APPENDIX 1

GLUCOSIM

The Glucosim has utilized two mathematical models based on pharmacokinetic diagrams of glucose and insulin (Puckett 1992) which represent the transport of glucose and insulin through major vessels to the capillaries. The glucose pharmacokinetic diagram contains tissues including heart, brain, liver, kidney and muscle where glucose is used for energy (Erzan et al. 2001). Glucose excretion by kidney and gastrointestinal tract were also included. The pharmacokinetic diagram for insulin includes the subcutaneous tissue as a source for insulin. It has been assumed by the researchers that the pancreas of a diabetic patient does not produce any insulin. Removal and degradation of insulin occurs mostly in liver, kidney and peripheral tissue. They degrade one-half, one-third and one-sixth respectively, of the insulin presented to them. Changes in blood flow would change these fractions, but the model flows are constant (Hillman 1976). A mass balance equation is written for each compartment in the model. The compartments represent actual body regions. The main disadvantage of these models is that the personal variations in physiological parameters are not taken into account. Therefore the outputs are average values and hence the simulator is advised for educational purpose only rather than providing medical advice. For a typical organ such as liver, the mass balances for glucose (\( G_L \)) and insulin (\( I_L \)) concentrations are

\[
\frac{dG_L}{dt} = \frac{1}{V_L} \left( Q_{HA} G_B + Q_{PV} G_{PV} - Q_L G_L - LGU + LGP \right) \quad (A1.1)
\]

\[
\frac{dI_L}{dt} = \frac{1}{V_L} \left( Q_{HA} I_B + Q_{PV} I_{PV} - Q_L I_L - LIR \right) \quad (A1.2)
\]

Where, \( LGP \) is Liver Glucose Production rate, \( LGU \) is Liver Glucose Utilization, \( LIR \) is Liver Insulin Removal rate, \( Q_L \) is Liver volumetric flow rate, and \( V_L \) is the effective volume in liver. \( Q_{HA} \) is the blood flow rate in
Hepatic Artery (HA), $Q_{PV}$ is the blood flow rate in Portal Vein (PV), $Q_L$ is the blood flow rate in Liver (L), $G_B$ is the glucose concentration in blood in mg/dl, $G_{PV}$ is the glucose concentration in PV, $I_B$ is the insulin concentration in blood in mU/dl, $G_L$ is the glucose concentration in liver, $I_L$ is the insulin concentration in liver in mU/dl.

In the overall model, it is assumed that changes in blood glucose and insulin concentration for each tissue are fast and the balances are in quasi-steady state shortly after a disturbance (i.e the carbohydrate intake). The resulting algebraic equations are incorporated in the glucose and insulin balances in the blood, yielding an overall model with two differential equations. In the detailed model all differential equations are preserved and it is possible to see the changes in glucose and insulin concentrations in individual tissues before reaching the quasi-steady state. Both models are capable of simulating the observed behavior of blood glucose and insulin levels of a patient. The screen shots of the simulator have been shown below in Figures A1.1 to A1.6.
Figure A1.1 Index page of Glucosim simulator

Figure A1.2 Glucosim simulator modes and options
Figure A1.3 Input settings of Glucosim simulator

Figure A1.4 Glucose and Insulin dynamics for 24 hours
Figure A1.5 Additional Inputs of Glucosim simulator

Figure A1.6 Physiological data obtained from Glucosim simulator
The data file shown in Figure A1.6 shows the values such as time in minutes, blood glucose in mg/dl, blood insulin in mU/dl, liver glucose production in mg/Kg min, stomach glucose in mg/Kg etc.. From this data file, first two columns of data i.e., time in minutes and blood glucose in mg/dl were used as the first data set for analyzing the proposed methods.