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Data Driven Identification of IDDM Patient Model

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***Abstract*—Prerequisite to the better living of an insulin dependent diabetes mellitus (IDDM) or type-1 diabetic patients is the closed loop blood glucose regulation via subcutaneous insulin infusion and continuous glucose monitoring system (SC-SC route). Closed loop control for blood glucose level in a diabetic patient necessarily uses an explicit model of the process. A fixed parameter full order or reduced order model does not characterize the inter-patient and intra-patient parameter variability. This paper deals with a real time implementation of online identification of frequency domain kernels from the input output data of an IDDM patient. The data-driven model of the patient is identified in real time by solving Volterra kernels up to second order using adaptive recursive least square (ARLS) algorithm with a short memory length of *M*=2. The frequency domain kernels, or the Volterra transfer function (VTF) are computed by taking the FFTs on respective time domain kernels for a specific length of extended input vector. The dynamic glucose-insulin process model of a IDDM patient in SC-SC route based on the work of Dalla Man *et. al*. has been constructed in hardware platform that acts as a virtual patient. The validation results have shown good fit of responses with nominal patient in simulation as well as with online identification.**

***Keywords*— diabetes mellitus, identification, nonparametric model, Volterra kernels, hardware realization.**

I. Introduction

In modern lifestyle pattern, intensive treatment of insulin dependent diabetes mellitus (IDDM) patient or type-1 diabetics is required to avoid later life complications resulting from sustained *hyperglycemia*. The treatment of Diabetes includes solving of the optimization problem of controlling the postprandial *hyperglycemia* while avoiding *hypoglycemia*. Proper dose of insulin needs to be applied to the bloodstream intermittently through subcutaneous or intravenous infusion for tight regulation of blood glucose (BG) level in the range of 70-144 mg/dl (*normoglycaemia*) in presence of normal meal and activity conditions of the patient [1-3]. The control of glucose-insulin processes is a non-trivial task requiring a model that can accurately predict the dynamic behaviour of the patient over its complete operating range. The closed loop process to determine insulin dosage is a stochastic one in presence of meal and activity disturbances, delays in the effect of meals, glucose measurement and subcutaneous insulin action involving interplay and patient parameter variability.

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The researchers so far have mainly used the first principle model in full order or Bergman's minimal model of the glucose-insulin (GI) process [4-11] for applying modern control algorithms. The model based control algorithms have performed very well, but the inherent uncertainty in the model (or patient parameters) has not been explicitly addressed [4]. Model based controllers based on off-line measurements from a fixed model take the detailed and dynamic model of the patients, constraints on insulin infusion rates and blood glucose concentration and provide optimal insulin rates [9]. But the main disadvantage of using parametric model in model based controller is that these models lack full information of nonlinearities in such a coupled biological system. On the contrary, nonparametric model decomposes arbitrary basis functions leading to most concise signal representation and best conditions of identification algorithms and model predictive control can easily be realized if the model can be perfectly identified from the process in real time [12-21].

The present work concentrates on the online identification of a nonparametric model of the glucose-insulin process using input output data from the patient. The nonlinear glucose-insulin process model of a IDDM patient in SC-SC path based on the work of Dalla Man *et. al.* [22-25] has been simulated in LabVIEW and run with input variations. The simulated model is then deployed into the microcontroller based cRIO (compact reconfigurable input output) hardware platform [26]. The cRIO unit has been used as the standalone real time virtual patient. The input-output data from this virtual patient model have been used to identify the model online. The Volterra transfer functions or the frequency domain Volterra kernels [14-21] of the model are computed by taking FFTs on respective time domain Volterra kernels using adaptive recursive least square (ARLS) algorithm [16, 18-21] all in real time on dSPACE hardware platform [27].

The next section gives an overview of the system. Section III details on the proposed identification methodology. A real time implementation with validation is given in section IV and concluding remarks are given in section V.

II. System Overview

Fig. 1 shows the block diagram of a closed loop insulin delivery system for blood glucose (BG) regulation of an IDDM patient that uses model based control.

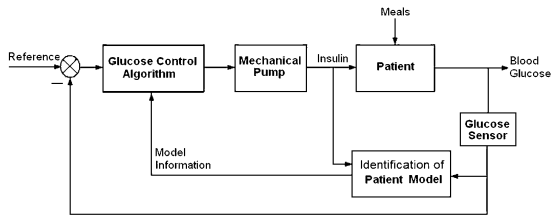

Figure 1. Closed loop blood glucose regulation in IDDM patient.

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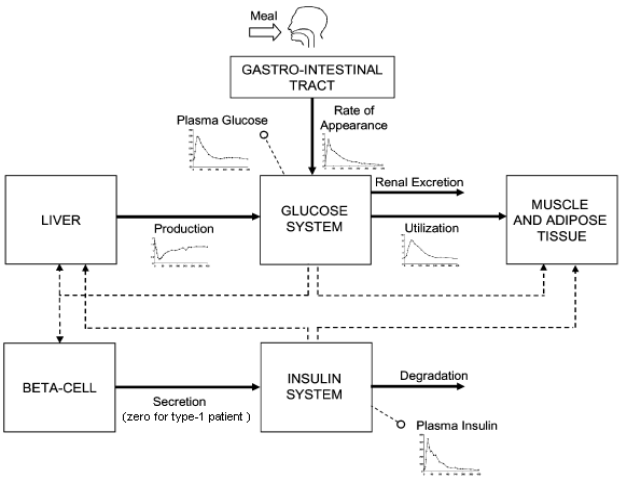

Figure 2. Scheme of the glucose insulin system [22].

A. *Model of Glucose-Insulin dynamics*

The model for glucose–insulin kinetics used in this paper is based on the dynamic equations used by Dalla Man *et.al.* [22] in the meal simulation model of the glucose-insulin system for type-1 diabetics. The structure of the meal simulation model shown in Fig. 2 includes glucose G and insulin I and the glucose fluxes, i.e., rate of appearance R_a, endogenous glucose production EGP, utilization U, renal extraction E, and insulin flux i.e. secretion S which is taken as zero for type-1 patient, and degradation D [22, 23]. The subcutaneous glucose kinetics used in this model has been developed by Magni *et. al.* [24]. The model has been successfully used by the researchers for *in-silico* trial for testing various control algorithms [25].

B. *Realization of Virtual Patient Model*

The nonlinear meal simulation model of the glucose-insulin system as described above has been reconstructed in LabVIEW simulation environment and deployed into a microcontroller based cRIO hardware platform [26] through ethernet port of PC. This is used as the standalone unit to serve as a virtual patient model. The analog input modules of cRIO are used to connect meal disturbance and insulin input. Glucose output is monitored from the analog output module. The input-output data is taken from the virtual patient cRIO module and connected through the ADC of dSPACE kit-1104 [27] for online identification of the patient. The output response from the patient and the identified model taken from DAC of the dSPACE unit are displayed as shown in Fig. 3.

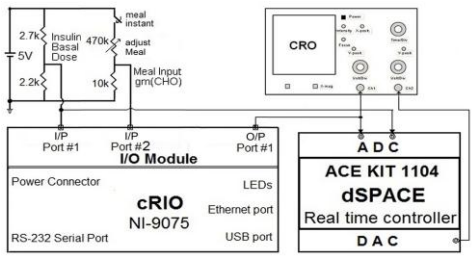

Figure. 3. Block Diagram of the connection of virtual patient model in cRIO with the identification routine in dSPACE real-time hardware.

III. Identification of Nonlinear Model Structure

Identification requires a proper choice of model structure. It involves selection of experimental parameters like sampling time and excitation signal. Block oriented models have been used by many researchers for identification of nonlinear systems. It gives insight to the complexity of the process, particularly for nonlinear processes and it has an advantage of approximating the nonlinear processes with higher accuracy with less computation time[12-21]. Nonparametric approaches represent the dynamic characteristics of the nonlinear system from expansion of the Volterra series. The adaptive recursive least square (ARLS) algorithm is used to optimize the kernels [14-16]. Frequency domain kernels directly describe the Volterra Transfer functions of the nonlinear process [15-21].

A. *Volterra kernels*

For a MISO system like the present one, with x_i number of inputs, where i=1, 2, … m, the output $y(t)$ for a memory length M is directly obtained from the generalized finite Volterra series in time domain up to second order kernel is expressed as

$$\begin{aligned} y(t) = & \sum_{\tau=0}^{M-1} g(\tau) + \sum_{i=1}^{m} \{ \sum_{\tau=0}^{M-1} g_i^{(1)}(\tau) x_i(t-\tau) \} + \\ & \sum_{i=1}^{m} \{ \sum_{\tau_1=0}^{M-1} \sum_{\tau_2=0}^{M-1} g_{ii}^{(2)}(\tau_1,\tau_2) x_i(t-\tau_1) x_i(t-\tau_2) \\ & + \sum_{j=i+1}^{m} \sum_{\tau_1=0}^{M-1} \sum_{\tau_2=0}^{M-1} g_{ij}^{(2)}(\tau_1,\tau_2) x_i(t-\tau_1) x_j(t-\tau_2) \} \end{aligned} \quad (1)$$

The self-kernels g_{ii} acting on a single input are symmetric and the cross-kernels g_{ij} acting on different inputs and they are asymmetric [12]. The second order Volterra structure for the present single-input single output GI process thus follows directly from equation (1) and the output of the process is:

$$y(t) = g^{(0)} + g^{(1)} * x(t) + g^{(2)} * x(t) * x(t) \quad (2)$$

where the 'g' denotes the respective Volterra kernels in time domain and '*' denotes the convolutions. The output $y(t)$ can also be expressed in terms of the nonlinear operators as:

$$y(t) = G(t)[x(t)] \quad (3)$$

G represents the gain of the Volterra model, which is sum of gains for a linear model and nonlinear models [12, 17] of different degrees of nonlinearity i.e.

$$G = G_1 + G_2 + \ldots\ldots \quad (4)$$

The first and second order Volterra kernels G_1 and G_2 for the SISO system are respectively given by:

$$G_1[x] = \sum_{\tau=0}^{M-1} g^{(1)}(\tau) x(t-\tau) \quad (5)$$

$$G_2[x] = \sum_{\tau_1=0}^{M-1} \sum_{\tau_2=0}^{M-1} g^{(2)}(\tau_1,\tau_2) x(t-\tau_1) x(t-\tau_2) \quad (6)$$

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B. *Implementation of the Block Oriented Models*

Since the higher order model is not very useful for computation and real time implementation purpose, the second order Volterra model having a short memory of M=2 has been considered here. The required Volterra kernels are computed online in adaptive way using recursive least square (ARLS) algorithm to select the filter coefficients [16-21] and update the same with new data set by minimizing a cost function:

$$J(t) = \sum_{\tau=0}^{t} \lambda^{t-\tau} e(\tau) = \sum_{\tau=0}^{t} \lambda^{t-\tau} (d(\tau) - y(\tau)) \quad (7)$$

where, $e(\tau)$ is the error signal and $d(\tau)$ is the desired signal and model output is $y(\tau)$. λ is a factor that controls the memory span of the adaptive filter.

C. *Frequency Domain Solution*

The frequency domain kernels of the Volterra series gives the nonlinear transfer function or the Volterra transfer function of the process which can be used for the design of Model based Controller [12-13, 15, 19, 21]. The frequency domain kernels have been computed by taking the FFTs on respective time domain kernels for a specific length of extended input vector.

The Fourier transform $G^{(k)}(f_1, f_2, \ldots f_k)$ of the k^{th} order kernel (nonlinear impulse response of order k) can be written as:

$$G^{(k)}(f_1, f_2, \ldots, f_k) = \sum_{q=0}^{Q} \sum_{\tau_1=0}^{M-1} \sum_{\tau_2=0}^{M-1} \cdots \sum_{\tau_k=0}^{M-1} g^{(k)}(\tau_1, \tau_2, \ldots, \tau_k) \sum_{q=0}^{k} \exp(-j2\pi f_q \tau_q) \quad (8)$$

where, Q is the maximum order of the kernel. The frequency domain kernels have been computed by taking the fast Fourier transforms (FFTs) of the respective k^{th} order time domain kernel (nonlinear impulse response of order k).

The online identification of the data driven model of the Glucose-Insulin process of a IDDM patient uses the overlap-save algorithm [19-21] with appropriate length N of model structure depending on the memory M. The insulin infusion level from and the glucose output produces the Volterra kernels $G_1$and G_2 of equations (5) and (6). Normal postprandial blood glucose level of 130*mg/dl* [23] is taken as the reference 'blood glucose' level for the ARLS filter. The flowchart of the identification process in frequency domain is shown in Fig. 4. The algorithm is listed below:

1. Considering the present data and one previous data and memory length M=2, the extended input vector for the present model structure of length $N=M(M+1)/2 + M = 5$ is created for the nonlinear part of the Volterra model.
2. By overlap-save algorithm, N no. of zeros are added left to the extended input vector and the time domain kernels are computed by ARLS algorithm from the extended input vector of size 2N.

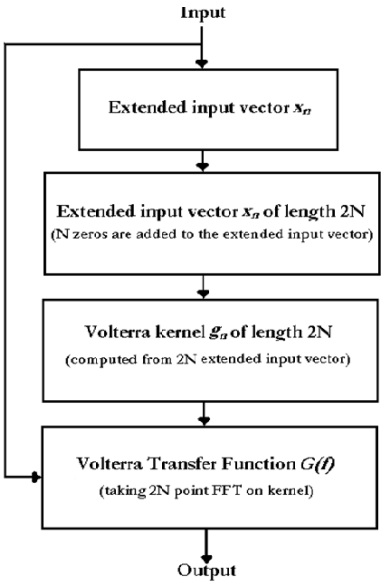

Figure 4. Flow chart of identification algorithm.

3. 2N point FFTs are taken on the kernel g(n) which acts as a nonlinear transfer function or the Volterra transfer function (VTF) of the process and then input data is multiplied with the VTF to generate the output.
4. The input–output data from the process is refreshed with the next sample of data and the steps 1–3 are repeated.

IV. Validation of Identification Algorithm

As the physiological process of an IDDM patient is completely lacking endogenous insulin secretion, the BG level rises to a large value in open loop. The identification algorithm in both simulation and hardware platform has been tested with 45g of glucose ingested at 8 a.m.(500min from start time), 70g at noon, and 70g at 8 p.m. and the target glucose level is 130 *mg/dl* as used in [23]. Fig. 5 shows the photograph of the hardware set-up for experimentation on the virtual patient model with cRIO and dSPACE 1104 kit to run in real time. The performance results exhibit a good match with the output both in the simulation result as shown in Fig. 6 and also from real time identification as shown in Fig.7.

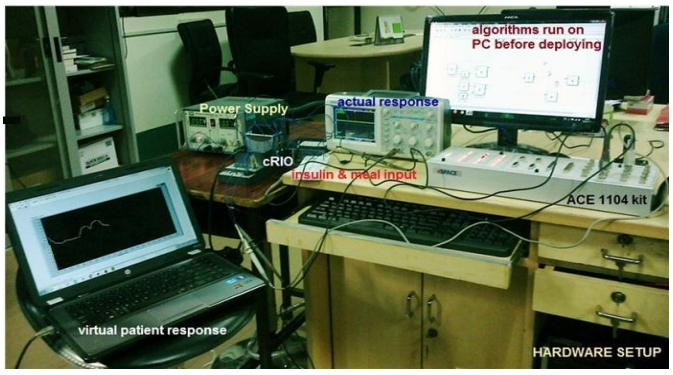

Figure 5. Photograph of Experimental Set-up with cRIO & dSPACE units.

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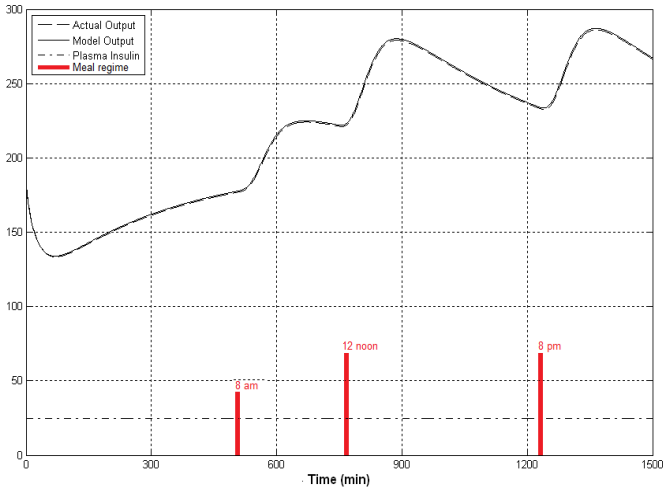

Figure 6. Simulation result of proposed algorithm with nominal model.

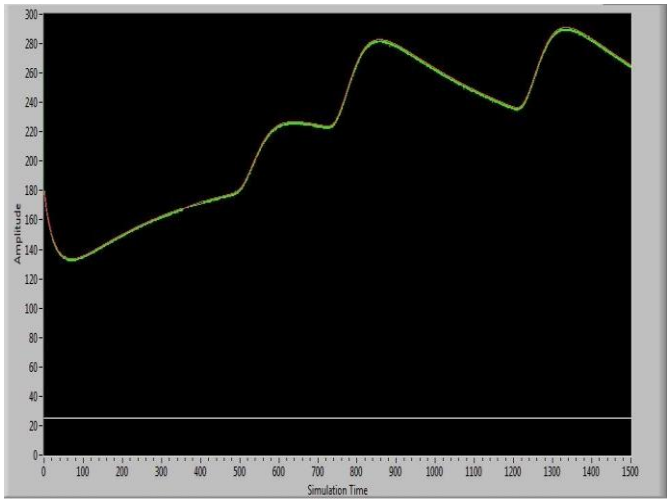

Figure 7. Response from online identification with Virtual patient model- red: Actual output, green: Identified model output and white: Plasma insulin.

v. Conclusion

A data driven block-oriented modeling in frequency domain for the nonlinear dynamic system of multivariable glucose-insulin process in IDDM patient has been presented. The algorithm has relatively short memory effects. The advantages of block-oriented model have been utilized with proper selection of Volterra kernels by ARLS algorithm and extended input vectors for the nonlinear process containing both deterministic insulin input as well as meal disturbance.

The online identification of the data driven model of the glucose-insulin process of the IDDM patient in hardware platform has been tested with the same amount of meal input ingested at the same instant of time as in the simulation experiment. The closeness of the glucose output from the cRIO model and the output of the identified model as shown in Fig. 7 confirms the model's accuracy for nominal patient in real time environment too.

Frequency domain Volterra term is expressed by means of a product with FFT inputs over the finite memory interval on time domain Volterra terms expressed by means of a multifold convolution integral. The set of kernels obtained from the present frequency domain Volterra model describes the nonlinear transfer functions or Volterra Transfer Function (VTF) of the nonlinear process in varied conditions of the patient that can be directly used in model based control.

The present method will be useful to the researchers for testing various model based control algorithms directly on the patient model derived from real time data of the patient instead of *in-silico* trial which uses a fixed UVa/Padova T1DM metabolic simulator model [25].

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