Diabetes Monitoring System

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Abstract:

This chapter reviews the current technologies for monitoring and intervention of diabetes. Especially various blood glucose concentration estimation, online signal monitoring and adaptive control mechanisms are discussed. Recent research has proposed many control engineering approaches for Type 1 diabetes and many algorithms of artificial pancreas have been proposed. This book chapter reviews the current state of the art and industrial standards on diabetes monitoring and control.

1. Measurements, Model Estimation and Control of Diabetes

Diabetes control is inherently an interdisciplinary field of study. Almost 50 years of research has been done on this which has proposed many models and closed control strategies to develop artificial pancreas. Diabetes is a metabolic disorder characterized by chronic hyperglacemia leading to microvascular and macrovascular complications. Diabetes can be divided in two categories – type 1 and type 2, although their pathogenesis is different. Type 1 diabetes is caused due to immune-mediated destruction of the beta-cells in the site of insulin secretion and production. This is not related to obesity but it can cause other cardiac complications. Type 1 diabetes is usually treated by insulin therapy to control hyperglycemia and for sustain life. Whereas in type 2 diabetes, the insulin secretion is inadequate which results in gyperglycemia. Usually the type 2 diabetes is related to increasing age (usually after 40), excess caloric intake, less physical activity, obesity which are play a big role in its development. It also causes other cardiovascular risks like dyslipidemia and hypertension. It has been estimated that almost 90% of the world diabetes population is of type 2 and 5-10% is of type 1. Over the years, diabetes leads to many other complications like diabetic retinopathy (leading to blindness), diabetic neuropathy (leading to limb loss), kidney failure, heart disease and stroke with double risk of dying.

The world health organization (WHO) has estimated that more than 180 million people in the world have diabetes which is likely to be doubled by 2020 [1]. Diabetes is the fifth highest case of death after communicable diseases, cardiovascular diseases, cancer and injury and also is a primary cause of death in low and middle income countries. Due to high complexity of this disease, studies of many disciplines are needed e.g. physiology and pathophysiology, dugs, artificial pancreas, transplantation, patient management, healthcare, systems biology.

The glucose insulin control system in the body is regulated by a complex neuro-hormonal control system. It is done by insulin which is the primary regulator of glucose homeostasis that promotes glucose utilization and inhibits glucose production for stored resources in the body. Counter-regulatory hormones like glucagon, epinephrine, cortisol, and growth hormone which work in different scales defends the body from life threatening hypoglycaemia. The insulin control and hypoglycaemia counter-regulation are balanced by neuro-modulation. Glucose in the body is produced by the liver and utilized in both insulin dependent (which includes central nervous system, red blood cells) and insulin independent tissues (muscle and adipose tissues). Insulin is secreted by the beta-cells in the pancreas, and then reaches the system circulation after liver degradation and finally cleared by the kidney. The glucose and insulin systems interact by feedback control signals e.g. after a meal when the glucose perturbation occurs, the beta-cells secret more insulin after sensing the high plasma glucose concentration. This promotes glucose utilization and inhibits the glucose production to balance the plasma glucose which are known as the insulin sensitivity and beta-cell responsivity both of which are

progressively deteriorated in type 2 diabetes. In type 1 diabetes, the beta cells becomes silent in response to the glucose perturbation and therefore, insulin must be provided exogenously into the patient's body to compensate for the hyperglycemia. However, often insulin treatment is risky and may lead to severe hypoglycaemia. Therefore, for type 1 diabetic patients it is challenge to maintain reduce hyper-glycemia without increasing the risk of hypo-glycemia. Blood glucose level is the measured quantity in such optimization and several control models have been developed to assist diabetes control. The following section reviews few models commonly used in diabetes control.

2. Minimal Models

Minimal models describes the key functionality, rather than describes the detailed substrate/hormone interactions. In addition minimal models on contrary are much simpler and for large detailed models, it is usually difficult to estimate all model parameters from *in-vivo* dynamic data. The desirable features for a minimal model include:

- Physiologically motivated
- Parameter estimation possible with good precision with a single dynamic response of the system
- The model parameters should vary within physiologically plausible ranges
- The whole system dynamics can be described with minimum number of parameters.

The glucose system is divided in many parts of a compartmental model [1] viz.

- Steady state insulin action
- Non-steady state insulin action
- Dynamic perturbation
- Dynamic perturbation with tracer

The response of plasma glucose and insulin to an oral or intravenous administration of glucose is given by the following system of ordinary differential equations (ODEs):

$$\begin{aligned} \frac{dG(t)}{dt} &= -a_1 G(t) - a_2 I(t) + J(t) \\ \frac{dI(t)}{dt} &= a_3 G(t) - a_4 I(t) \end{aligned} \tag{1}$$

where, the system parameters are given as:

G: plasma glucose,

I: plasma insulin,

J: glucose input either as an intravenous injection or the absorption rate of glucose during a meal or an oral glucose tolerance test.

The minimal model assumes that glucose kinetics can be described by one compartment and the remote insulin controls both the net hepatic glucose balance and peripheral glucose disposal:

$$\begin{aligned} &\frac{dQ_1(t)}{dt} = \mathrm{NHGB}\big(Q(t), I'(t)\big) - R_d\big(Q(t), I'(t)\big) + D \cdot \delta(t), \quad Q(0) = Q_b \\ &\frac{dI'(t)}{dt} = -k_3 \cdot I'(t) + k_2 \cdot \big[I(t) - I_b\big], \quad I'(0) = 0 \\ &G(t) = \frac{Q(t)}{V} \end{aligned} \tag{2}$$

where, the parameters are given by:

Q: plasma glucose mass,

Q_b: basal value of the plasma glucose mass,

I: plasma insulin concentration,

I_b: basal value of the plasma insulin concentration,

D: glucose dose,

V: glucose distribution volume,

k_2, k_3 are the rate parameters.

The net hepatic glucose balance (NHGB) depends upon plasma glucose and remote insulin (I') as:

$$\mathrm{NHGB}\left(Q(t), I'(t)\right) = \mathrm{NHGB}_0 - \left[k_5 + k_6 \cdot I'(t)\right] \cdot Q(t), \tag{3}$$

where, R_d is the rate of glucose disappearance from the peripheral tissues and given by:

$$R_d\left(Q(t), I'(t)\right) = R_{d0} + \left[k_1 + k_4 \cdot I'(t)\right] \cdot Q(t) \tag{4}$$

This nonlinear model is usually reparametrized in order to be uniquely identifiable as:

$$\begin{aligned} &\frac{dQ(t)}{dt} = -\left[p_1 + X(t)\right] \cdot Q(t) + p_1 \cdot Q_b + D \cdot \delta(t), \quad Q(0) = Q_b \\ &\frac{dX(t)}{dt} = -p_2 \cdot X(t) + p_3 \cdot \left[I(t) - I_b\right], \quad X(0) = 0 \\ &G(t) = \frac{Q(t)}{V} \end{aligned} \tag{5}$$

with the following relations:

$$\begin{aligned} X(t) &= \left(k_4 + k_6\right) \cdot I'(t) \\ p_1 &= k_1 + k_5 \\ p_2 &= k_3 \\ p_3 &= k_2 \cdot \left(k_4 + k_6\right) \\ p_4 &= NHGB_0 - R_{d0} = p_1 \cdot Q_b. \end{aligned} \tag{6}$$

The meaning of the parameters are:

X: insulin action,

p_1: fractional (i.e. per unit distribution volume) glucose effectiveness,

p_2: rate constant of the remote insulin compartment where the insulin action emanates from,

p_3: scale factor which governs the amplitude of insulin action.

This model allows the estimation of insulin sensitivity as:

$$S_I^{IVGTT} = \frac{p_3}{p_2} \cdot V \quad \left(\mathrm{dl/kg/min\ per\ } \mu\mathrm{U/ml}\right), \tag{7}$$

where, S_I^{IVGTT} is a steady-state measure which means it does not account for how fast or slow the insulin action takes place.

Another mass balance equation is also used by describing the rate of appearance of glucose into plasma (Ra) as:

$$\frac{dQ(t)}{dt} = -\left[p_1 + X(t) \right] \cdot Q(t) + p_1 \cdot Q_b + Ra(t, \boldsymbol{\alpha}), \quad Q(0) = Q_b \tag{8}$$

with $\alpha = \left[\alpha_1, \alpha_2, \cdots, \alpha_N \right]$ the parameter vector describing *Ra*.

In the dynamic perturbation with tracer category, another important quantity is the endogenous glucose production (EGP) responsible for negligible or negative action of insulin on the liver and is given by:

$$EGP(t) = EGP_b - GE^L \cdot \left[G(t) - G_b \right] - X^L(t) \cdot G(t), \quad EGP(0) = EGP_b \tag{9}$$

where, the parameters are given as:

EGP_b : basal endogenous glucose production,

GE^L : liver glucose effectiveness,

G: glucose concentration and G_b being its basal value,

X^L is the liver insulin action or the deviation from insulin.

This follows the following dynamical system:

$$\frac{dX^L(t)}{dt} = -p_2 \cdot X^L(t) + p_3^L \left[I(t) - I_b \right], \quad X^L(0) = 0, \tag{10}$$

where, p_2: rate constant describing the dynamic action of insulin action on glucose production,

p_3^L : scale factor governing amplitude of hepatic insulin action.

An improved model has been suggested in [1] as:

$$EGP(t) = EGP_b - k_G \cdot \left[G(t) - G_b \right] - X^L(t) - X^{Der}(t), \quad EGP(0) = EGP_b \tag{11}$$

where X^L can be described by the system of ODEs:

$$\begin{aligned} \frac{dX_1(t)}{dt} &= -p_2^L \cdot X_1(t) + p_3^L \cdot \left[I(t) - I_b \right], \quad X_1(0) = 0 \\ \frac{dX^L(t)}{dt} &= -p_2^L \cdot X^L(t) + p_3^L \cdot X_1(t), \quad X^L(0) = 0 \end{aligned} \tag{12}$$

and

$$X^{Der}(t) = \begin{cases} k_{GR} \cdot \dfrac{dG(t)}{dt}, & \text{if} \quad \dfrac{dG(t)}{dt} \geq 0 \\ 0, & \text{if} \quad \dfrac{dG(t)}{dt} < 0 \end{cases} \tag{13}$$

where the two parameters are:

p_2^L: rate constant describing dynamics of insulin action on glucose production,

p_3^L: scale factor governing amplitude of hepatic insulin action,

k_{GR}: parameter governing magnitude of glucose derivative control.

The endogenous glucose production can be calculated by using the endogenous glucose concentration (G_{end}) which indicates the compartment of total glucose concentration measured in plasma due to glucose production. The quantity G_{end} is related to the endogenous glucose production EGP by the integral equation:

$$G_{end}(t) = \int_0^t h(t,\tau) \cdot EGP(\tau) \cdot d\tau + G_b \cdot h(t,0) \tag{14}$$

where, $h(t,\tau)$ is the time-varying impulse response of glucose system given by tracer minimal model and G_b is basal glucose.

The whole body to tissue model usually employs tracer elements and is described the following ODEs:

$$\begin{aligned}
\frac{dC_c(t)}{dt} &= K_1 C_p(t) - (k_2 + k_3) C_c(t) + k_4 C_e(t), \quad C_c(0) = 0 \\
\frac{dC_e(t)}{dt} &= k_3 C_c(t) - (k_4 + k_5) C_e(t), \quad C_e(0) = 0 \\
\frac{dC_m(t)}{dt} &= k_5 C_e(t), \quad C_m(0) = 0
\end{aligned} \tag{15}$$

and

$$C(t) = (1 - V_b)\left(C_c(t) + C_e(t) + C_m(t)\right) + V_b C_b(t) \tag{16}$$

where, the parameters are given as:

C_p: Fluorodeoxyglucose (FDG) plasma arterial concentration,

C_c: Extra-cellular concentration of FDG normalized to tissue volume,

C_e: FDG tissue concentration,

C: Total ^{18}F activity concentration in the region of interest,

K_1 [ml/ml/min] and k_2 [min^{-1}] are the exchange between plasma and extracellular space,

k_3 [min^{-1}] and k_4 [min^{-1}] are the rate of transport in and out of the cell,

k_5 [min^{-1}] is the rate of phosphorylation,

V_b: fractional blood volume in the region of interest,

C_b: whole blood tracer concentration.

From these models one can calculate the fractional uptake of the FDG, K [ml/ml/min] as:

$$K = \frac{K_1 k_3 k_5}{k_2 k_4 + k_2 k_5 + k_3 k_5} \tag{17}$$

More details of this model can be found in [1].

For an insulin system, firstly an insulin kinetics model in steady state and insulin secretion can be investigated. The C-peptide concentration measurements (C) are linear in a wide range of concentration and related to the basal pancreatic secretion by the following convolution integral:

$$C(t) = \int_0^t h(t-\tau) \cdot SR(\tau) \cdot d\tau \tag{18}$$

where, h is the impulse response function of this system.

As described before, during IVGTT, the basal insulin secretion model is given by the pancreatic secretion rate (SR) as:

$$SR(t) = m \cdot F(t) \tag{19}$$

with F as the ready releasable insulin given by the ODE:

$$\frac{dF}{dt} = -m \cdot F(t) + Y(G,t), \quad F(0) = F_0 \tag{20}$$

with F_0 the amount of insulin released immediately after the glucose stimulus and $Y(G,t)$ is the provision of new insulin which depends on the glucose level:

$$\frac{dY(G,t)}{dt} = -\frac{1}{T} \cdot \left[Y(G,t) - Y(G,\infty) \right], \quad Y(0) = 0. \tag{21}$$

3. Maximal Models

Compared to the minimal models as described above, the maximal models are more detailed or fine-grained, nonlinear, higher order and with large number of parameters to estimate. Usually such models are not possible to estimate without running large experimental investigations. However, such models have been widely used for simulation purpose to check model validity. A healthy state simulator has been described in [1] on 204 nondiabetic subjects with simulation models of plasma glucose, plasma insulin, endogenous glucose production, glucose rate of appearance, glucose utilization, insulin secretion etc. Maximal models have also been used for prediabetes and type 2 diabetes simulator, type 1 diabetes simulator with unit process models and forcing functions for the liver, gastro-intestinal tract, muscle and adipose tissue, beta cell. *In-silico* subject simulation has been reported in [1] with a feedback controller and simulated insulin pump for type 1 diabetes. For the insulin secretion the following mass balance equations are used for the intermediate pool (I):

$$\frac{dI(t)}{dt} = M(g,t) - r \cdot I(t) - p^+ \cdot I(t) + p^- \cdot \int_0^\infty h(g,t) \cdot dg \tag{22}$$

where, M is the mobilization flux and r is the rate of reinternalization.

The readily releasable pool (RRB) can be described by the time varying density function $h(g,t)$ that indicates the amount of insulin in the RRP in beta-cells with a threshold between g and (g + dg). The granules are primed with rate p^+ and they are assumed to loose the capacity with rate p^-. It is also considered that if the granule is in a triggered beta-cell it will fuse with rate f^+ which leads to the following equation:

$$\frac{dh(g,t)}{dt} = p^+ \cdot I(t) \cdot j(g) - p^- \cdot h(g,t) - f^+ \cdot h(g,t) \cdot \theta(G-g). \tag{23}$$

Here, $\theta(G-g)$ is the Heaviside step function which takes the value of unity for $G > g$ and zero otherwise. Also, I is total intermediate pool, the primary flux $p^{+}I$ distributes among cells with threshold g, described the time constant function $j(g)$.

4. Diabetes Monitoring Signals and Controls

Various signal processing techniques have been historically used since 1970s during in-hospital monitoring of blood glucose concentration and other substances like insulin, C-peptide, glucagon etc. New continuous glucose monitoring (CGM) systems have emerged recently that are capable of monitoring glucose concentration as frequently as every 5 minutes. These CGM monitoring devices are minimally invasive, portable, measuring glucose subcutaneously and assessing blood glucose concentration indirectly though interstitial fluid sampling. Although the measurement accuracy are not fully solved yet but this technology shows high potential for real-time prevention and treatment of hypo- and hyper-glycemia. Amongst various signal processing methods, glucose-insulin oscillations, peak detection and spectral/correlation analysis, hormone pulsatility and use of approximate entropy are notable. Other challenges of continuous glucose monitoring with time series data include CGM sensor calibration, CGM vs. blood glucose measurement, filtering, prediction, hypoglycaemia vs. hyperglycemia alert etc.

Several architectures have been proposed for glucose control. This includes safety algorithms and real-time control. In various real-time control schemes, the feedback and feedforward control, autoregressive moving average exogenous (ARMAX) and nonlinear ARMAX system identification, proportional integral derivative (PID) control, model predictive control (MPC) with quadratic cost and constraints on the manipulated variables (insulin pump), real-time detection and estimation using Kalman filter are notable [1]. For tuning the control loops various strategies have been adopted e.g. control variability grid analysis, robustness vs. personalization of the controller parameters, run to run control and behavioural analysis etc. More in-depth models, signals and control strategies for diabetes are discussed in [1] and the large number of references therein.

Recently, Turksoy *et al.* [2] introduced a multi-module multivariable adaptive control strategy for artificial pancreas for type 1 diabetes. The artificial pancreas collects information from many sensors, computes the optimal insulin amount to be infused and the then manipulates the infusion rate of the pump. A recursive model of glucose concentration dynamics is first estimated using the ARMAX method of system identification. The controller takes various inputs e.g.

- Glucose and activity feedback
- Hypoglycemia detection and carbohydrates suggestion
- Meal detection and hyperglycemia prevention
- Exercise classification
- Fault detection and diagnosis.

Using these inputs the multivariable adaptive controller drives the insulin infusion pump for the patient. The measurements in this scheme are used as – continuous glucose monitoring sensor and wearable biometric sensors. The study in [2] also concluded with clinical experiments that the multivariable approach provides better results than the single variable version using only CGM measurement.

Meal detection has further been researched in [3] for nine patients with type 1 diabetes over 27 different main meals. The multivariable adaptive artificial pancreas system includes a minimal model similar to equation (1), followed by unscented Kalman filter for state estimation of the nonlinear system. The CGM measurements are used for nine subjects during breakfast, lunch, dinner to validate the algorithm. A similar analogue PID based glucose control algorithm was implemented in [4] using a β-cell model and comprising of an ODE and the sigmoid function, known as the Hill equation. For type 1 diabetes

control using artificial pancreas, PID and sliding mode reference conditioning based safety auxiliary feedback control has been implemented in [5] with enhanced robustness and fault-tolerance properties.

A model predictive iterative learning control (MPILC) scheme has been proposed in Wang *et al.* [6] for artificial pancreatic β-cells in type 1 diabetes. This involves a virtual patient which uses an autoregressive exogenous (ARX) model. Robustness of the MPC and ILC on repetitive and non-repetitive diets, robustness to subject variations, set-point updating have also been investigated.

For type 1 diabetes patients an improved overnight safety scheme has been proposed in Facchinetti *et al.* [7] for online failure detection of the glucose sensor and insulin pump system. There are two cases considered viz. CGM sensor failure and continuous subcutaneous insulin infusion (CSII) pump failure. The failure detection employ a Kalman predictor and online prediction and alert module. The method was validated on *in-silico* data of 100 virtual subjects and also real type 1 diabetes mellitus (T1DM) data. Robustness of the failure detection monitoring system against noise and domain of validity has also been investigated on these two databanks.

In the field of closed loop control of diabetes, the MPC has been found to have wide applicability over conventional therapy in the development of artificial pancreas with various modules e.g. data handling/filtering, state estimation/update, closed-loop control algorithm, safety supervision algorithm, actuation, data-logging and outcome measures etc. [8]. For modular control the two important issues are – design flexibility, incremental testing, regulatory approval and deployment. The safety supervision algorithm has various elements like insulin request classifier, correction filter, other elements like hypoglycaemia indicators etc. This system is based on a linear MPC which has linearized model of the nonlinear insulin-glucose dynamics. Also, the MPC works on the difference between the CGM signal and the patient's nominal blood glucose profile with improved individualization capability and has been validated on *in-silico* experiments.

5. Non-invasive Diabetes Monitoring

Recently, more works are devoted on non-invasive monitoring of diabetes. As an example, Pai *et al.* [9] used a cloud computing platform to implement a photoacoustic spectroscopy system with detailed calculation of the signal to noise ratio (SNR). In the calibration and testing phase, several well-known signal processing operations like pre-processing, feature extraction (e.g. positive/negative peaks, max/min peak, peak to peak amplitudes), followed by *in-vitro* and *in-vivo* testing, glucose estimation using polynomial kernels. The estimation performances were compared with respect to three accuracy measures: root mean square error (RMSE), mean absolute difference (MAD), mean absolute relative difference (MARD) which results in a kernel based calibration model for continuous non-invasive glucose monitoring using photoacoustic measurements. The algorithm has been deployed in mobile cloud computing platform with internet of things (IoT) devices, internet gateway, cloud services with dataflow pipelines like data processing, data analytics, data storage, application control etc. the embedded back-end implementation was tested against power consumption, security, *in-vitro* testing, system stability, safety, *in-vivo* testing etc.

Much of the future research in this domain are expected to have few key functionalities: unobtrusive sensing, modelling the onset and progress of diabetes mellitus and user-centred approach [10]. Zarkogianni *et al.* [10] reviewed various emerging technologies for the management of diabetes mellitus. Amongst the commercially available devices only two uses non-invasive methods like Raman spectroscopy (HG1-c by C8 Medisensors) and thermal ultrasound and electromagnetic (GlucoTrack by Integrity Applications Ltd.). These devices has been benchmarked against other invasive devices by Dexcom, Medtronic and Abbott with detailed comparison of the sensor lifetime, sensor warm up time, frequency of calibration, frequency of recording, accuracy etc. Several artificial intelligence (AI) models for type 2 diabetes risk prediction and early diagnosis has been reviewed in [10] e.g. fuzzy neural networks (FNN), adaptive neuro-fuzzy inference system (ANFIS), support vector machine

(SVM), linear discriminant analysis (LDA), adaptive network based fuzzy inference system and mixture of experts (ME) and their performances are compared using classification accuracy, sensitivity, specificity etc. For long-term risk modelling several statistical models e.g. cox regression, Tobit survival regression, Cox proportional hazard model and fractional polynomials, univariate and multivariate logistic regression, survival analysis, Weibull proportional hazard regression, Markov model etc. have been used for different size of cohorts (55, >1000, >5000, >1.2 million etc.). Moreover, several glucose prediction models are compared in [10] based on AI and autoregressive models. Long term implanted sensor/telemetry systems are studied in [11] for glucose monitoring for patients with diabetes. Raman spectra of blood has also been used for glucose monitoring devices in [12].

6. Recent Research Trends in Diabetes Monitoring and Control

Diabetes monitoring and control is emerging as a prominent research discipline. In the Scopus search some patterns were retrieved for the first 2000 highest cited papers on this topic. The word-clouds in Figure 1 shows that in the papers titles, few frequently used words are: diabetes, glucose, type1 and 2, insulin, monitoring along with some relatively less used words like cardiovascular, glycemic, close-loop, management, self-monitoring, pump etc. These word frequencies show the relative research efforts and different sub-areas in this field which are actively growing. Figure 2 also shows a bar chart of type of recently published works which shows there were many more journal research articles than review articles, followed by conference papers, short survey and letters.

Figure 1: Word-clouds of the titles of recent diabetes monitoring research papers. Datasource: Scopus.

Similar to exploring the article titles, next Figure 3 shows the indexed and author's keywords in the top 2000 papers in this active research area. As opposed to the title based text analysis, often the keyword based analysis is capable of capturing finer technical details or an emphasis of fewer most popular technologies. In both the word-clouds, apart from diabetes, the most frequent words were glucose, insulin, blood, monitoring, continuous, control etc. which shows the finer details of the technologies gradually increasing over the years. While exploring the citation patterns in this research field in Figure 4, it is clear that the citations of the papers on diabetes monitoring has rather a drooping characteristics, at least for the upper quartile. The gradual decrease in the median citation from year 2000 almost follows an exponential trend, because the citation dynamics is usually a cumulative phenomenon and as such recent technological advancements take years to get assimilated in clinical practice. Also there are more outliers in the papers between the years 2001-2013 as shown in Figure 4 which indicate there are few highly impactful papers, compared to the citation of average papers published in the recent years. Next

we, explore the source titles of the top 2000 papers on this topic as shown in Figure 5. It is evident that most of the impactful papers were published in the journals like Diabetes Care (American Diabetes Association), Diabetes Technology and Therapeutics (Liberto Pub.), Journal of Diabetes Science and Technology (Sage), Diabetic Medicines (Wiley), Diabetologia, Diabetes (American Diabetes Association), The Lancet, IEEE Transactions on Biomedical Engineering etc. A more focussed study on mobile health technologies for diabetes mellitus ranging the years 2011-2017 and using 3 databases – ScienceDirect, SpringerLink and IEEEXplore have been reported in [13].

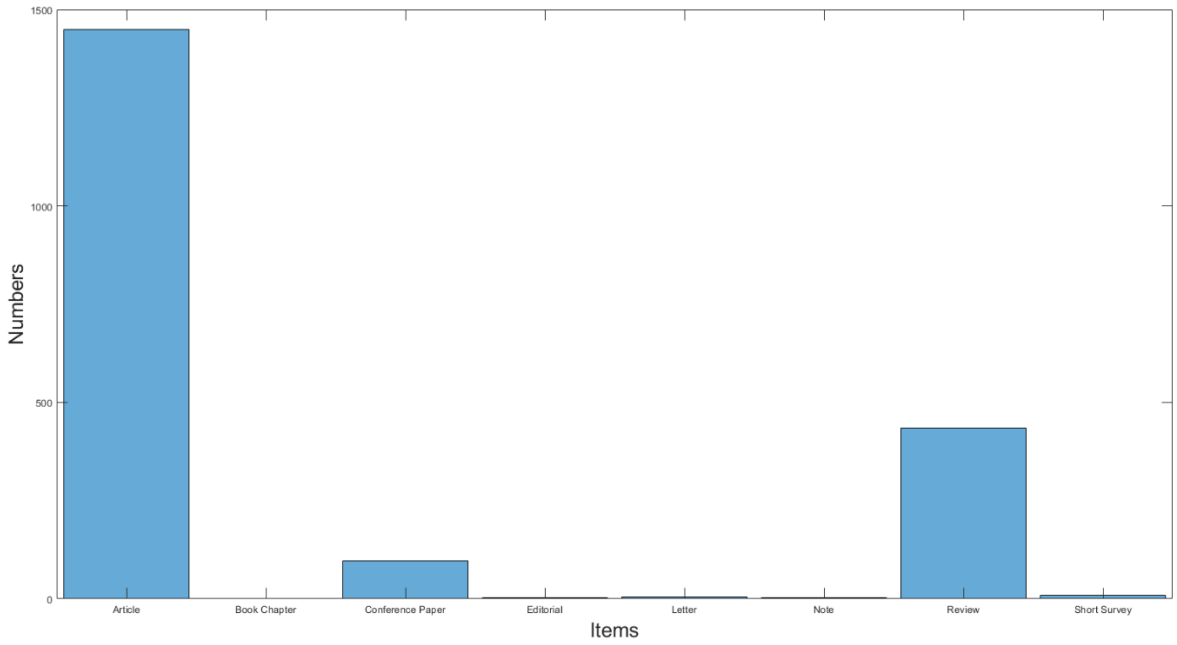

Figure 2: Type of recent papers on diabetes monitoring system. Datasource: Scopus.

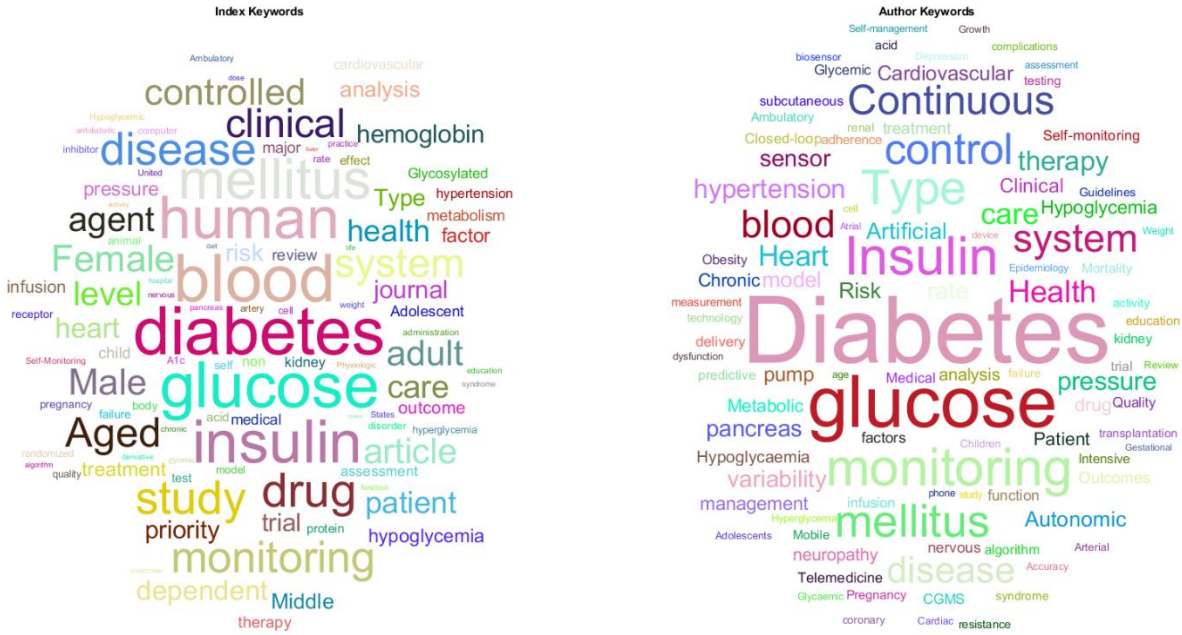

Figure 3: Indexed and author's keywords for recent papers on diabetes monitoring system. Datasource: Scopus.

With the advent of 5G and smart technologies several personalized options has opened to analyse big healthcare data on clouds [14]. The 5 goals of such technology using 5G are – cost-effectiveness,

comfortability, personalization, sustainability, smartness. The 5G-smart diabetes architecture in [14] has three layers – sensing layer, personalized diagnosis layer, data sharing layer. The performance was validated using machine learning algorithms like decision tree, artificial neural network (ANN), SVM, ensemble etc. which suggests on prevention and treatment of diabetes using recommendations like diet, sport, data sharing in a social network etc.

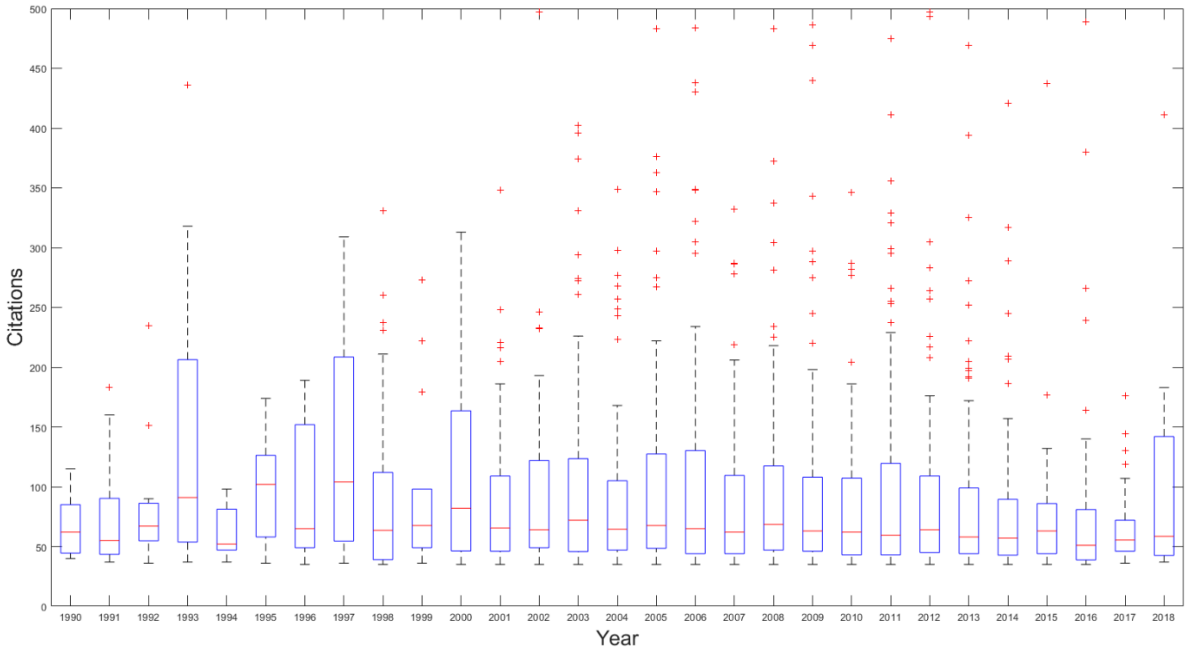

Figure 4: Year-wise citations of recent papers on diabetes monitoring system. Datasource: Scopus.

Figure 5: Source titles for recent works on diabetes monitoring system. Datasource: Scopus.

7. Conclusion

This book chapter reviews the recent trends in diabetes monitoring using the top 2000 cited articles and report text analytics results on past research activities and emerging trends in this domain. It also reviews various diabetes monitoring and control models available in the literature which are primarily divide din two categories – minimal and maximal models. Although the citation trends suggest that fundamental research in this domain is nearly to a saturated level. However, there are many

commercialization activities and patents issued recently on this topic [15], which shows a new opportunity to grow new industries in this domain which needs a good and affordable business model particularly for low and medium income countries of the developing world where diabetes is emerging almost in the scale of a large epidemic.

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