FRANKFURT UNIVERSITY OF APPLIED SCIENCES

SAFETY CRITICAL SYSTEMS

[Project Status Report by Group H]

BIONIC PANCREAS SIMULATOR

Under the guidance of:

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ABSTRACT

"Bionic Pancreas" is a term very commonly used today for the '*Insulin and Glucagon Pumps*'. It is a portable electronic device used by people suffering from hyperglycaemia or hypoglycaemia in order to maintain a stable blood glucose level. The aim of our project is to design a simulator that can work as a real world Bionic Pancreas which is a safety critical system. This document will help in understanding the problem statement, requirements, system design and other development activities related with the simulation of an Insulin/Glucagon Pump System.

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1. INTRODUCTION

1.1 PROBLEM STEATEMENT

Diabetes is characterized as “a metabolic disorder in which the body is not able to regulate the levels of glucose in the blood” [1]. The cause for this disorder is the lack of insulin hormone, which is responsible for synthesis of glycogen. More specifically, “Insulin enables the body’s cells to absorb and use this glucose. Without it, glucose does not enter the body cells and it cannot be used as fuel to support their continued function” [2].

On the other hand, in case patients suffering with Hypoglycaemia, there is deficiency of glucose in the bloodstream [3]. This situation is a result of the lack of glucagon hormone that breaks down glycogen from liver and release into the bloodstream.

A personal Insulin and Glucagon pump for people suffering from diabetes should be simulated with software. Pumps can be programmed to release small doses of insulin continuously (basal), or a bolus dose close to mealtime to control the rise in blood glucose after a meal. This delivery system most closely mimics the body's normal release of insulin[11].

A personal Insulin and Glucagon pump is an external (or internal) device that mimics the function of the pancreas. It uses an embedded sensor to measure the blood sugar level at periodic intervals and then injects Insulin and/or Glucagon to maintain the blood sugar at a ’normal’ level.

1.2 TASK DISTRIBUTION

	Schedule	Task Contribution	Involved Members
1	Week 45 – Week 47 [2015.Nov.01] to [2015.Nov.21]	Requirement Analysis	Manoj Murugan, Sneha Sahu, Varun Varadarajan, Manjunatha Shetty
2	Week 48 – Week 50	Mathematical Model	Manjunatha Shetty
3	Week 51 – Week 01	Interface Design and Code Implementations	Sneha Sahu
4	Week 02 – Week 03	Testing and Code Modifications	Sneha Sahu, Varun Varadarajan
5	Week 04 – Week 05 [2016.Jan.24] – [2016.Feb.04]	Final Documentation	Manoj Murugan, Sneha Sahu, Varun Varadarajan, Manjunatha Shetty

2. REQUIREMENTS

2.1 FUNCTIONAL REQUIREMENTS

- ✓ Current blood glucose reading must be shown in the Interface
- ✓ Graph and Range Indicator should work in sync with the current blood glucose reading.
- ✓ Battery level, Insulin Bank and Glucagon Bank should be maintained effectively.
- ✓ One dose of Insulin/Glucagon should not exceed the pre-defined max Single Dose limits
- ✓ Simulator must ring an alarm bell when Blood glucose goes out of normal range.
- ✓ When status of battery, insulin or glucagon bank drops below a certain limit, alarm along with pop-up message is generated.

2.2 SAFETY REQUIREMENTS

Blood Glucose Range[8]: the simulator must be fed with the safe blood sugar range –

Dangerous/Unsafe: blood glucose < 70mg/dl

Safe: blood glucose between 70 and 120 mg/dl

Undesirable: blood glucose > 120 mg/dl.

Hormone Dosage Limit: we need to maintain a dosage limit for both the hormones, i.e. there should be a minimum and maximum single dose limit for both Insulin and Glucagon.

Simulator Mode: in automatic mode, the simulator should be efficient enough to maintain blood glucose within the defined normal range; i.e. auto-calculate the amount of hormone to be injected, by referring to patient's previous and current blood glucose values.

Monitoring Period: the simulator should keep updating its data at frequent intervals(every 10 minutes)[11].

Alerts and Warnings: In case of any discrepancy, immediate alert/warning should be generated.

2.3 SOFTWARE REQUIREMENTS

Platform: Windows 10 (64 bits) Operating System

Programming Language: Java Eclipse IDE, Java FX framework

Tools: ObjectAid, ArgoUML, MsExcel

3. ENGINEERING PROCESS

3.1 PROCESS MODEL

Choosing good process model effect on project Cost, time and performance. Keeping the timeframe of the project, delivery deadlines and weekly targets in the picture, the team decided to choose V-Model as the software engineering process for this project. The process model covers the following aspects in our project [10] –

- ✓ System Initiation/Planning
- ✓ Requirements Analysis and Specification
- ✓ Functional Specification or Prototyping
- ✓ Partition and Selection
- ✓ Architectural Design and Configuration Specification
- ✓ Detailed component Design Specification
- ✓ Software Integration and Testing
- ✓ Documentation Revision and System delivery
- ✓ Deployment and Installation
- ✓ Training and Use
- ✓ Software Maintenance

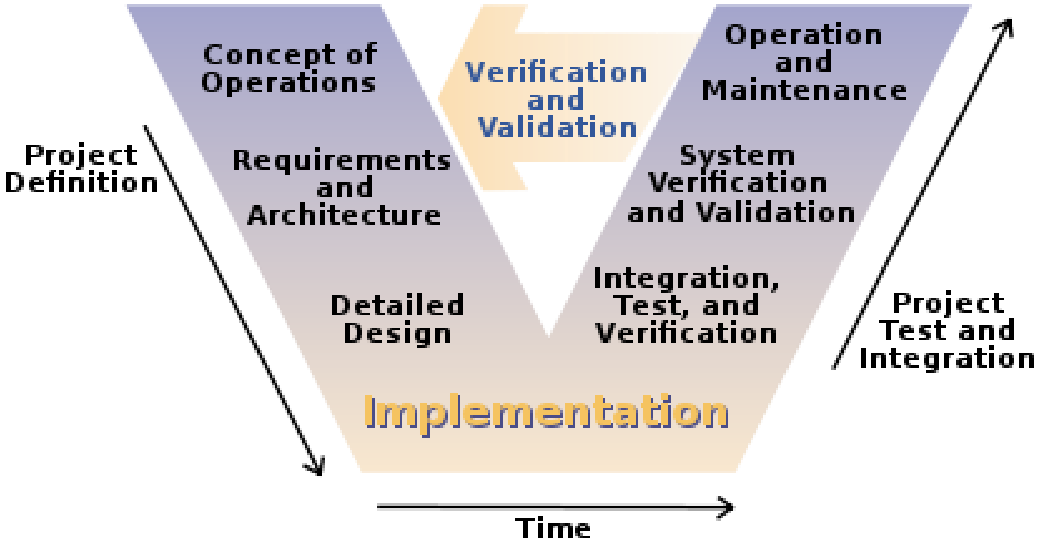

Fig.1: V-Model [9]

<u>Approach to the Project Using V-Model</u>

The V-Model represents a software development process (also applicable to hardware Development) which may be considered as an extension of the waterfall model. Instead of moving down in a linear way, the process steps are bent upwards after the coding phase, to form the typical V shape. The V-Model demonstrates the relationships between each phase of the development life cycle and its associated phase of testing. The horizontal and vertical axis represents time or project completeness (left-to-right) and level of abstraction (coarsest-grain abstraction uppermost), respectively.

3.2 <u>HAZARD AND RISK ANALYSIS</u>

we have tried to identify hazardous scenarios which can hamper the functioning of the system and thereby health of user –

Identified Hazards	Hazard Probability	Associated Risk	Risk Level	Preventive Measure
Timer Failure	Low	There will be inconsistency in the change in Blood sugar level and computed Hormone Injection	High	Implement an efficient timer; monitor change in blood glucose and Hormone computation every 10 minutes [~5 seconds in Simulator]
Power Failure	Low	Simulator shuts down	High	Implemented Battery Alert Notification along with an effective alarm [~90% in simulator]
Blood Glucose Sensor Failure	High	Incorrect blood glucose reading and hence incorrect Hormone dosage computation	High	No preventive action since sensors do not compute blood glucose level but simply take reading; [Implemented automatic sensor check that runs every 5 sec of simulator]
Hormone Overdose	Medium		High	Set maximum single dosage limit and re-compute Hormone Dose
Empty Hormone Bank	High	No further hormone dose possible	Medium	Alert Notification along with effective alarm, in case Insulin/Glucagon bank goes below a certain level [~90% in simulator]

4. MATHEMATICAL MODEL

After extensive search of literature, we have adopted the below mathematical model for computing changes in Blood glucose levels and Insulin/Glucagon injection dose in our Simulator.

4.1 Insulin Kinematics

Our model mimics how the concentration of glucose in the blood varies as time progresses. The formula is based on variables such as initial/ concentration of glucose, amount of carbohydrates in meal, glycaemic index and the rate at which insulin is released.

The form of the minimal model [4] is:

$$\frac{dC}{dt} = -k_1 C \qquad \frac{dG}{dt} = k_1 C - k_2(G - G_0)$$

On solving both the differential equations we can determine G(t) as follows.

$$G(t) = A_0 \frac{k_1}{(k_2-k_1)}(e^{-k_1 t} - e^{-k_2 t}) + G_0.$$

Symbol	Definition
G	Glucose level in the blood
G_0	Baseline value of glucose in blood
C	Concentration of carbohydrates in stomach
C_0	Amount of carbohydrates in the meal
k_1	Glycemic index
k_2	Rate at which insulin is released
t	Time

Fig.2: Variables and their representations [4]

The values for parameters – $A_0 = 121.7$, $G_0 = 90.0$, $k_1 = 0.0453$, and $k_2 = 0.0224$

Time (minutes)	Blood Glucose Levels	
	Experimental Data	Theoretical Model
0	90	90
30	151	151.09
60	137	136.89
90	118	117.98
120	105	105.33
180	94	94.2
240	92	91.1
320	91	90.8

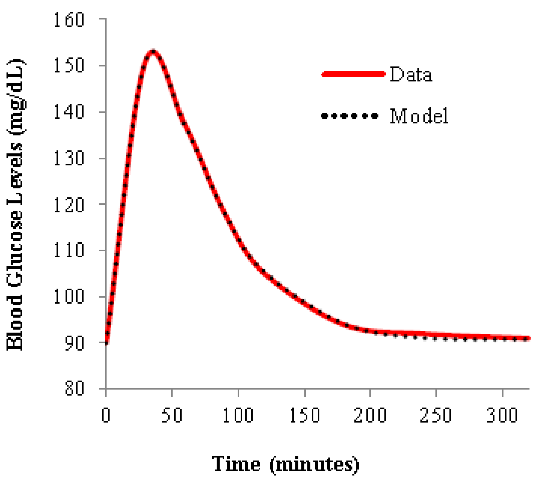

Fig.3: Blood glucose levels for the experimental data and theoretical model in equation [4]

It can be seen clearly from Fig.3 that the graphs for the theoretical model and experimental data are almost identical.

4.2 Glucagon Kinematics

Glucagon is a key catabolic hormone consisting of 29 amino acids. Described by Roger Unger in the 1950s, glucagon was characterized as opposing the effects of insulin [5]. Glucagon plays a major role in sustaining plasma glucose during fasting conditions by stimulating hepatic glucose production.

Glucagon is secreted by α-cells in pancreas which constitute not more than 10-15% of total volume. Despite this fact, glucagon is a powerful peptide hormone which has almost immediate on blood glucose even administered in very small quantities. The clinical findings for glucagon administration show that when the glucagon was administered intravenously the average time of the maximal response of the blood sugar was 25.2 minutes, with a range of 17 to 40 minutes. When given intramuscularly the average time of the maximal response was 31.6 minutes with a range of 15 to 56 minutes for 0.05, 0.02 and 0.1 mg of glucagon per kg body weight given [6].

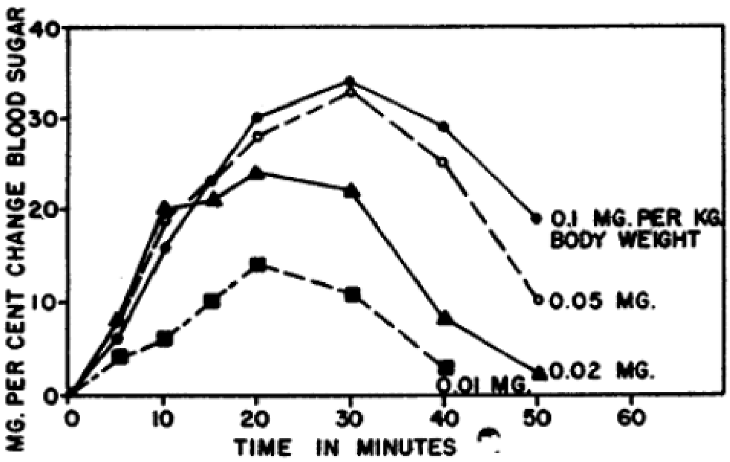

Fig.4: The average responses to a variety of glucose doses [6].

4.3 Hormone Dosage Computation

Blood sugar level is monitored continuously every 10 minutes[~5 sec in simulator] and corresponding amount of hormone dosage is injected if blood sugar is out of normal range.

a. Dosage Computation is based on the following factors[7] –
b. the reading for most recent blood sugar level [~ BSL].
c. patient's average body weight assumed as 72 Kg. in our prototype.
d. 1 unit of Insulin cause the blood sugar to drop by 45 mg/dl [~ I=45].
e. 1 unit of Glucagon will enhance the blood sugar level by 3 mg/dl [~G=3].

InsulinDose = minimum[Imax, (BSL - Rmax)/I];
GlucagonDose = minimum[Gmax, (Rmin - BSL)/G]

where, Rmax = upper limit of safe blood sugar level
Rmin = lower limit of safe blood sugar level
Imax = maximum Single Insulin Dose = 1
Gmax = maximum Single Glucagon Dose = 2

5. DESIGN CONSIDERATIONS

5.1 SIMULATOR ALGORITHM

1) Launch Application GUI
2) At Launch – all display parameters like BSL, timer, battery level, Hormone Banks, Graph Axes, message box is initialized.
3) Every 1 hour [~30 seconds] BSL drops by 1 unit, keeping into mind that human body loses some amount of sugar throughout the day[11].
4) Whenever, there is change in carbohydrates, "*blood glucose sensor*" changes BSL as per the mathematical model described in Unit 4.
5) For any change in BSL done by "*blood glucose sensor*" the following steps are performed –
   a. check if BSL is within safe range and alert if not.
   b. update information for Range Indicator and message box.
   c. compute Insulin/Glucagon dose, which get stored in a hash map.
6) Every 10 minutes [~5 seconds], the display settings are refreshed to get latest readings – BSL, Insulin/Glucagon Dose, Insulin/Glucagon amount in bank and battery level. [Battery level reduces by 0.5% every 5 seconds of simulator]
7) Based on these parameters, the other sections – Range indicator, message box and graph display gets modified.
8) Whenever, the battery level or hormone bank goes below certain limit, give pop up message and sound alert.

5.2 SEQUENCE FLOW DIAGRAM

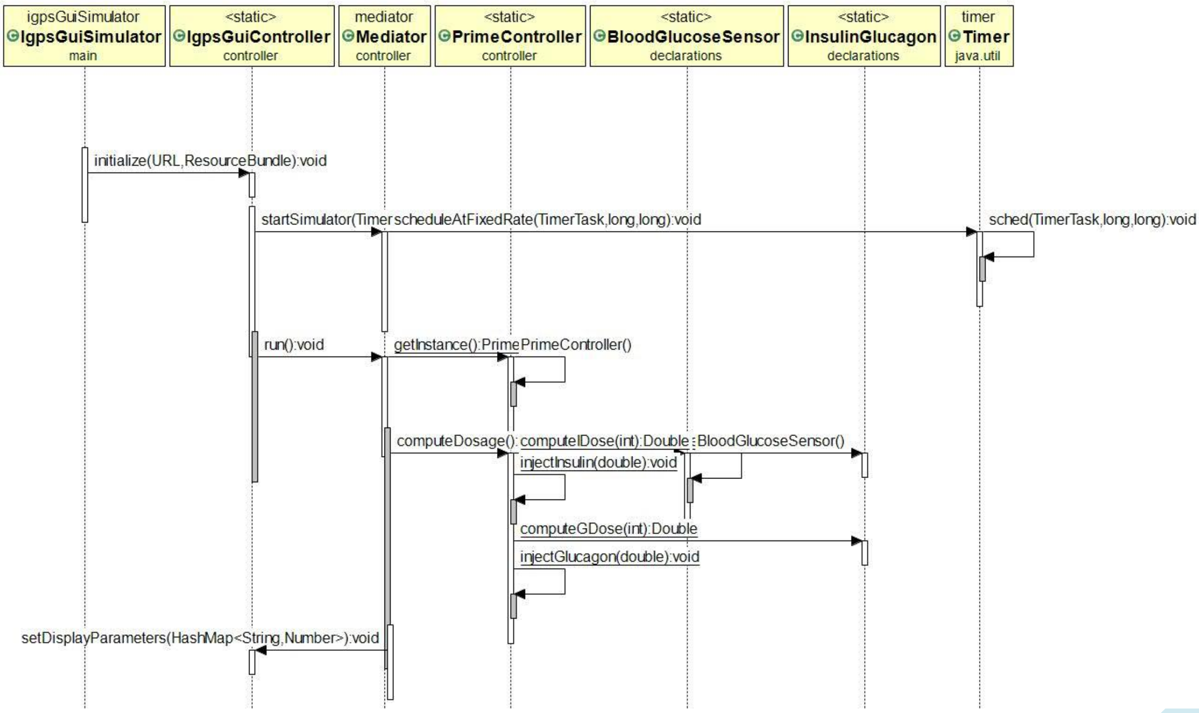

Fig.5: Simulator sequence flow

5.3 CLASS DIAGRAM

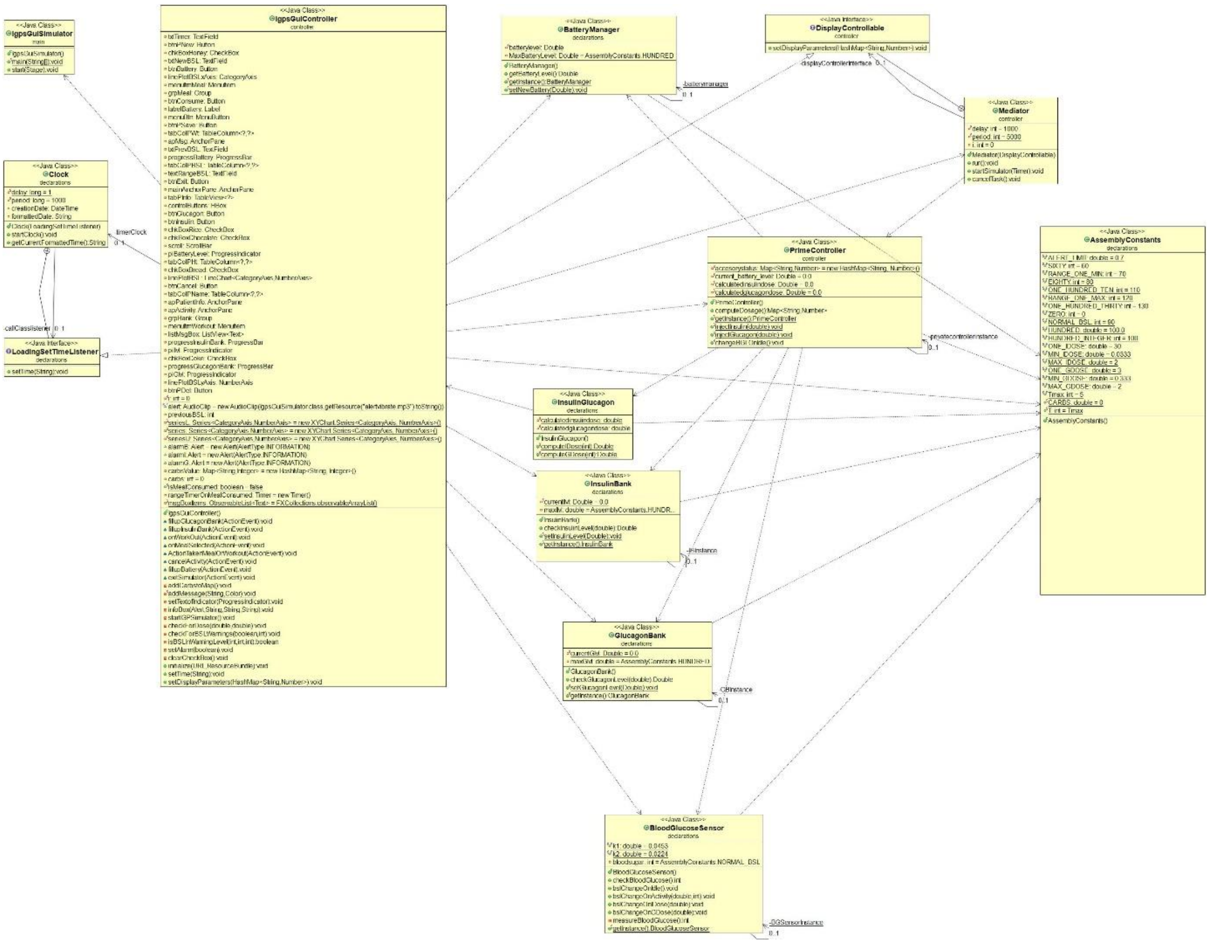

Fig.6: Simulator classes and their references

5.4 HUMAN MACHINE INTERFACE

In this section, we have laid importance on the interaction model between user and the pump and how we tried to match the software simulation as close as possible to a real Insulin pump. The idea we followed is to keep the User Interface of the pump as user friendly as it can be, thus enabling a better human-machine interface.

The Bionic Pump

Fig.7 below displays the main view of our simulator. The middle –left area depicts the live charts of the following values:

- Sugar Level along Y-Axis ranging from 0-130 depicts the value of current blood sugar level in mg/dl at the current time.
- The X-axis depicts the current time.
- The green line indicates the Upper limit of Blood sugar level
- The red line indicates the lower limit of blood sugar level
- The yellow line indicates the current Blood sugar level plot

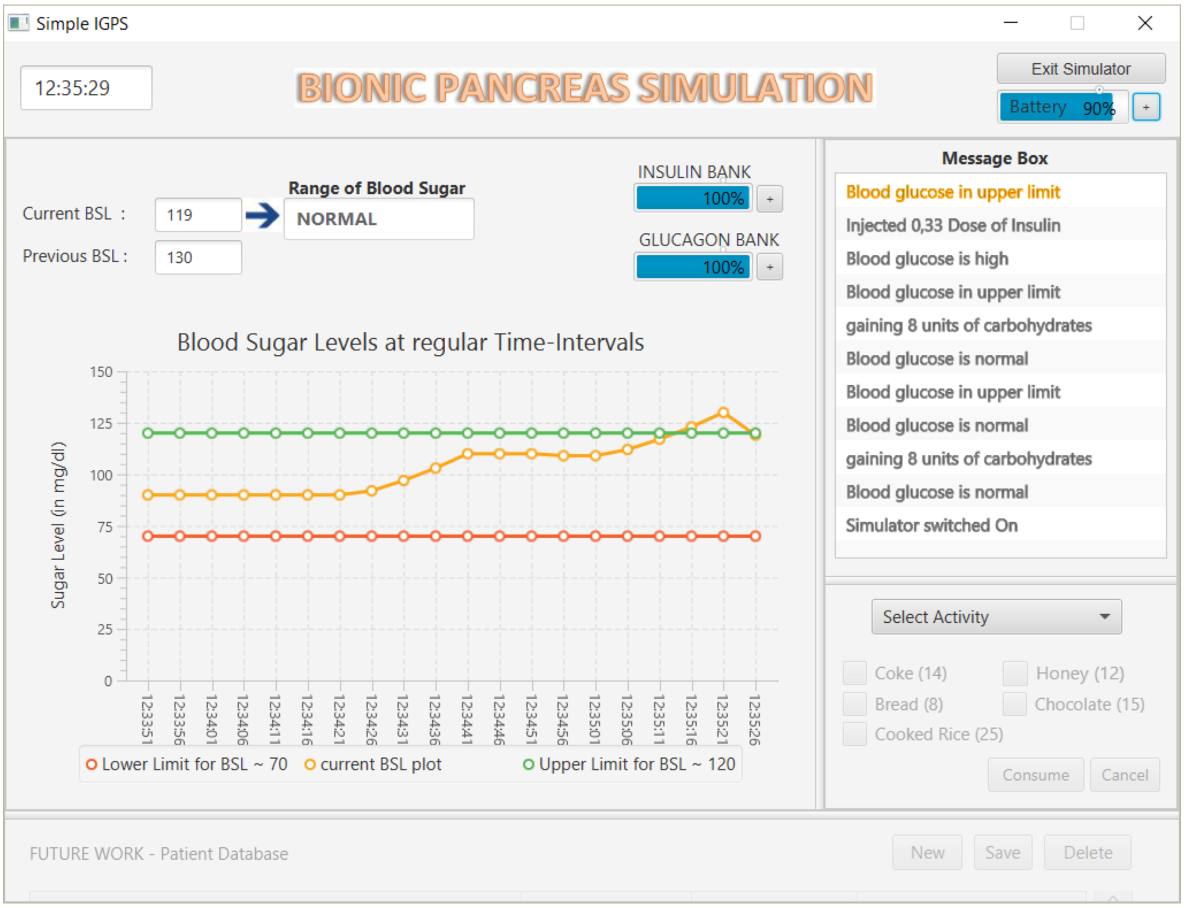

Fig.7: Bionic Pancreas Simulator

Every 5 seconds the graph is refreshed appending the new BSL value at the end. The scale of 5 seconds, in reality refers to 10 minutes. So 5 seconds on the graph is equivalent to 10 minutes for a real Insulin Pump.

In this Figure, just above the graph, there is a small text box where user can see the numerical form of the blood sugar level depicted in the chart. This helps to quickly spot the exact value of the parameter and the charts help to analyze the change in Blood sugar level against current time. The range of blood sugar is also depicted in the same panel which here is showing as “Normal”. Other values for the section being – “High Sugar” and “Below safe”.

Beside the blood sugar indicator, we have the insulin and glucagon supply indicators in the pump. One unit of insulin is equivalent to 45mg/dl reduction in Blood Sugar level and for one unit of glucagon intake, there is an increase of 3mg/dl in Blood sugar level.

The right top area has the panel with battery level indicator and Exit simulator. The warning pop up window appears if the battery level goes below 90 percent, which can be modified as per user need.

The Bionic Pump

The right area of our interface below the battery indicator contains the activities we can apply to blood glucose levels to test the insulin pump. The buttons are given with some predefined scenarios. They will vary the blood glucose levels based on the activity selected.

- If "Go for Workout" activity is selected, there is a negative change in the blood glucose level by 10 units of carbohydrate, which is shown in the graph in Fig.8b. It decreases gradually with time.

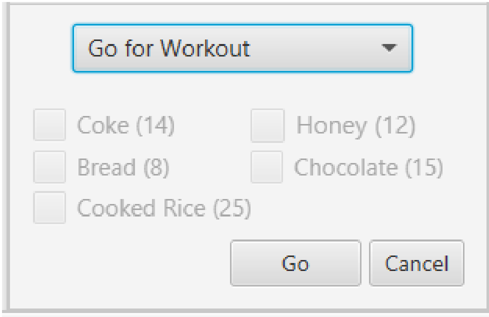

Fig.8a

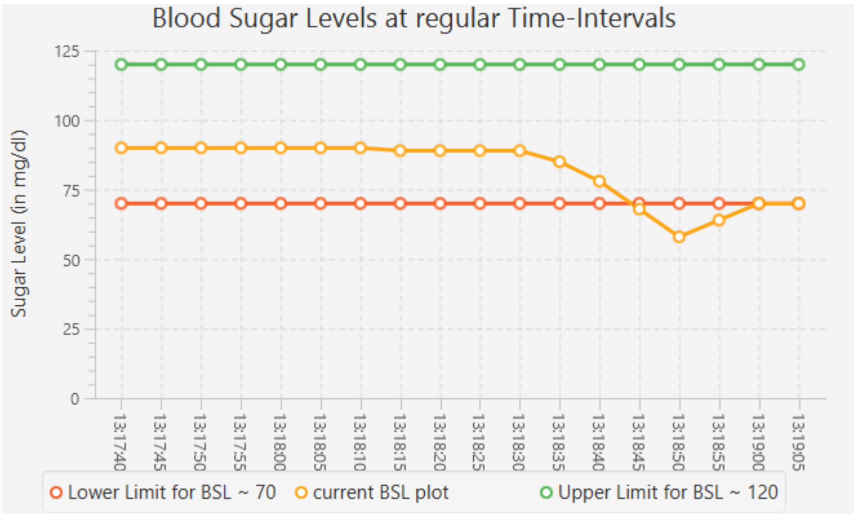

Fig.8b

- If "Proceed for a meal" activity is selected, it enables manual selection options of meals with their carbohydrate metrics which are coke, bread, honey, chocolate and cooked rice. The blood sugar level increases according to the total units of meals consumption.
- As shown in the graph in Fig.9b, there is a gradual increase in the blood sugar level with time.

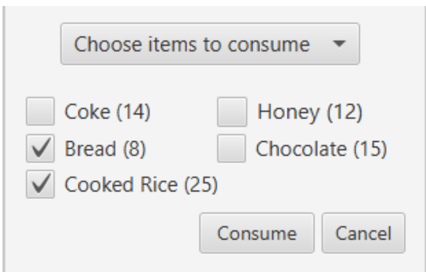

Fig.9a

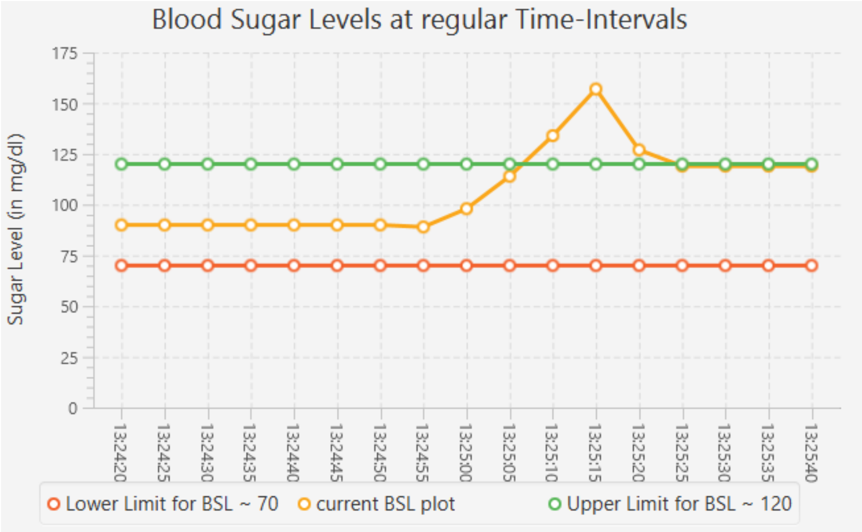

Fig.9b

Usability Features

The lines indicating the blood glucose levels in the graph is colored appropriately to identify the exact blood glucose level at a particular time. The current BSL is denoted by yellow color, the upper limit line is indicated in green and the lower limit line in red. There is a message box in the form of a text box in the right area of our interface above the activities buttons, which indicates the messages as and when an activity occurs with respect to the insulin pump.

The messages indicated in the message box are as follows:

- Blood Sugar level is normal indicated in green color
- Blood sugar level in lower or upper limits indicated in yellow color i.e. at 120mg/dl and 70mg/dl
- Blood Sugar level when normal the yellow line in the graph plots between the Upper scale limit and lower scale limit i.e. between 70mg/dl and 120 mg/dl
- When Blood sugar level is high and low, the yellow line plots beyond the upper and lower scale limits in the graph i.e. above 120 mg/dl and below 70 mg/dl
- Units of Carbohydrates gained and lost is displayed in the message box

6. FUTURE ENHANCEMENTS

Since it's a minimalistic simulation of Insulin/Glucagon pump, there is a huge scope for future enhancements. Few important ones being –

1. Give a platform for run-time user customisation for setting threshold limits – battery level and hormone banks.
2. Include manual injection of Insulin/Glucagon hormones.
3. Incorporate a refresh button that would re-plot the graph from index 1.
4. Include a daily dosage limit for both the hormones.

5. Maintain a database that can help to generate weekly/monthly reports for doctor's use.
6. Provide daily/weekly suggestions on the food intake based upon his previous diet statistics.
7. Implement a SOS to nearby or close relatives in case of emergencies.

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