF) to quantify the capability of HFT in denoising the combined effects of random noise and double Laplace noise. With the trials conducted with 500 simulated data sets, it is observed that the RMSE is minimum in HFT method compared with the KF in almost all the trials.

Since KF method needed 6 hours tuning period, we also adopted the same initial training slot so as to have a uniformity in the conduction of experiment and comparison of results. The denoising capability of both the methods are analyzed in low and high SNR regions. The HFT provides perfect smoothing by the intelligence of sensing the variations in the noise variance of different noise distributions. The KF method has been developed with only white Gaussian noise in mind. Therefore when tested with combination of WGN and Double Laplace noise, the performance of KF is little lower. The results clearly prove that the HFT mechanism is able to capture and remove the combined noise effects in a superior way than the other methods. This shows that the artificial neural network in HFT is trained well with physiological variations of each individual and it tracks the glucose profile perfectly, neglecting the various noise effects in the CGM time series. The denoising effect of HFT in a representative noisy glucose profile is shown in figure 8.

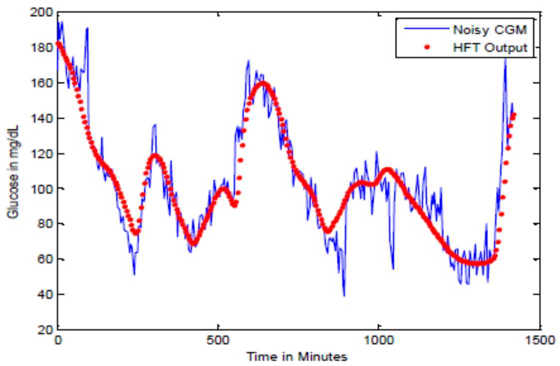

Fig : 8 Denoised CGM signal from HFT

The efficiency of HFT can very well be observed with the comparison shown in figure 9.

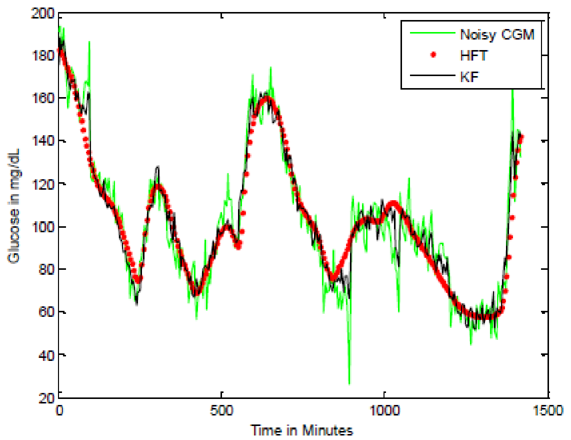

Fig.9 Denoised CGM signal from KF , HFT

The smoothing performance of HFT is corroborated with graphical representation of the enlarged view of time frame of 16 to 19 hours in figure 10 and time frame of 5 to 10 hours in figure 11 which are of different SNR values.

The figures clearly shows the oscillations in noise variance in KF output when compared with HFT which gives a smoother output. This smoothness is due to the ability of the artificial intelligent neural network that is being trained with EKF algorithm in capturing the non linear dynamics of the glucose profile.

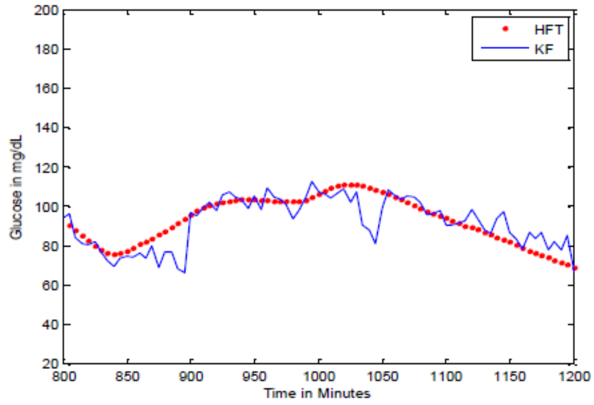

Fig .10: Enlarged view of time frame 800-1200 minutes

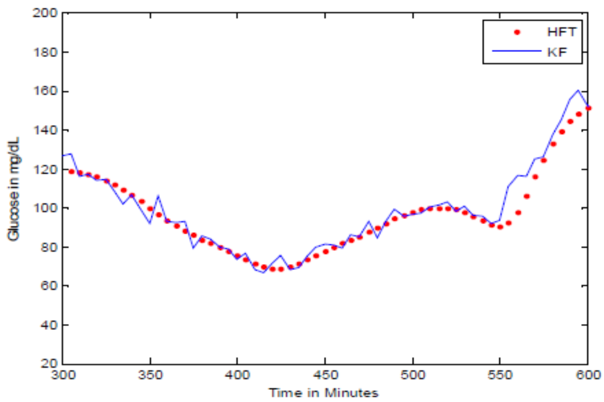

Fig.11: Enlarged view of time frame 300-600 minutes

4.2 Quantitative Analysis

The effect of denoising is quantitatively analyzed with three indexes as in [18] i.e RMSE(calculated between the denoised and real profile), the time delay(calculated as the time shift which minimizes the distance between true and denoised signal) and SRG,the smoothness relative gain(calculated as the normalized difference between energy of second order differences of the original and denoised CGM signals), in order to evaluate the regularity increase of the denoised with respect to original CGM profile. The RMSE obtained for HFT is with a mean of 5.5 ± 1.6 and for KF it is 8.3 ± 2.6. The delay introduced in the HFT is slightly higher ie. 1.9 minutes as an average whereas that of KF is 0.9 minutes. This delay is due to the estimation of neural weights with respect to the varying noise variances. SRG is high 0.95 thanks to the intelligence of neural network. The experiments were conducted with different scenarios and some representative results are listed in table 1.

S. No	RMSE (mg/dL)		Time Delay (min)		SRG	
	KF	HFT	KF	HFT	KF	HFT
1	6.1	**4.3**	0.42	**0.54**	0.88	**0.91**
2	4.3	**2.5**	0.11	**0.19**	0.89	**0.92**
3	7.8	**5.1**	0.22	**0.35**	0.76	**0.89**
4	9.4	**3.9**	0.18	**0.31**	0.65	**0.95**
5	10.9	**6.1**	0.90	**1.53**	0.5	**0.99**
6	5.7	**3.3**	0.23	**1.15**	0.74	**0.89**
7	3.8	**1.0**	0.15	**0.39**	0.56	**0.88**
8	8.1	**4.2**	0.75	**1.21**	0.81	**0.95**
9	7.3	**5.7**	0.80	**0.91**	0.69	**0.88**
10	6.7	**3.0**	0.75	**0.89**	0.78	**0.90**
11	5.9	**4.1**	0.67	**0.71**	0.67	**0.89**
12	8.6	**5.2**	0.33	**0.42**	0.61	**0.87**
13	9.3	**5.5**	0.15	**0.71**	0.74	**0.91**
14	10.5	**6.1**	0.19	**0.65**	0.59	**0.87**
15	9.0	**5.7**	0.32	**0.43**	0.74	**0.99**

Table 1: Performance Comparison of HFT and Kalman Filter

5 Discussion

Initially the approach of extended Kalman filter was used by Knobbe and Buckingham for the estimation of blood glucose and physiological parameters (i.e time lag **'t'**) [12]. Their model includes five state variables, each one has its own variance which have to be trained. Whereas Fachinetti et al., focused on EKF for improving the accuracy of CGM data by enhanced calibration in cascade to the standard device calibration. [17] Even though their model has apparently six states, the true unknown variables are only three. But different description of the variables(i.e random walk process). Here in our work we also adopted the random walk model approach for BG and sensor gain deviation parameter. The model order are fixed with Akaike information criteria and the coefficients are arrived with weighted least squares estimation. The estimated state values and their variances are sent to a neural network as parameters. The network is trained initially with these values and are altered gradually to meet out the required criteria of minimum RMSE. This approach is a newer one and we claim that the updation of neural weights and biases by EKF procedure will perform good for interindividual and intra individual variability of SNR of CGM time series.

6 Conclusion

The Continuous Glucose Monitoring is very much essential for prevention of Diabetic complications. Perfect filtering of various types of noise distributions in CGM data enables it to be used for further processing like Hypo/Hyper glycemic alert generation and as control input to closed loop artificial pancreas. Conventional filtering methods are not sufficient to track the variations of physiological signal neglecting the noise effects. Our proposed work comprising the intelligent artificial neural network with extended Kalman filter algorithm has proved its success in denoising the CGM signal with simulated data sets. The time lag that occurs in the HFT due to enormous computations of neural network can be nullified by the latest high speed processors.

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