iGLU 1.1: Towards a Glucose-Insulin Model based Closed Loop IoMT Framework for Automatic Insulin Control

Prateek Jain[1], Amit M. Joshi[2] and S. P. Mohanty[3]
Malaviya National Institute of Technology, Jaipur, India. [1,2]
University of North Texas, Denton, TX , USA.[3]
Email: prtk.ieju@gmail.com[1], amjoshi.ece@mnit.ac.in[2], saraju.mohanty@unt.edu[3]

Outline of the Talk

- Introduction
- Related Works
- Our Vision iGLU-Automatic Glucose Monitoring and Control in IoMT Framework
- Framework of Diabetes Control System – The iGLU 1.1 of the current paper
- Novel Contributions of the current Work
- Proposed Automatic Glucose Control model
- Simulation and Results
- Conclusions and Future Research

The Problem of Diabetes

- Diabetes is a disease that occurs when your blood glucose, also called blood sugar, is too high. Blood glucose is your main source of energy and comes from the food.
- Diabetes is caused by the deficiency of insulin with respect to the generated glucose in the body.
- This is a condition in which the muscles, fat and liver cells of the body do not consume insulin effectively.

Type 1 Diabetes

• If person has type 1 diabetes, the body does not make insulin. Immune system attacks and destroys the cells in pancreas that make insulin. It can appear at any age. People with type 1 diabetes need to take insulin every day to stay alive.

Type 2 Diabetes

•Type 2 diabetes is the most common diabetic stage which is most commonly seen in the people over the world. In this type of diabetes, the pancreas will be able to generate some amount of insulin.

Gestational Diabetes

• Gestational diabetes develops in some women when they are pregnant. Most of the time, this type of diabetes goes away after the baby is born. However, if lady had gestational diabetes, she will have a greater chance of developing type 2 diabetes later in life. Sometimes diabetes diagnosed during pregnancy is actually type 2 diabetes.

Diabetes is a Global Crisis

- An estimated 463 million adults are living with diabetes worldwide.
- Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the developed countries.
- The greatest increase in prevalence is, however, occurring in low- and middle-income countries including in Asia and Africa, where most patients will probably be found by 2030.
- The risk of getting type 2 diabetes has been widely found to be associated with lower socio-economic position across countries.

Diabetes is a Global Crisis

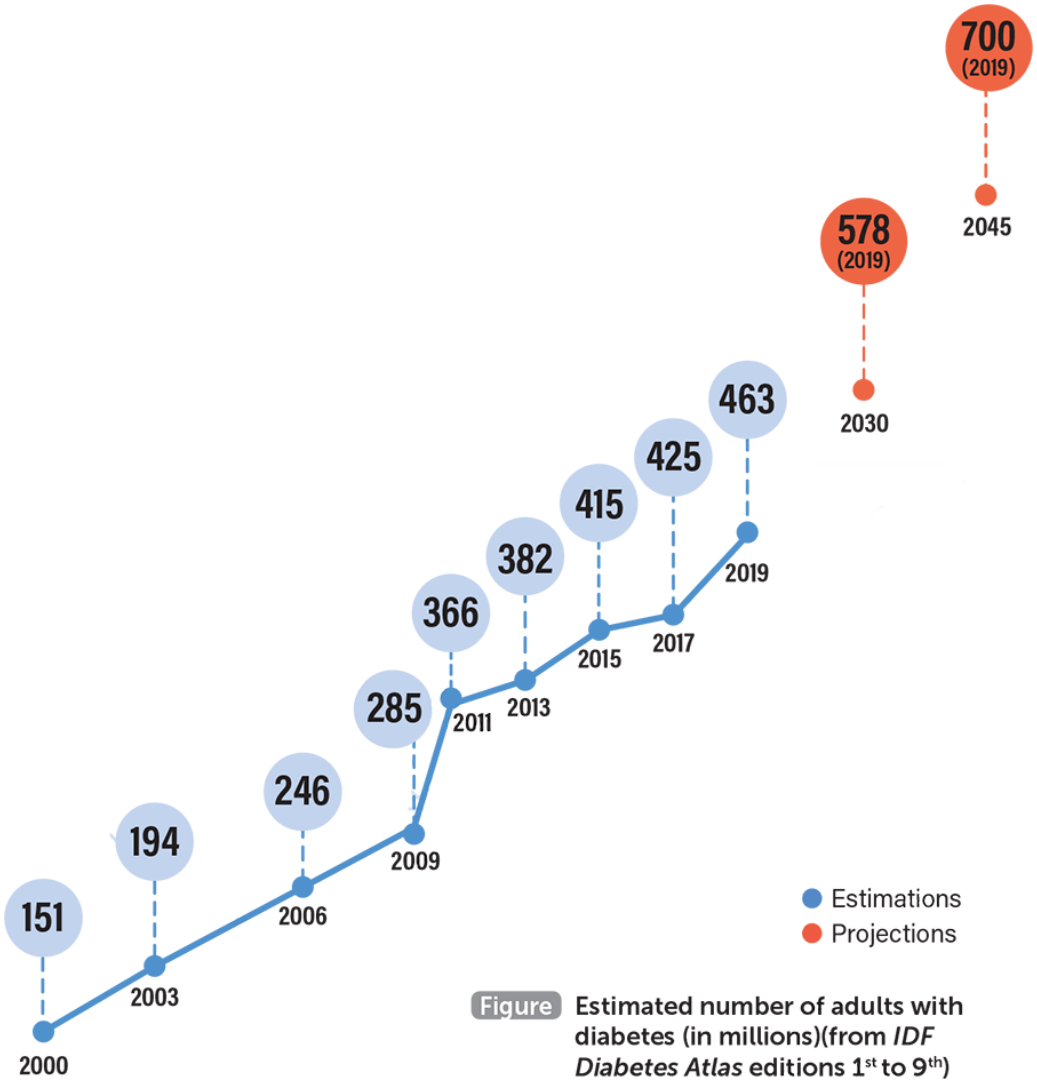
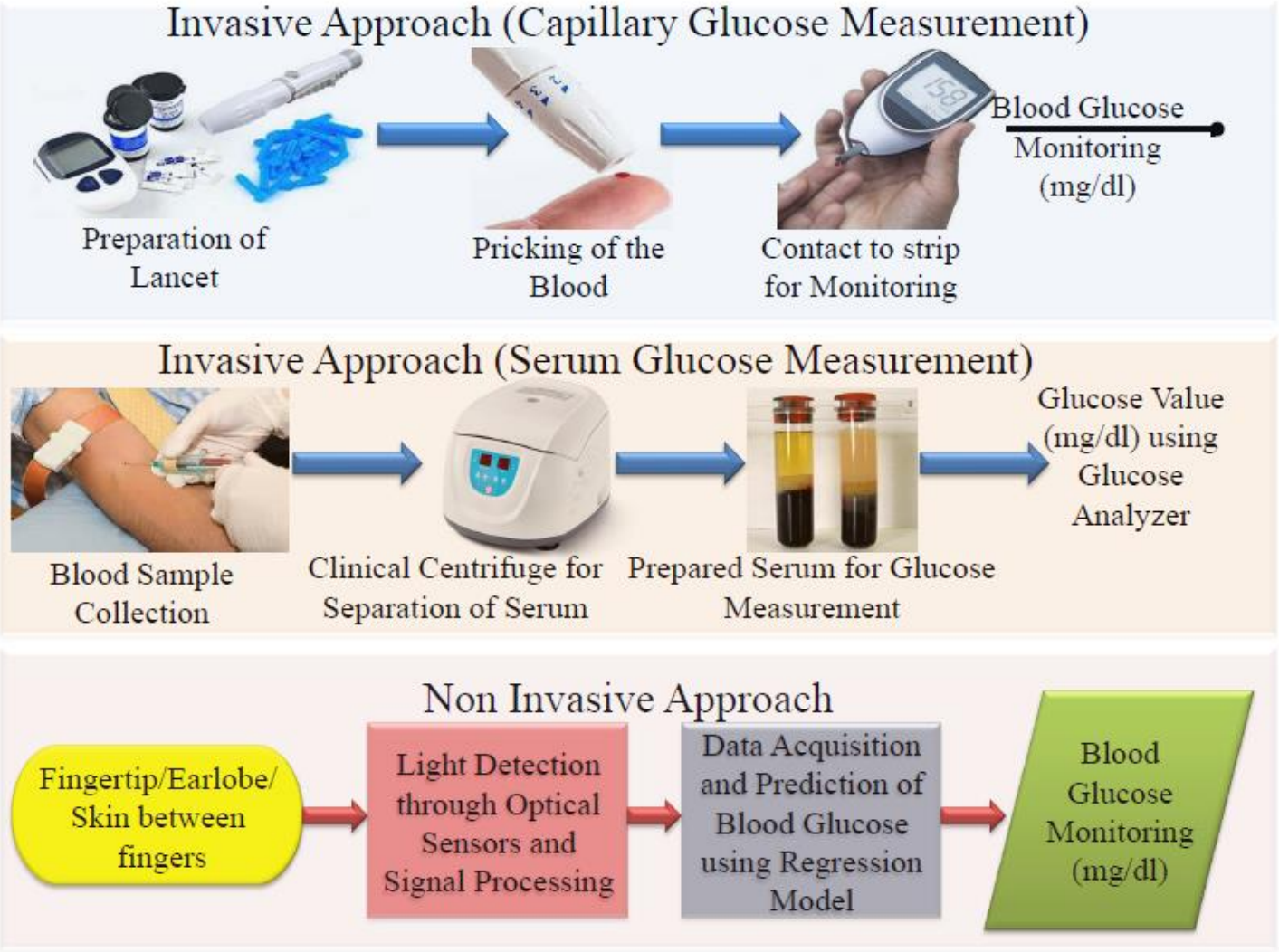


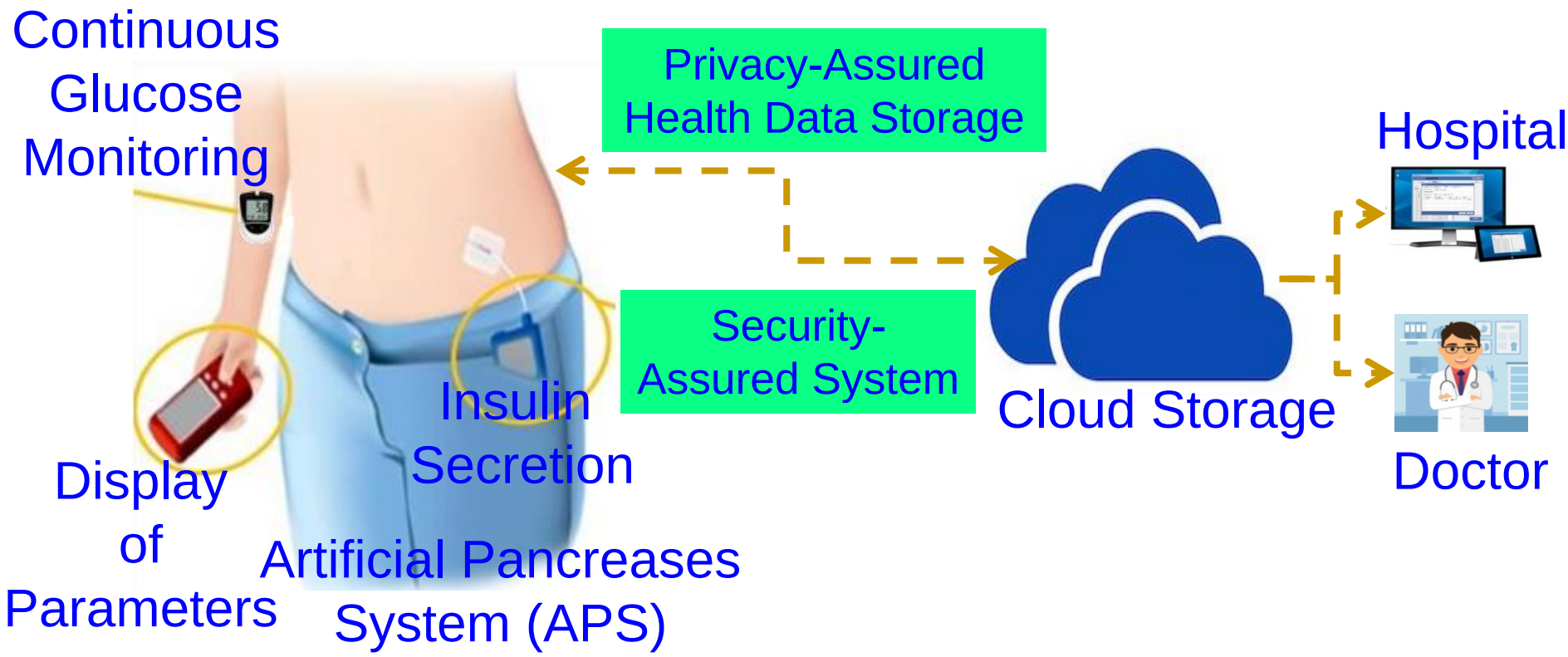
Figure Estimated number of adults with diabetes (in millions)(from *IDF Diabetes Atlas* editions 1st to 9th)

Source: https://diabetesatlas.org/en/sections/worldwide-toll-of-diabetes.html

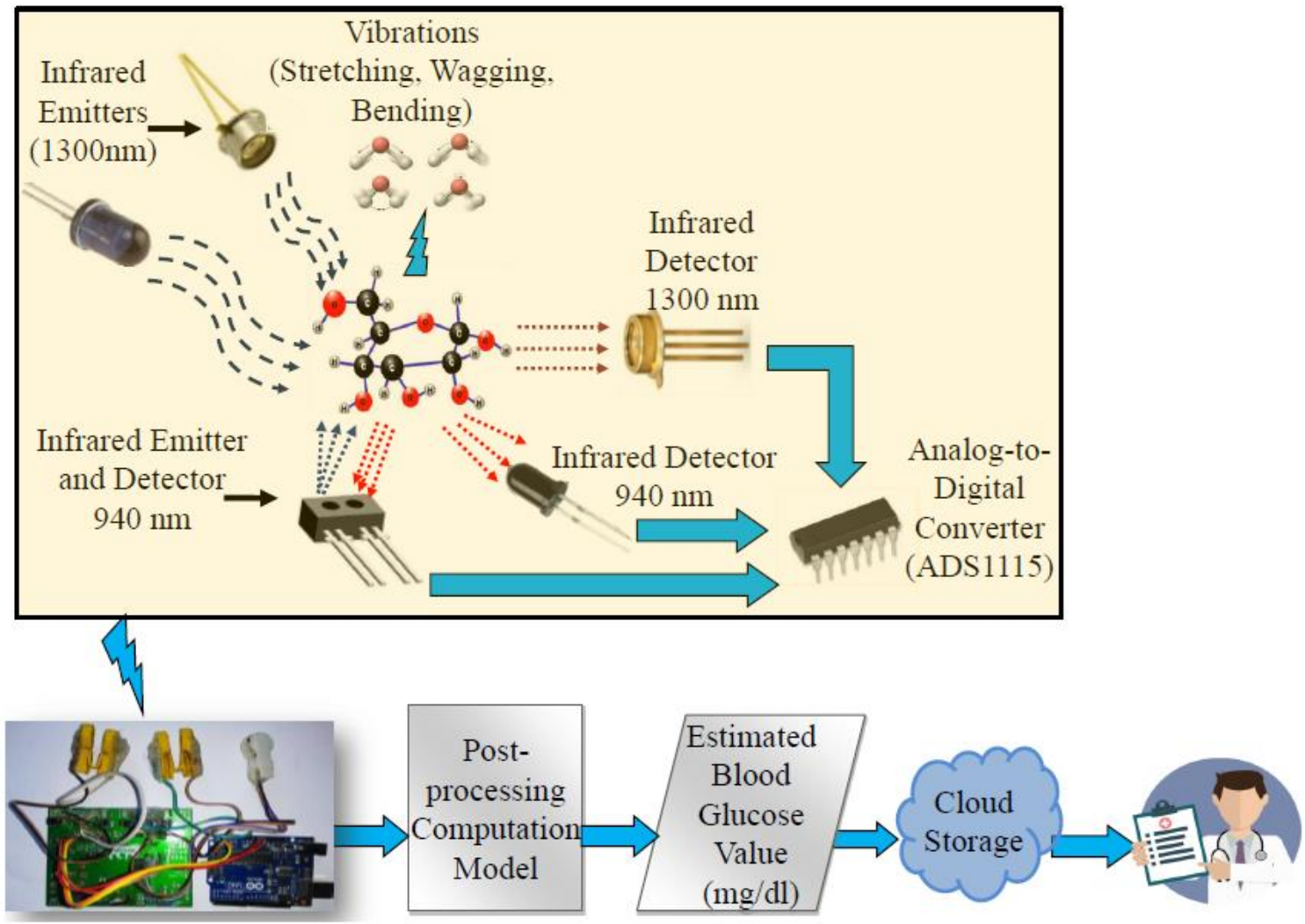
Noninvasive Detection is Needed



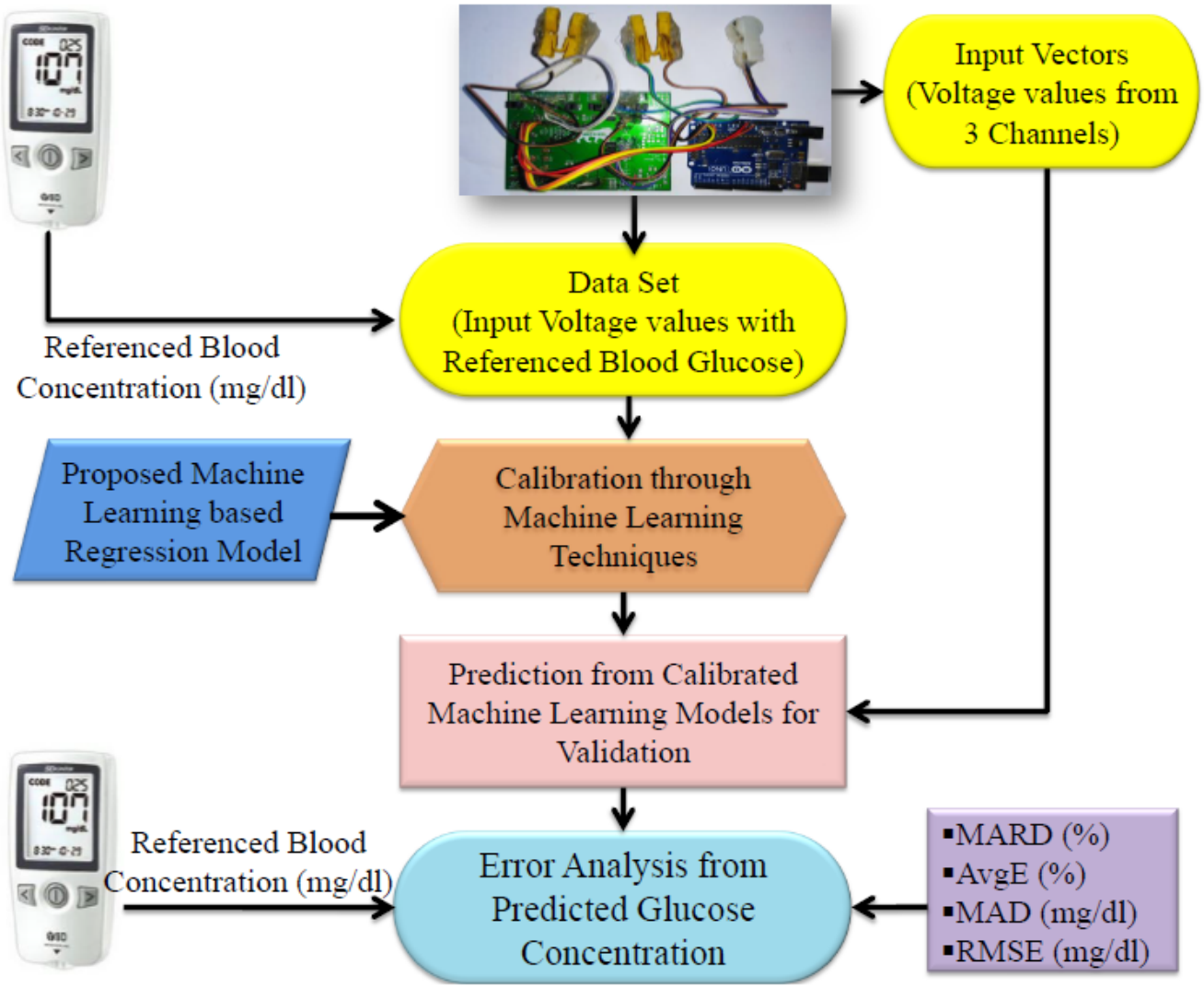
Our Vision – iGLU (Intelligent Noninvasive Monitoring and Control)



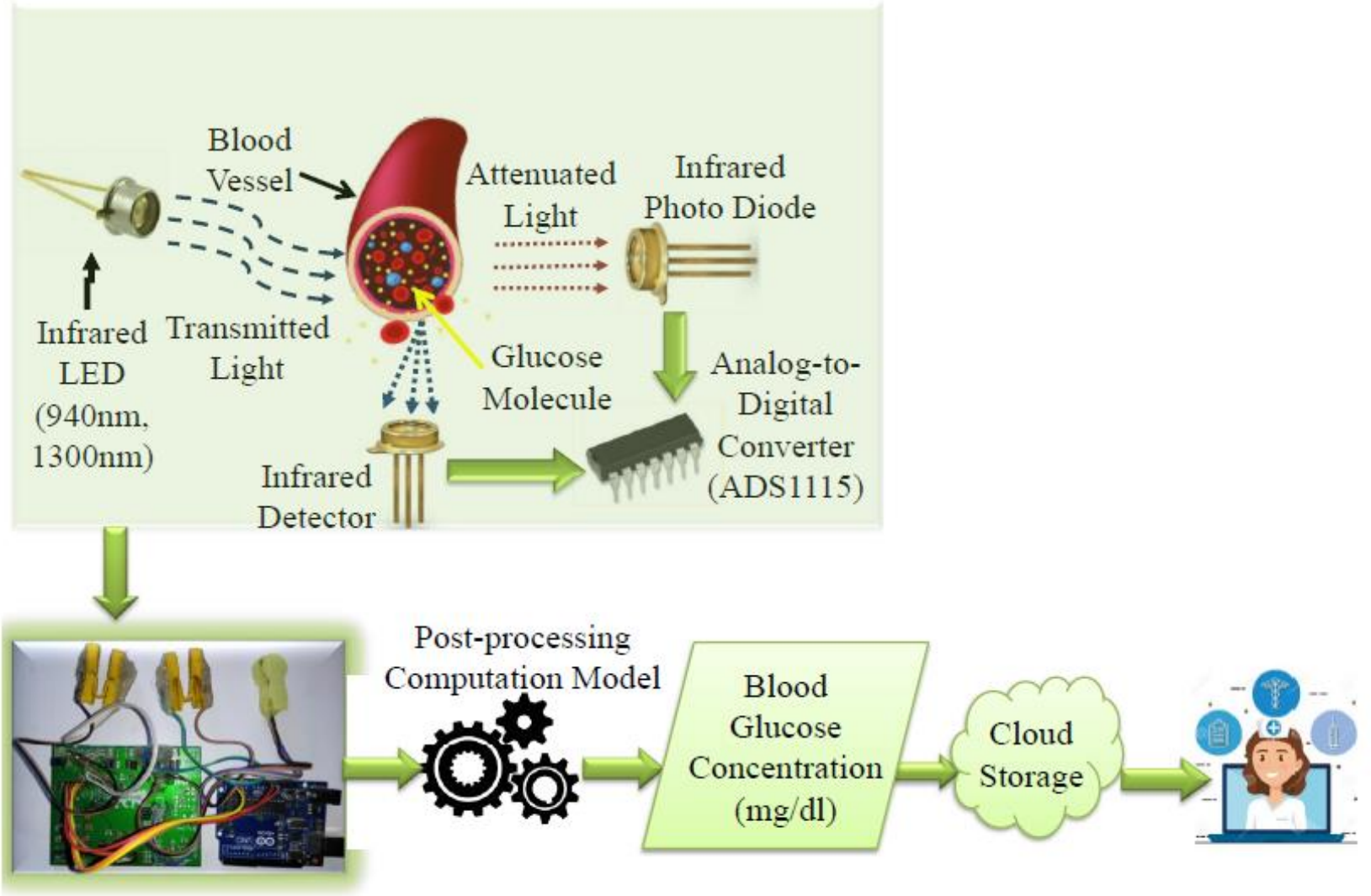
iGLU 1.0:


Vibrations
(Stretching, Wagging,
Bending)
Infrared
Emitters
(1300nm)
Infrared
Detector
1300 nm
Infrared Emitter
and Detector
940 nm
Infrared Detector
940 nm
Analog-to-
Digital
Converter
(ADS1115)
Post-
processing
Computation
Model
Estimated
Blood
Glucose
Value
(mg/dl)
Cloud
Storage

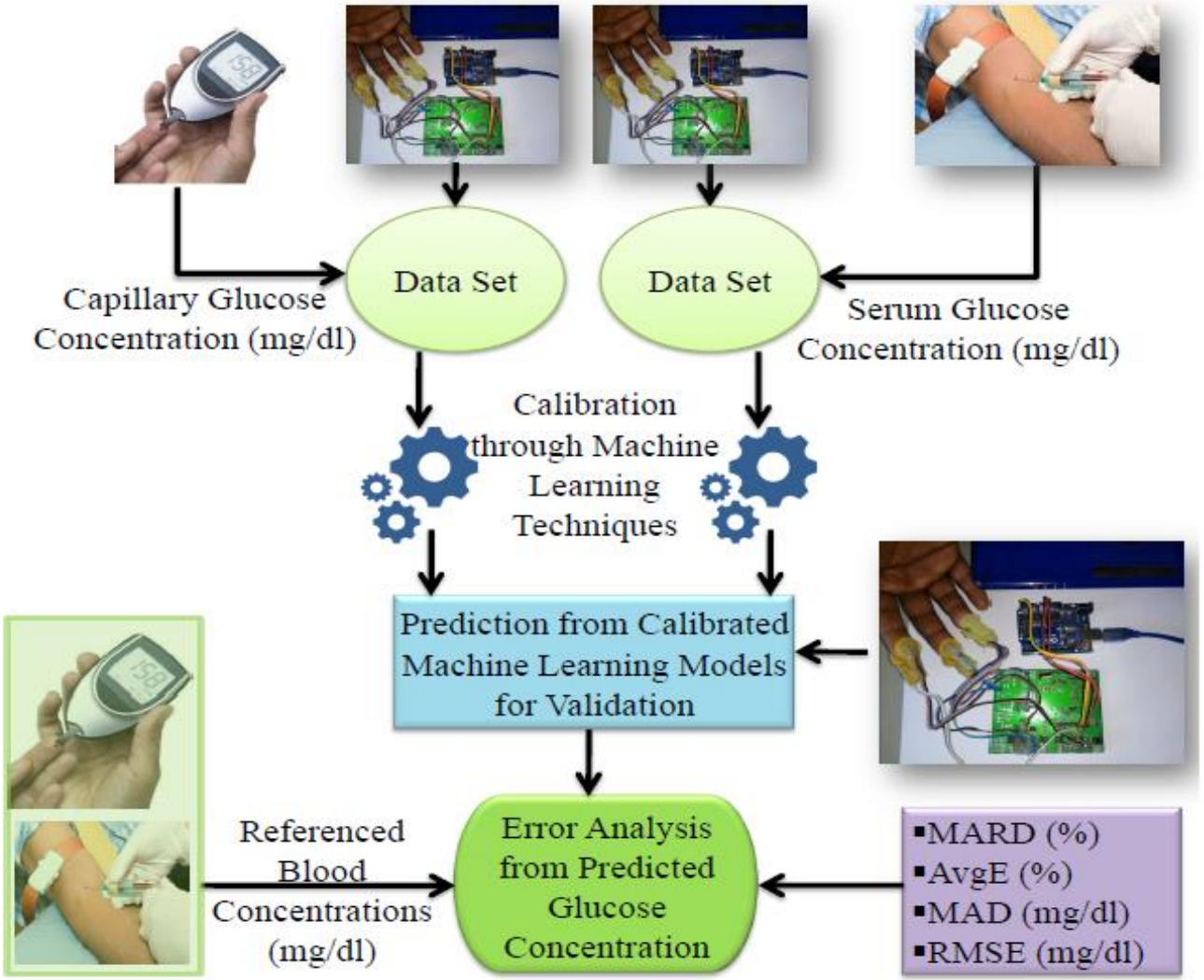
iGLU 1.0:


Input Vectors
(Voltage values from
3 Channels)
Data Set
(Input Voltage values with
Referenced Blood Glucose)
Referenced Blood
Concentration (mg/dl)
Proposed Machine
Learning based
Regression Model
Calibration through
Machine Learning
Techniques
Prediction from Calibrated
Machine Learning Models for
Validation
Referenced Blood
Concentration (mg/dl)
Error Analysis from
Predicted Glucose
Concentration
▪MARD (%)
▪AvgE (%)
▪MAD (mg/dl)
▪RMSE (mg/dl)

iGLU 2.0:


Blood Vessel
Attenuated Light
Infrared Photo Diode
Infrared LED (940nm, 1300nm)
Transmitted Light
Glucose Molecule
Analog-to-Digital Converter (ADS1115)
Infrared Detector
Post-processing Computation Model
Blood Glucose Concentration (mg/dl)
Cloud Storage

iGLU 2.0:

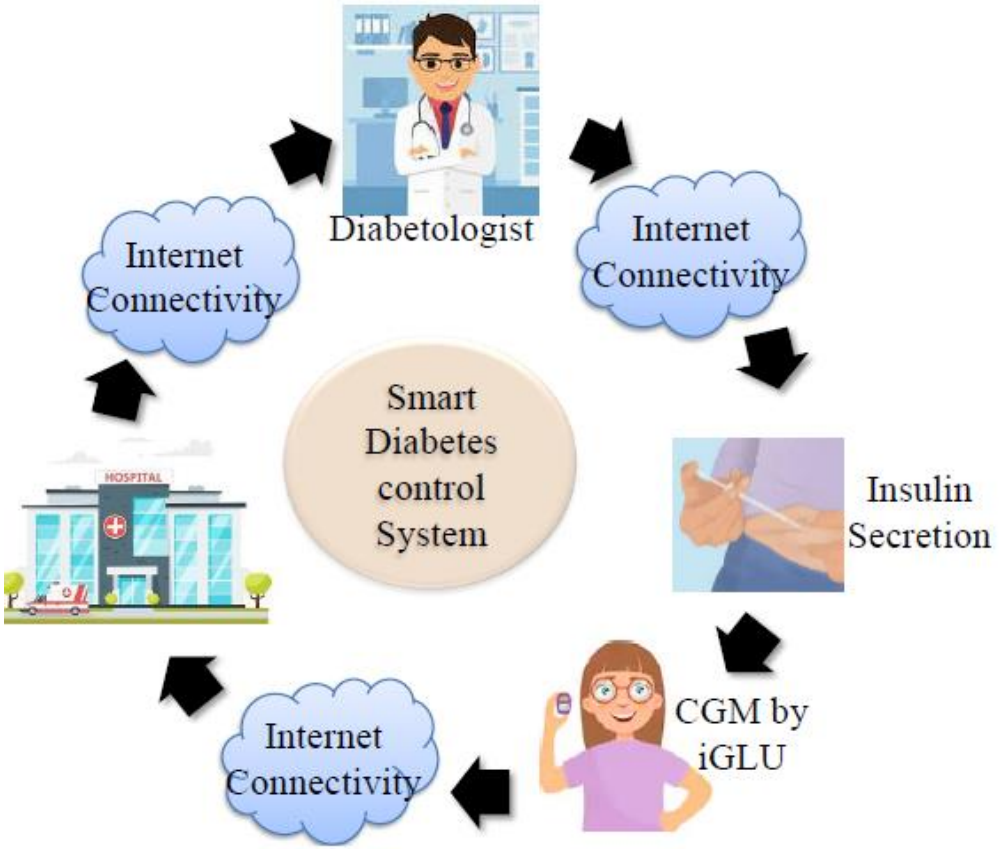

Capillary Glucose Concentration (mg/dl)
Data Set
Data Set
Serum Glucose Concentration (mg/dl)
Calibration through Machine Learning Techniques
Prediction from Calibrated Machine Learning Models for Validation
Referenced Blood Concentrations (mg/dl)
Error Analysis from Predicted Glucose Concentration
▪MARD (%)
▪AvgE (%)
▪MAD (mg/dl)
▪RMSE (mg/dl)

iGLU 1.1: Novel Contributions

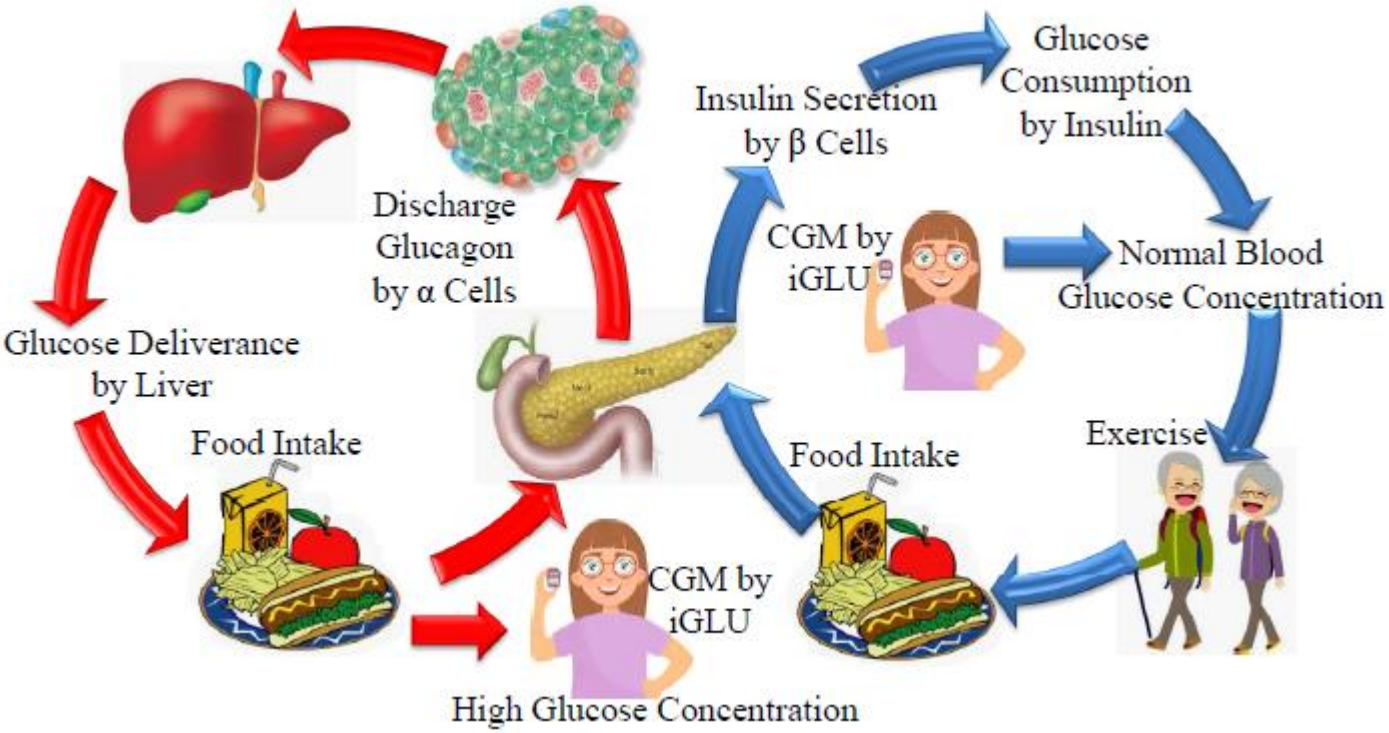
- A novel glucose-insulin model is proposed which represents an artificial pancreas system (APS) with continuous glucose monitoring.
- Four different cases have been considered to validate the proposed glucose-insulin model. In this modeling, glucose consumption parameters have also been determined.
- Proposed model (APS) are integrated with IoMT framework for remote located diabetic patients to provide prescribed diet and insulin plan and diagnosis with the help of diabetologist.

Framework of Diabetes Control System

- When the human body has a problem to maintain the amount of blood glucose then, the condition refers to Diabetes.
- The unhealthy lifestyle is the prominent factor in magnifying the chance of being a diabetic patient.
- The unbalanced diet is one of the main factors for the occurrence of diabetes Mellitus.
- Therefore, diagnosis and treatment of diabetes Mellitus are attracting points of research in smart healthcare.
- Time to time, the glucose values have been monitored by a diabetologist and insulin secretion has been recommended accordingly



Glucose Insulin Control Closed Loop System



Works of Diabetes Control

- The first glucose-insulin mathematical model has been explored to estimate the coefficients of normal blood regulation.
- An FDA approved Uva/Padova Simulator was represented for glucose-insulin control system.
- In the way of diabetes regulation, an intelligent PID controller (iPID) has been introduced for type 1 diabetic patients.
- A lot of models have been presented with different parameters in terms of meal detection and glucose-insulin concentration measurement.

Limitations of Existing Approaches for Diabetes Control

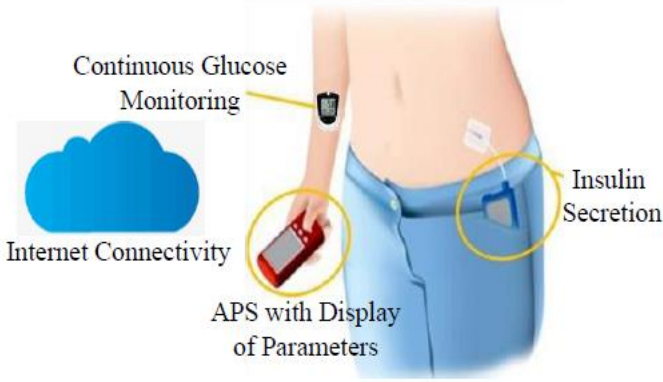
- Various parameters such as glucose absorption rate, net hepatic glucose balance, peripheral glucose utilization and renal excretion rate are required to determine the glucose consumption in the body.

- parameters are necessary to determine the blood glucose level regulation with scheduled diet and necessary insulin secretion plan.

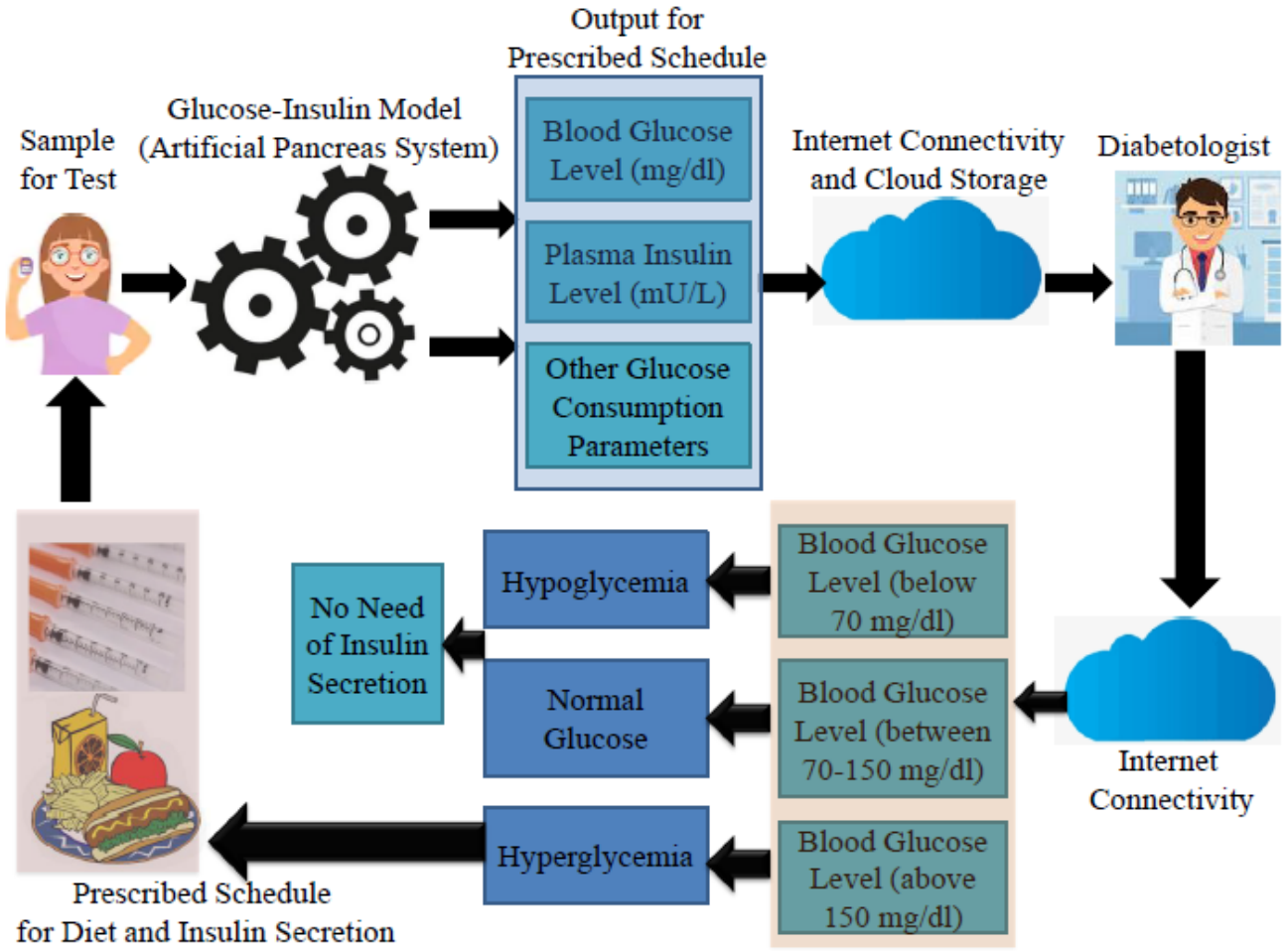
- A glucose-insulin mathematical model is required to control the blood glucose level of type 1 diabetic patients with prescribed diet and insulin secretion plan.

iGLU 1.1: Automatic Glucose Control in IoMT Framework

- The proposed work summarizes the glucose-insulin model to estimate the glucose consumption parameters with the integration of IoMT framework for a consultancy from diabetologist.
- This proposed model can create an environment, in which different cases of diabetes can be analyzed in terms of controlling of net glucose level, plasma insulin level and glucose excretion.
- In this proposed system, glucose-insulin based APS system determines the various parameters of glucose consumptions along with plasma insulin and glucose level for precise treatment of remote located diabetic patients.



Proposed APS model with IoMT framework



Proposed Model for Glucose and Insulin Relationship

The presented differential equations along with secondary relations constitute the computing model. The variation in plasma insulin I_P is expressed by the following expression:

$$\frac{dI_P}{dT} = \left(\frac{I_{absorb}}{V_{oi}}\right) - P_{ie} \times I_P \qquad (1)$$

P_{ie} is the rate constant of insulin elimination. I_{absorb} is insulin absorbance rate and V_{oi} is the insulin distribution volume. The rate of change of active insulin follows first order kinetics which is represented as:

$$\frac{dI_{Act}}{dt} = (P_1 \times I_P) - (P_2 \times I_{Act}) \qquad (2)$$

Where P_1 and P_2 are rate constants which represent the insulin action delay. The absorption rate of insulin is represented as

$$I_{absorb}(t) = \left(\frac{I_{type} \times t \times T_{D50}^5 \times D}{t[T_{D50}^5 + t^5]^2}\right) \qquad (3)$$

t is the time period from insulin injection. T_{D50} is the time at which 50% of the total dose D has been consumed and I_{type} is a specific parameter in terms of insulin absorption for different types of insulin (short, intermediate and long-acting).

Continues…

$$T_{D50}^{5} = p \times D + q \tag{4}$$

$$I_{absorb}(t) = \left(\frac{I_{type} \times t(p \times D + q) \times D}{t[p \times D + q + t^{5}]^{2}} \right) \tag{5}$$

If insulin regimen contains more injections. then, totally absorbed insulin I_{absorb} will be the sum of individual absorbed insulin from multiple injections. The steady-state insulin has been represented for steady-state:

$$I_{steady}(t) = I(t) + I(t+12) + I(t+24) + I(t+48) \tag{6}$$

From the above expression, it is concluded that this expression is not applicable for short-acting insulin. For steady-state absorbed insulin:

$$I_{Act,steady}(t) = I_{Act}(t) + I_{Act}(t+12) + .. + I_{Act}(t+48) \tag{7}$$

The equilibrium insulin level can be expressed in terms of steady-state active insulin:

$$I_{equil}(t) = P_2 \left(\frac{I_{Act,steady}(t)}{P_1} \right) \tag{8}$$

This is considered to compute net hepatic glucose balance (NHGB) and peripheral glucose uptake. The insulin level is responsible for the periphery and hepatic control action.

Continues…

$$I_{equil}(t) = P_2\left(\frac{I_{Act}(t) + I_{Act}(t+12) + .. + I_{Act}(t+48)}{P_1}\right) \quad (9)$$

The change in glucose values with respect to the time represented by the differential Eqn. 10:

$$\frac{dG_{plasma}}{dt} = \frac{[NHGB(t) + G_{abgut}(t)]}{V_g} - \frac{[G_{aiu}(t) + G_{ren}(t)]}{V_g} \quad (10)$$

where, $G_{abgut}(t)$ = Absorbed glucose from the gut

$G_{aiu}(t)$ = Consumption of peripheral and insulin independent glucose

$G_{ren}(t)$ = Renal glucose excretion

V_g = glucose distribution volume

$[NHGB(t)+G_{abgut}(t)]/V_g$= Total body glucose without consumption

$[G_{aiu}(t)+G_{ren}(t)]/V_g$ = Consumed and renal excreted glucose

According to Michaelis-Menten relationship,

$$G_{aiu}(t) = \left(\frac{G_{plasma}[(c.S_p.I_{equil} + G_{ii})(k + G_{ref})]}{G_{ref}(k + G_{plasma})}\right) \quad (11)$$

c = Slope between peripheral glucose and insulin level

G_{ii} = Insulin independent glucose utilization

G_{ref} = Reference glucose for consumption

[Sp ×Iequil] = Effective insulin level

Continues…

The glucose concentration in gut contains the mean in the form of carbohydrates which is represented as the following:

$$\Delta G_{gut} = G_{Emp} - (K_{gabsorb} \times G_{gut})$$

G_{gut} = The amount of glucose in gut

G_{Emp} = Gastric emptying

$K_{gabsorb} \times G_{gut}$ = Glucose consumption for systemic circulation.

TABLE : Parameters of iGLU 1.1 System

iGLU 1.1 Parameters	Descriptions
P_{ie}= 5.4 l/hr	Rate constant of insulin elimination
P_1= 0.025 /hr	Rate constant of insulin delay action
k= 10 mmol/l	Michaelis constant
G_{ii}= 0.54 mmol/hr/kg	Insulin independent glucose utilization
G_{ref}= 5.3 mmol/l	Reference glucose for consumption
c= 0.015 mmol/hr/kg/mU*l	Slope b/w peripheral glucose and insulin
$k_{gabsorb}$= 1/hr	Constant for glucose absorption from gut
V_{oi}= 0.142 l/kg	Insulin distribution volume
V_g= 0.22 l/kg	Distribution volume of glucose

iGLU 1.0 – Experiments - Datasets

Table: Baseline characteristics of samples

Samples Basic Characteristics	Calibration	Validation and Testing
Age (Years)	**Gender Wise Samples**	
Male:- 22-77	Male:- 53	Male:- 64
Female:- 17-75	Female:- 44	Female:- 29
Age (Years)	**Prediabetic**	
Male:- 22-65	Male:- 18	Male:- 11
Female:- 26-75	Female:- 13	Female:- 10
Age (Years)	**Diabetic**	
Male:- 30-68	Male:- 16	Male:- 17
Female:- 30-73	Female:- 14	Female:- 11
Age (Years)	**Healthy**	
Male:- 22-65	Male:- 19	Male:- 36
Female:- 17-70	Female:- 17	Female:- 08

iGLU 1.0 – Experimental Results

- **RM1:- Absorption and reflectance of light at 940 nm wavelength**
- **RM2:- Absorption of light at 940 nm and 1300 nm**
- **RM3:- Reflectance of light at 940 nm and absorption of light at 1300 nm**
- **RM4:- Combination of all three channels**

Statistical Analysis using MPR kernel based calibration with polynomial degree 3.

	R^2 value	$mARD$ (%)	$AvgE$ (%)	MAD (mg/dl)	$RMSE$ (mg/dl)
RM1	0.42	30.74	24.78	53.22	73.68
RM2	0.46	28.58	22.33	47.61	66.94
RM3	0.43	29.76	23.70	50.83	69.73
RM4	**0.81**	**4.66**	**4.61**	**7.55**	**11.95**

Statistical Analysis using MPR kernel based calibration with polynomial degree 4.

	R^2 value	$mARD$ (%)	$AvgE$ **(%)**	MAD (mg/dl)	$RMSE$ (mg/dl)
RM1	0.32	43.68	32.81	59.66	75.22
RM2	0.28	30.21	27.68	52.77	72.11
RM3	0.33	32.34	34.32	57.78	70.21
RM4	**0.56**	**10.61**	**10.69**	**10.23**	**17.46**

iGLU 1.0 – Experimental Results

Statistical Analysis of calibration of proposed model and existing techniques.

Regression Model	$mARD$ %	$AvgE$ %	MAD mg/dl	$RMSE$ mg/dl
Logistic	15.11	16.63	27.78	39.06
SVR	8.03	7.71	12.34	18.04
DNN	6.65	7.30	12.67	21.95
MPR3(RM4)	**4.66**	**4.61**	**7.55**	**11.95**

Statistical Analysis of validation of proposed combination and existing techniques

	$mARD$ %	$AvgE$ %	MAD mg/dl	$RMSE$ mg/dl
Logistic	25.57	27.54	48.29	71.08
SVR	8.22	9.35	16.81	29.94
DNN	7.32	7.03	9.89	11.56
MPR3	**6.01**	**6.08**	**11.30**	**18.29**

iGLU 2.0 – Experiments - Datasets

Samples Basic Characteristics	Capillary Glucose	Serum Glucose	Capillary Glucose	Serum Glucose
	Calibration		**Validation and Testing**	
Age (Years)		**Prediabetic Samples**		
Male:-18-80	Male:-23	Male:-13	Male:-18	Male:-10
Female:-17-75	Female:-20	Female:-16	Female:-16	Female:-09
Age (Years)		**Diabetic Samples**		
Male:-18-80	Male:-30	Male:-18	Male:-14	Male:-15
Female:-17-75	Female:-19	Female:-12	Female:-12	Female:-12
Age (Years)		**Healthy Samples**		
Male:-18-80	Male:-09	Male:-08	Male:-07	Male:-05
Female:-17-75	Female:-12	Female:-07	Female:-07	Female:-08
Age (Years)		**Total Samples**		
Male:-18-80	Male:-62	Male:-39	Male:-39	Male:-30
Female:-17-75	Female:-51	Female:-35	Female:-35	Female:-29

iGLU 2.0 – Experimental Results

Table:- Statistical Analysis of calibration of proposed model and existing techniques

Regression Model	MARD %	AvgE %	MAD mg/dl	RMSE mg/dl
CSVR (Capillary)	31.85	27.32	59.42	79.66
Serum	26.69	32.55	51.92	73.32
MGSVR (Capillary)	31.36	26.82	58.43	77.83
Serum	26.50	24.66	47.75	66.01
FGSVR (Capillary)	14.31	12.49	27.36	45.06
Serum	12.31	10.45	20.96	31.09
DNN (Capillary)	29.06	22.14	46.47	62.51
Serum	9.11	8.95	19.47	27.95
MPR3 (Capillary)	6.07	6.09	13.28	19.71
Serum	4.86	4.88	9.42	13.57

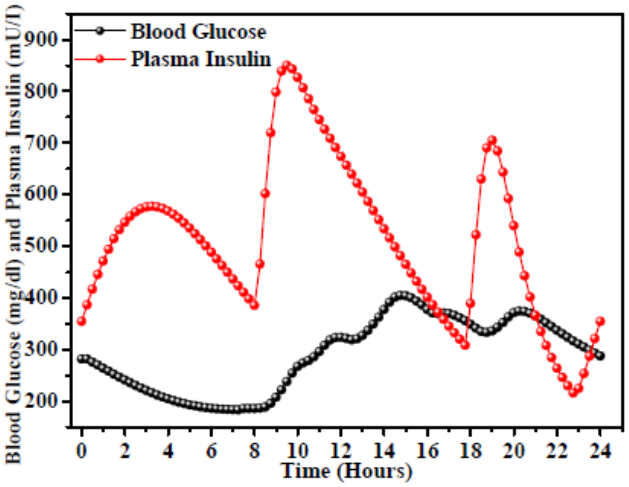
iGLU 2.0 – Experimental Results

Table:- Statistical Analysis of Validation of proposed model and existing techniques

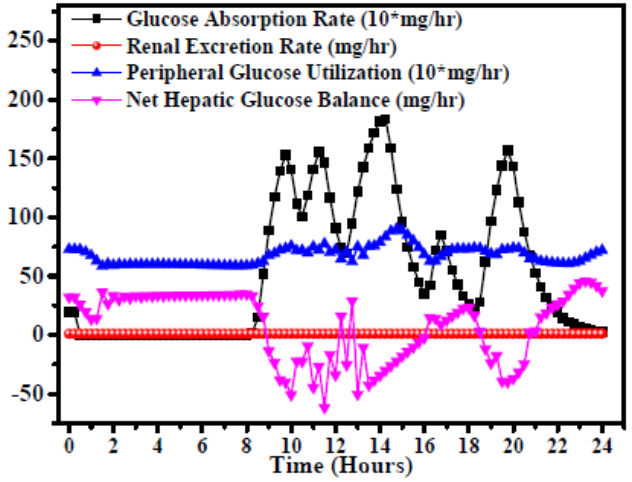
Regression Model	$mARD$ %	$AvgE$ %	MAD mg/dl	$RMSE$ mg/dl
FGSVR (Capillary)	14.09	11.45	25.20	41.18
Serum	**9.17**	**9.12**	**19.09**	**27.34**
DNN (Capillary)	11.67	10.02	21.81	34.05
Serum	**23.19**	**22.14**	**45.07**	**59.74**
MPR3 (Capillary)	7.74	7.70	16.08	22.46
Serum	**5.009**	**4.97**	**9.74**	**12.98**

Validation with Multiple Cases and Results

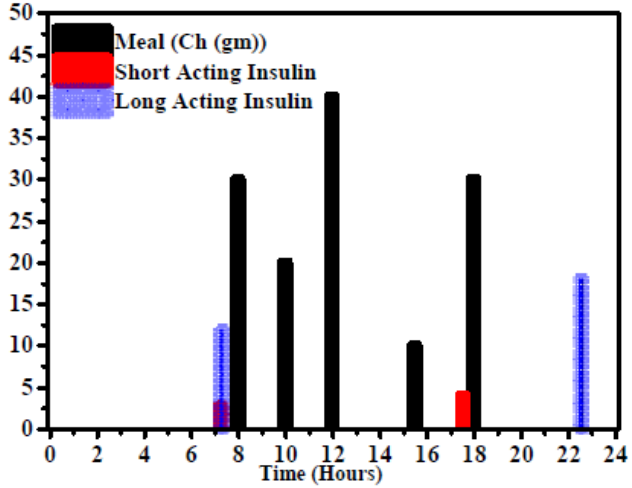
Case 1: A woman wants to control her sugar level. Her weight is 70 Kg. and is taking three injections of intermediate and/or short-acting insulin every day. A woman desires to start her family but consistently has had considerably high blood glucose levels after morning, despite the number of attempts to normalize her control in anticipation of becoming pregnant. Clearly, diet schedule for glucose regulation will not be good during pregnancy. According to this condition, the blood glucose is monitored frequently.



(a) Blood glucose and plasma insulin (case 1)



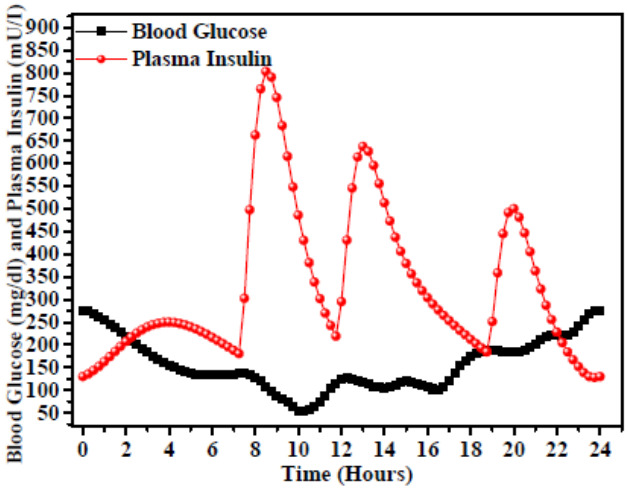
(b) Functional paremeters of glucose (case 1)



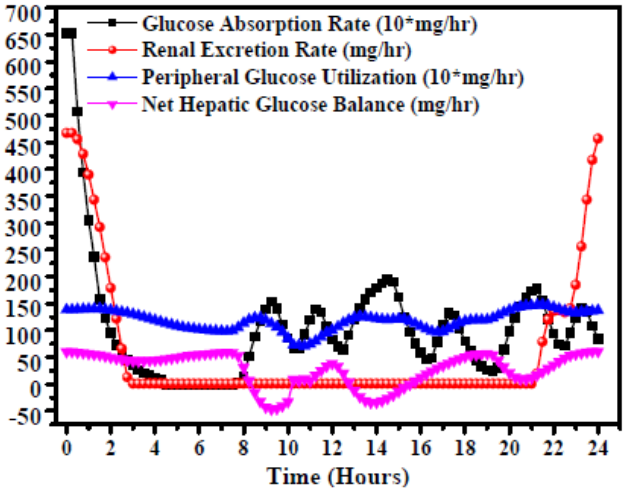
(c) Diet and insulin secretion (case 1)

Continues…

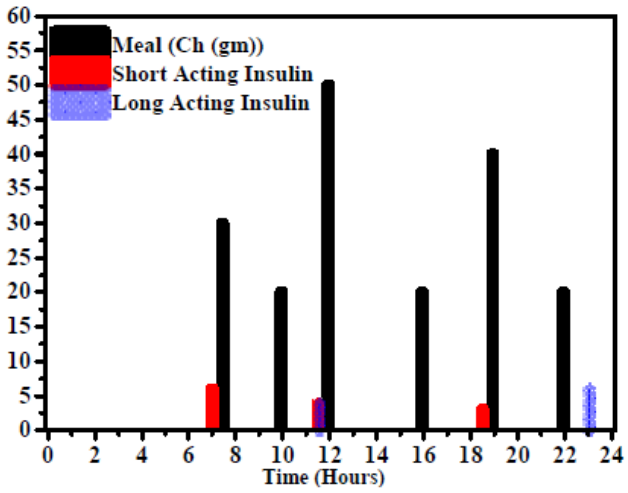
Case 2: A person aged 45 was confirmed as having diabetes at an early age. The weight of the person is 68 Kg. He is following the prescription for combined short and/or intermediate-acting insulin dose four times per day. According to his continuous glucose monitoring, he leads to higher glucose level during the night but he has a low glucose level in the morning. For this condition, the plasma insulin level is monitored frequently with diet and insulin secretion schedule**.**



(d) Blood glucose and plasma insulin (case 2)



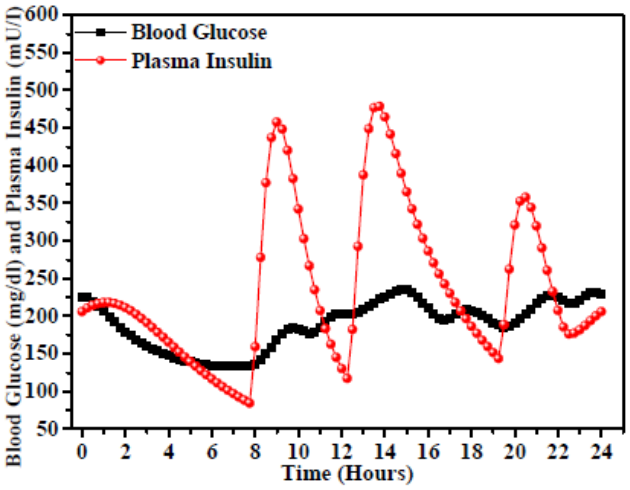
(e) Functional paremeters of glucose (case 2)



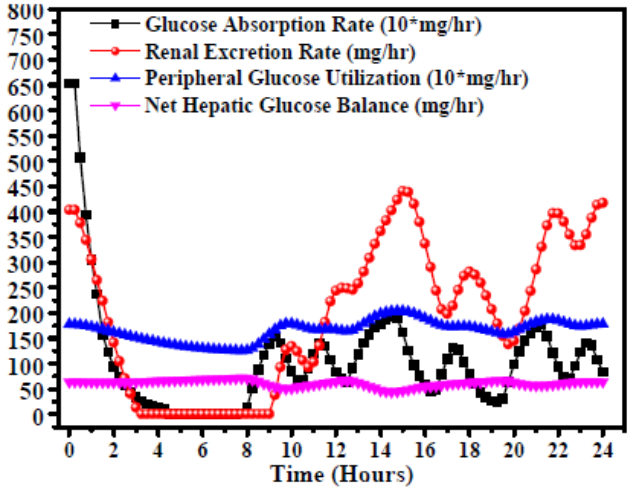
(f) Diet and insulin secretion (case 2)

Continues…

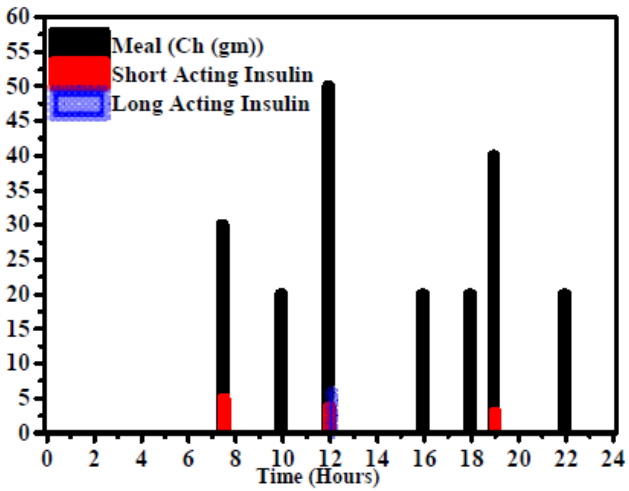
Case 3: This overweighed patient aged 58 is insulin dependent (type 1 patient) has had the main problem of gaining weight. The weight is 98 Kg. She is sensitive to take insulin secretion, because the more insulin she will take, the more she has to eat. She smokes and is at higher risk of a heart attack. By adjusting her carbohydrates intake and insulin regimen accordingly may help her reduce weight without going 'hypo'. For this condition, the plasma insulin level is monitored frequently with diet and insulin secretion schedule.



(g) Blood glucose and plasma insulin (case 3)



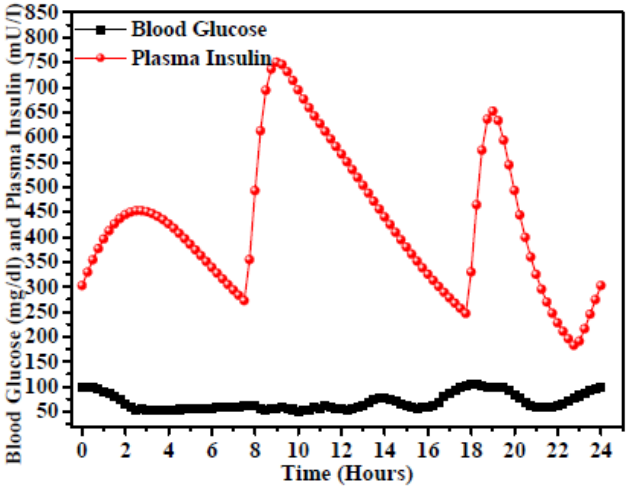
(h) Functional paremeters of glucose (case 3)



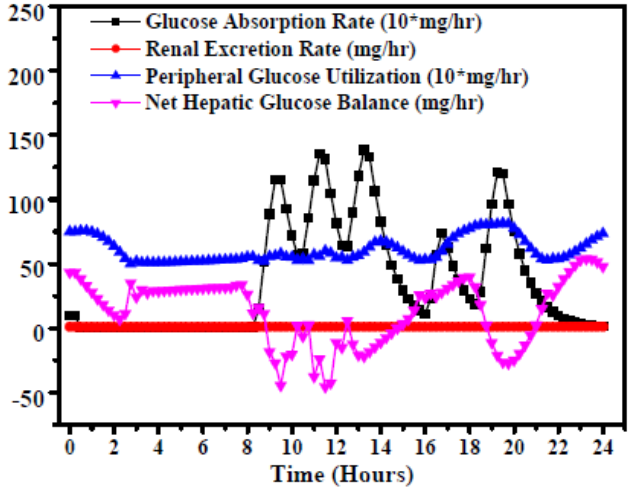
(i) Diet and insulin secretion (case 3)

Continues…

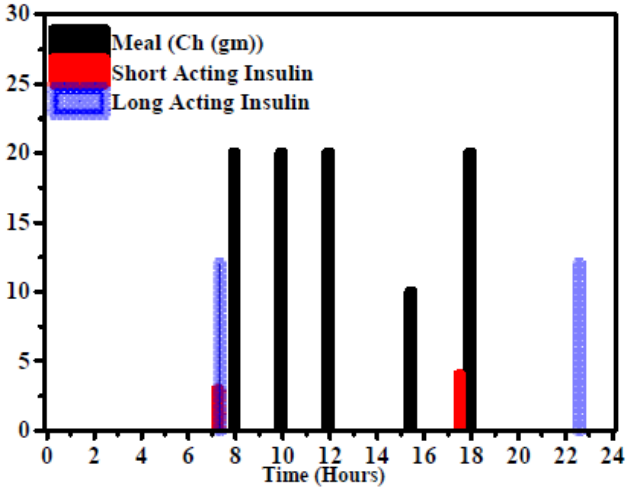
Case 4:- An eighteen years old insulin-dependent patient is weighted 70 Kg and has just shifted from his home first time for University. He is also not a good cook. He appears pretty awful in mornings. He leads to the pretty low glucose level in the morning, at times being at risk of going 'hypo'. By altering his prescribed insulin dose, his glucose level may not be actually so low in the morning.



(j) Blood glucose and plasma insulin (case 4)



(k) Functional paremeters of glucose (case 4)



(l) Diet and insulin secretion (case 4)

Results

TABLE II: Comparison with Previous Works

Works	Parameters	Model-Simulator	Cases
Magdelaine, et al. [13]	Glucose and insulin dynamics	Uva/Padova Metabolic Simulator	Virtual data of type 1 diabetic patients
Turksoy, et al. [14]	Meal detection with CGM	Uva/Padova Metabolic Simulator	Virtual data of nine subjects
Xie, et al. [15]	Basal-bolus insulin sensitivity	Uva/Padova Metabolic Simulator	Virtual data of two subjects
MohammadRidha, et al. [16]	Meal detection using iPID model	Uva/Padova Metabolic Simulator	Virtual data of ten subjects
Proposed Work	Glucose Consumption parameters	MATLAB for model simulation	Four possible cases of diabetic patients recommended by diabetologist

Conclusion

Control of Diabetes Mellitus

- To control the Type 1 diabetes mellitus, a glucose-insulin modeling based artificial pancreas system has been proposed with continuous blood glucose monitoring.
- A mathematical model has been proposed which shows the relationship between active equilibrium insulin in the human body to the plasma glucose.
- In proposed work, glucose consumptions in different modes (glucose profiles) have also been presented which are modeled mathematically with plasma and gut glucose.

Future Directions of this Work

- There is a requirement to design a real-time artificial pancreas system for Type 1 diabetic patient.
- The proposed system should have the functionality to balance the glucose and insulin level in the human body with a scheduled meal and bolus insulin secretion plan.
- The system is required to be the real-time wearable device with monitoring all glucose profiles of the human body.
- The proposed real-time artificial pancreas system needs to be portable, easy to handle, wearable device and cost-effective solution.

References

- P. Jain, A. M. Joshi, and **S. P. Mohanty**, "iGLU 1.0: An Accurate Non-Invasive Near-Infrared Dual Short Wavelengths Spectroscopy based Glucometer for Smart Healthcare", *arXiv Electrical Engineering and Systems Science*, arXiv:1911.04471, November 2019, 23-pages.
- P. Jain, A. M. Joshi, and **S. P. Mohanty**, "iGLU: An Intelligent Device for Accurate Noninvasive Blood Glucose-Level Monitoring in Smart Healthcare", *IEEE Consumer Electronics Magazine (MCE)*, Vol. 9, No. 1, January 2020, pp. 35-42.
- P. Jain, A. M. Joshi, N. Agrawal, and **S. P. Mohanty**, "iGLU 2.0: A New Non-invasive, Accurate Serum Glucometer for Smart Healthcare", *arXiv Electrical Engineering and Systems Science*, arXiv:2001.09182, January 2020, 19-pages.
- Jain, A. M. Joshi, and **S. P. Mohanty**, "iGLU 1.1: Towards a Glucose-Insulin Model Based Closed Loop IoMT Framework for Automatic Insulin Control of Diabetic Patients", in *Proceedings of the 6th IEEE World Forum on Internet of Things (WF-IoT)*, 2020, pp. Accepted.

Thank You !!!

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