SIMULATING THE IMPACT OF DIET AND EXERCISE ON BLOOD GLUCOSE LEVEL FOR PEOPLE WITH TYPE 2 DIABETES

by

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ABSTRACT
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This thesis describes the design of a discrete-event simulator that tracks the blood glucose level and glycated hemoglobin level as a person goes through her daily diet and exercise activities. This thesis also reports results of simulations performed using the simulator that show the changes in blood glucose level and glycated hemoglobin level as a diabetic person makes specific changes to her diet/exercise routine.

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1. Introduction

Diabetes has reached epidemic proportions. It is estimated that this disease affects more than 29 million people in USA (9.3% of the population) [1] and more than 347 million people worldwide [2]. Type 2 diabetes, often associated with a sedentary life style and obesity, accounts for 90% to 95% of all diagnosed cases of diabetes in adults in USA [1].

Diabetes results in persistently elevated blood glucose levels that cause many serious complications such as heart disease, blindness, and kidney failure and lower-limb amputation. In 2010, diabetes was listed as a cause of death in 234,051 death certificates in USA [1]. The direct medical costs of diabetes in USA were estimated to be $176 billion in 2012 with an extra $69 billion cost attributed to disability, work loss and premature death caused by the disease [1].

In a non-diabetic person metabolic homeostasis maintains the blood glucose levels within a narrow range (70 to 125 mg/dL) with mean 100 mg/dL. A number of hormones, primarily insulin and glucagon, help the body achieve this effect. As the blood glucose level becomes high, the pancreas releases insulin, which causes liver and muscle/fat-tissue cells to remove glucose from the blood. As the blood glucose level becomes low, the pancreas releases glucagon, which causes the liver cells to release stored glucose into the blood stream. In Type 1 diabetes, the pancreas does not produce enough insulin and in Type 2 diabetes, cells within muscles/liver/fat-tissues have a reduced

response to insulin (known as insulin resistance) and thus fail to efficiently remove glucose from the blood. Type 1 diabetics need frequent insulin injections just to survive, while Type 2 diabetics can manage their condition via diet control, exercise and medication (including insulin). This research is focused on Type 2 diabetes, hereafter referred to simply as diabetes.

Due to insulin resistance, the blood glucose level of a diabetic person may become much higher than normal following a carbohydrate rich meal. For example, it is not unusual for a diabetic person to have a post-meal blood glucose level approaching 300mg/dL or higher. In the absence of medication or vigorous physical activity, the elevated blood glucose level may persist for several hours. People with diabetes usually take medicine (including insulin) that help reduce their blood glucose levels via many different mechanisms. Also, any vigorous physical activity, such as walking or running, allows the cells to absorb glucose from the blood via an insulin-independent pathway [3], [4] and thus reduces the blood glucose level. Besides reducing blood glucose levels, physical exercise also helps diabetic people reduce weight, which can significantly improve their condition. Hence, people with diabetes need to be very careful about their diet and must exercise regularly.

A diabetic patient undergoes a laboratory test every 3 months to measure the fraction of glycated hemoglobin (HbA1c) in her blood. Glycated hemoglobin is formed as a result of the attachment of a glucose molecule to a hemoglobin molecule inside an

erythrocyte (also known as a red blood cell). A new erythrocyte does not have any glycated hemoglobin. The rate of glycation of hemoglobin molecules at any given point in time is considered directly proportional to the prevailing glucose level in the blood at that time. A hemoglobin molecule, once glycated, stays glycated until the erythrocyte carrying this molecule dies. Hence the fraction of glycated hemoglobin in blood, henceforth referred to as the HbA1c level, is considered a reliable indicator of long term average blood glucose level.

In this thesis, we describe the design of a discrete-event simulator that tracks a person's blood glucose level and HbA1c level as she goes through her daily diet and exercise activities. Then, we describe simulation results that illustrate how the simulator quantifies the impact of specific changes in a person's diet/exercise routine on her blood glucose levels and HbA1c level. We anticipate the simulator to serve as a useful tool for diabetes research especially in situations where monitoring/experiments on human/animal subjects is not feasible.

2. Simulator Design

2.1 Simulator Core

The discrete-event simulator has the following core components:

Simulation Controller:

This unit takes as input a timed sequence of diet, exercise and rest activities for several months. At the start of a simulation, these activities are read into a priority queue. The priority of an activity is same as its occurrence time. The unit fires each activity at its specified occurrence time. The unit is also responsible for incrementing time once all the activities scheduled for the current time have been fired.

Human Body: This unit performs the following tasks:

Glycemic Adjustment: This unit adjusts the blood glucose level in a specified manner following the occurrence of a diet/exercise/rest activity. At present, the simulator supports only a linear change in blood glucose level following the occurrence of a diet/exercise activity (as discussed later, the impact of a rest activity is somewhat different). Also, an activity is assumed to impact the blood glucose level only until the occurrence of the next activity. A diet activity causes the blood glucose level to increase at a linear rate associated with that activity. An exercise activity causes the blood glucose level to decrease at a linear rate associated with that activity. A rest activity also causes the blood glucose level to decrease but the rate of decrease decreases with time.

In the simulations reported in this document, we have used the rest activities to limit the impact a diet/exercise activity on blood glucose level. For example, placing a rest activity 2 hours after a diet activity limits that diet activity's impact to those 2 hours. Finally, the blood glucose level is constrained to stay within specified bounds (lower bound 100 mg/dL and upper bound 400 mg/dL in the simulations reported in this document) irrespective of the rate of change in effect.

Future modifications to the simulator will enable a diet/exercise activity to impact the blood glucose level beyond the occurrence of the next event. In particular, it will be possible for the simulator to take in account all the diet/exercise activities so far in the day while deciding the rate at which the blood glucose level will change.

Hemoglobin Glycation: The hemoglobin molecules primarily reside inside erythrocytes (or red blood cells). An adult human body has 20-30 trillion erythrocytes at any given time [5]. Each erythrocyte contains approximately 280 million hemoglobin molecules [6].

The simulator assumes that all hemoglobin molecules residing inside an erythrocyte glycate together and when that happens the erythrocyte itself is assumed to have glycated. The probability of glycation of an unglycated erythrocyte is assumed to be proportional to the prevailing blood glucose level. An erythrocyte, once glycated, is assumed to stay glycated until it dies. The "Human Body" unit causes erythrocytes to take birth, possibly glycate in response to prevailing blood glucose level and finally die

after completing their lives. This unit takes as input the rate at which new erythrocytes are born, their lifetime distribution and the probabilities of an erythrocyte's glycation in a unit time in response to various prevailing blood glucose levels. This unit maintains data structures recording the number of glycated/unglycated erythrocytes in existence for each possible age. At each time instant, this unit allows some new erythrocytes to take birth, some erythrocytes to die as per their lifetime distribution and some unglycated erythrocytes to glycated based on the prevailing blood glucose level. In the simulations reported later, new erythrocytes take birth at rate 138888888 per minute, each erythrocyte is assumed the live for 120 days and an unglycated erythrocyte gets glycated during a minute with probability

$$G_p = G_{ps} * L + G_{pc}$$

Where G_{ps} is glycation probability slope and G_{pc} is a glycation probability constant and L is the current blood glucose level in mg/dL. After extensive experiments, we used the following values for these constants: G_{ps} = 0.0000000021 dL/mg and G_{pc} = .0000007. These values provide the best match with the mapping between average blood glucose level and HbA1C value reported in the literature [5][7].

2.2 Simulation Configuration File Generator

This unit generates simulation configuration files containing the timed sequence of diet/exercise/rest activities for several months. Each activity is associated with a linear rate of change in blood glucose level that will come in effect when this activity is fired. In addition, a configuration file contains the following information:

1. Initial fasting blood glucose level
2. Rate of erythrocyte birth and death
3. Rate at which erythrocytes glycate at different blood glucose levels
4. Decrease rates associated with rest activities
5. Constraints on minimum and maximum values of blood glucose level
6. Glycation probability slope and constant.

3. Class Diagrams

The simulator is implemented in C++ and consists of the following classes.

3.1 Simulator Core

This module consists of 6 classes

1. Humanbody
2. SimCtl
3. PriQElt
4. PriQ
5. Event
6. Linear_Change

For each simulation, one **SimCtl** instance and one **Humanbody** instance is created. These two instances exist until the end of the simulation. The main task of **SimCtl** instance is to create an object of **PriQ** class from the given profile information. Each profile is consists of list of **Events**. An **Event** object consists of event time, event rate, event group etc. **PriQ** is a priority queue that holds Events and fires them at specified times.

Main operations of **SimCtl** are listed bellow

i. add_linear_change_event: This method adds a new event in the **PriQ** object.

ii. fire_event: this method will find a new event from the priority queue during the simulation time of 90 days period.

SimCtl also track simulation clock time during the simulation with an attribute n_ticks.

The **Humanbody** instance simulates a human body with given profile information like min blood glucose level, maximum blood glucose level, glycation probability slope, glycation probability constant etc. The **Humanbody** instance has the following main attributes

i. BGL : track blood glucose level at any time t during simulation

ii. Rate : rate of current event

iii. AvgBGL : track Average BGL so far during simulation

iv. HbA1C : keeps A1C value after the simulation

v. AgeBins: it keeps track of glycated and non-glycated hemoglobin during simulation.

vi. minBGL : minimum allowed BGL for that profile

vii. maxBGL : maximum BGL allowed for that profile

viii. G_{fast} : fasting blood glucose level

List of main Operations for **humanbody** instance

i. changeRate : this method change the current rate of BGL update by a new rate

ii. UpdateAvgBGL : in every clock tick this method update AvgBGL

iii. UpdateBGL: this method update current BGL with the corresponding rate in every minute. For meal and exercise event it use equation 1 and 2 and for artificial decease rate it uses equation 7.

iv. Update: this method update glycated hemoglobin and BGL in every clock time.

3.2 Simulation Configuration File Generator Module

This module consists of the following classes.

1. ProfileGenerator
2. Profile
3. ProfEvent
4. EventDayTime

Profile Generator Class creates profile data base taking profile configuration information **Profile** class is responsible for creating new profile with given user input as list of **event** and others related profile info like fasting blood glucose level G_{fast} , number of events, Peak of BGL due to each events etc. Profile class can also update profile and create new profile from given profile and update instruction.

ProfEvent class Creates Event list for new Profile. Each instance of **ProfEvent** consists of one event list representing a whole day food exercise habit of a user.

Main attributes of **ProfEvent** class are

i. eDateTime: it is an instance of **EventDayTime** which tells the time info for that **ProfEvent** instance.

ii. changeR : rate of changes in BGL due to this event

EventDayTime class is basically a structure which is consists of 4 fields: Event day, time, minute seconds. It tells the exact time of an event in 90days span simulation time.

A **profile** has a list of events and others humanbody information like fasting blood glucose level, RBC birthrate etc. Which represent the food exercise habit of a person.

The module has two additional classes: **FilManager** and **SimConfig.** File manager is used for disk read-write operations where **SimConfig** instance provide configuration information like number of total profile in the simulator, number of events in each profile , simulation time, glycation probability slope , glycation probability const etc.

3.3 Result Log module

This module keeps records of all simulation results after the simulation. The main attributes of this class are listed bellow.

i. **AvgBGL** : 2d vecotr which records Average blood glucose level of each profile and its version
ii. **HbA1C** : 2d vecotr which records A1C value of each profile and its version
iii. **All_Points** : 3d vector which records all BGL reading before and after each events for each profile and its different versions during simulation.

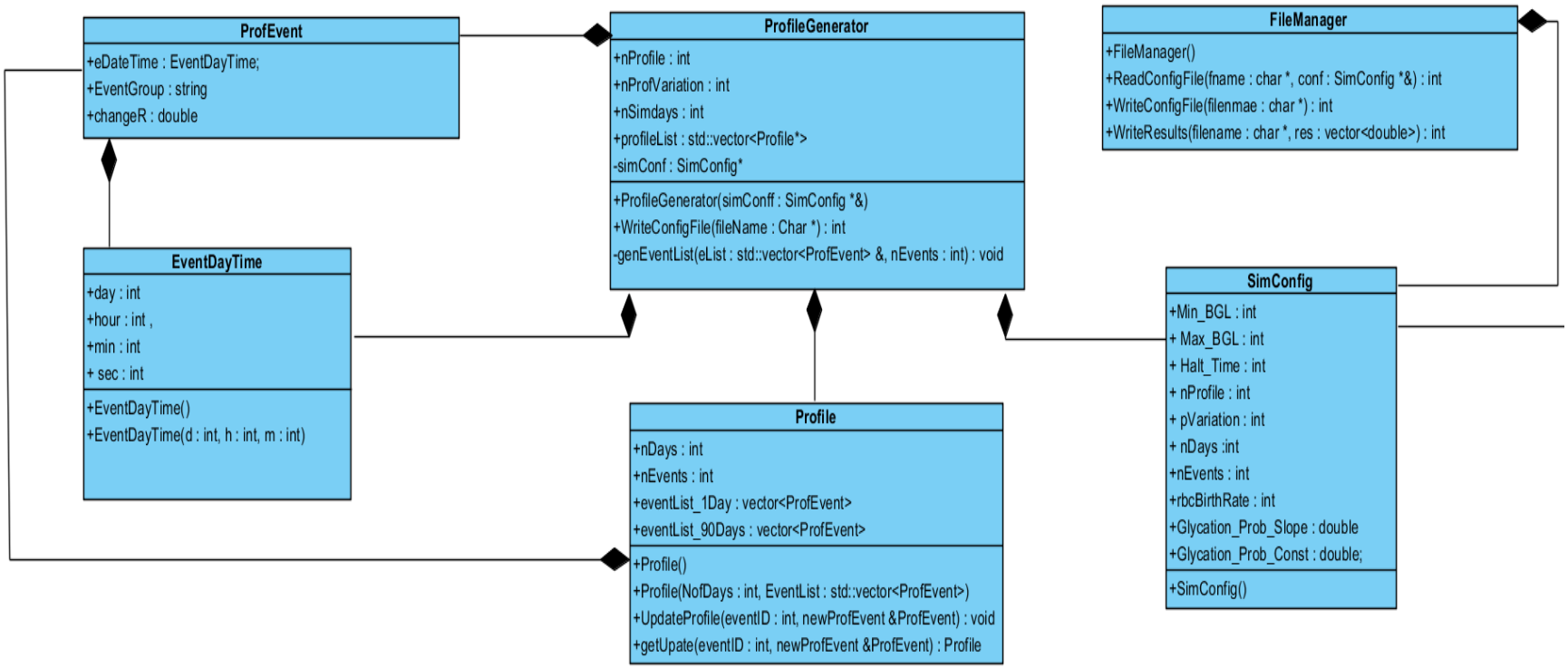

Figure 1 : Class diagram of configuration file Generator module

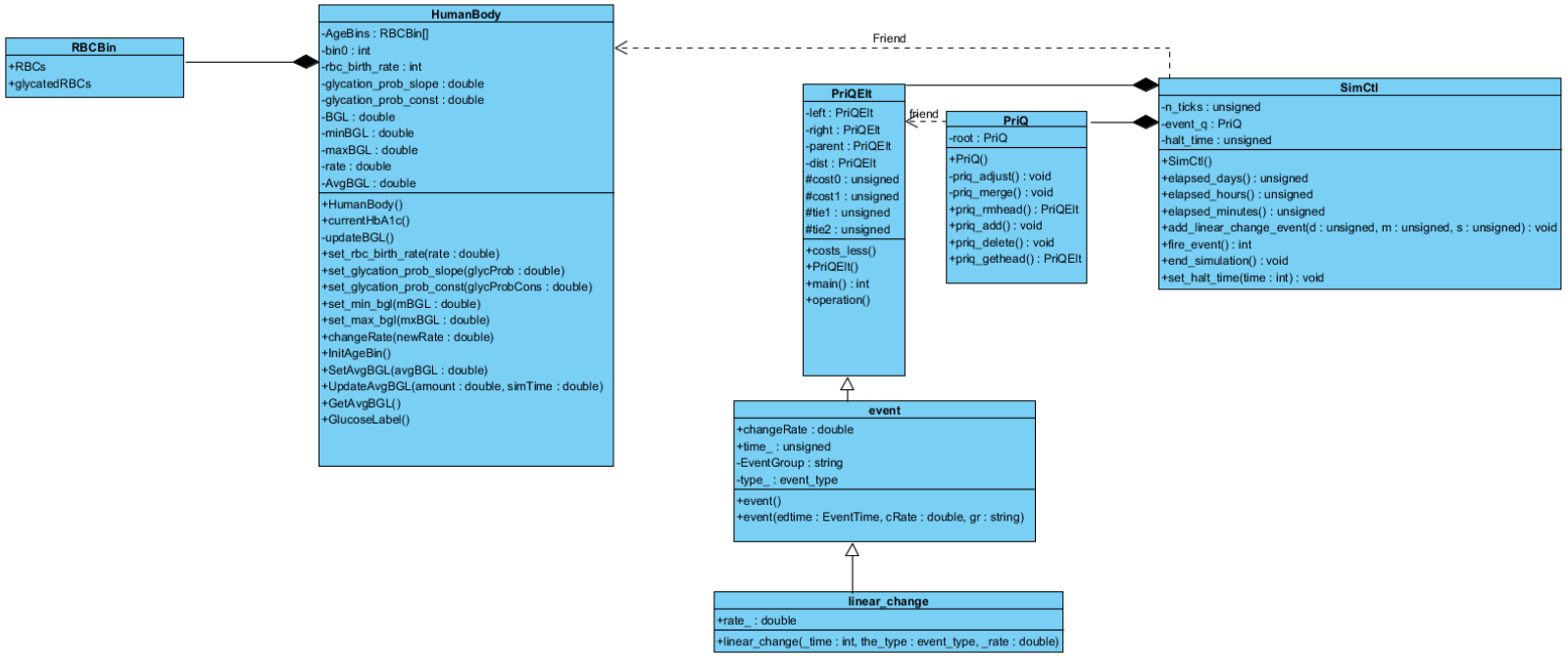

Figure 2 : Simulation core class diagram

Figure 3 : results log module class diagram

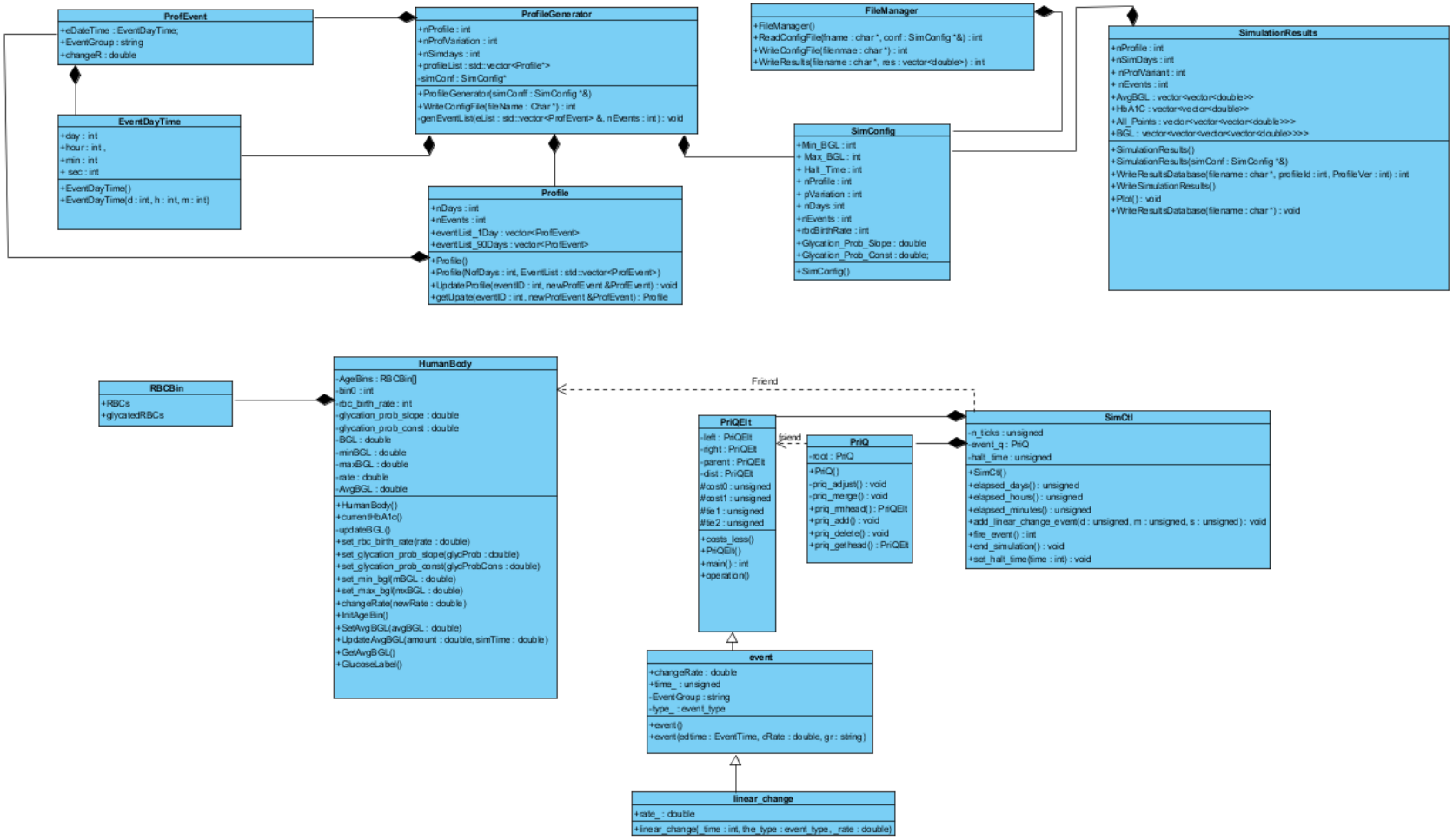

Figure 4 : class diagram of the simulator

4. Simulation Results

We simulated 4 sets of profiles, where each profile represents a person with Type 2 Diabetes. A profile consists of the following information:

1. Fasting blood glucose level (BGL): BGL after 8 hours of fasting
2. Metabolic rates : changes in BGL after meal intake or after exercise
3. Food habits : list of daily food intake activities
4. Exercise habits : list of daily activities involving physical exercise
5. Rate of decrease in BGL during rest/sleep.

We used same glycation probability constant .0000007 and glycation probability slope 0.0000000021 dL/mg for all profiles. So, an unglycated erythrocyte glycates with probability (L * 0000000021 + 0000007) during a second when the prevailing BGL is L.

We simulated each profile for 90 days and obtained the log of the blood glucose levels throughout the simulation. We also noted the average blood glucose level and HbA1c level at the end of the simulation. This was followed by introducing various interventions (in terms of modified/new diet/exercise activities) in this person's daily routine, simulating the modified routine for 90 days and noting the impact in terms of blood glucose levels and HbA1c value. The studied interventions included reduction in the amount of consumed breakfast/lunch/dinner such that the rate of increase in BGL following the meal reduces by 30%. This is referred to as a "30% reduction in breakfast/lunch/dinner" in the following discussion.

4.1 Profile 1

Our first profile is that of a type-2 diabetic person who does not do any exercise and takes breakfast, lunch and dinner as daily food. This person has initial fasting BGL 130 mg/dL. Table 2 shows the linear rate of BGL change per minute due to each meal intake. Each meal intake affects BGL for 2 hours. For example, if BGL of this person before lunch is 140 mg/dL, the peak BGL after lunch (achieved 2 hours after lunch) will be 140 + .67 * 120 = 220 mg/dL. Table 2 shows sample impact of each type of meal on BGL. After that, the BGL starts to decrease as per the rates associated with rest/sleep shown in Table 3.

Table 1 : Profile 1 metabolic rates

Meal	Rate per minute mg/dL
Breakfast	0.666667
Lunch	0.80
Dinner	0.90

Table 2 : Blood Glucose reading after different event

Event	Before mg/dL	After mg/dL
Breakfast	130	208
Lunch	155	250
Dinner	151	258

Table 3 shows the decrease in BGL per minute during different hours of rest/sleep. These rates involve a geometric reduction in value with time.

Table 3: Decrease in BGL per minute during rest

Hour	Decrease in BGL (mg/dL /minute)
1	0.286655
2	0.238879
3	0.199066
4	0.165888
5	0.13824
6	0.1152
7	0.096
8	0.08

Figure 5 shows the changes in blood glucose level over 3 days for this profile. If this person continues with this profile for 90 days, his HbA1C level would be 7.2% and his average BGL would be 184 mg/dL. If this person decreases his breakfast intake by 30 % his average BGL after 90 days falls to 166mg/dL and his HbA1c value becomes 6.9% (Figures 6, 7, 8). In addition to breakfast, if he reduces his lunch intake by 30 % then his average BGL after 90 days falls to 149mg/dL and HbA1c value becomes 6.7 % (Figure 6, 7, 8). Finally if he reduces all breakfast, dinner and lunch by 30% than his average BGL after 90 days falls to 136mg/dL and HbA1c value becomes 6.5% (Figure 6, 7, 8). Figures 9, 10 and 11 show this person's BGL two hours after breakfast, lunch and dinner respectively over 90 days under various interventions.

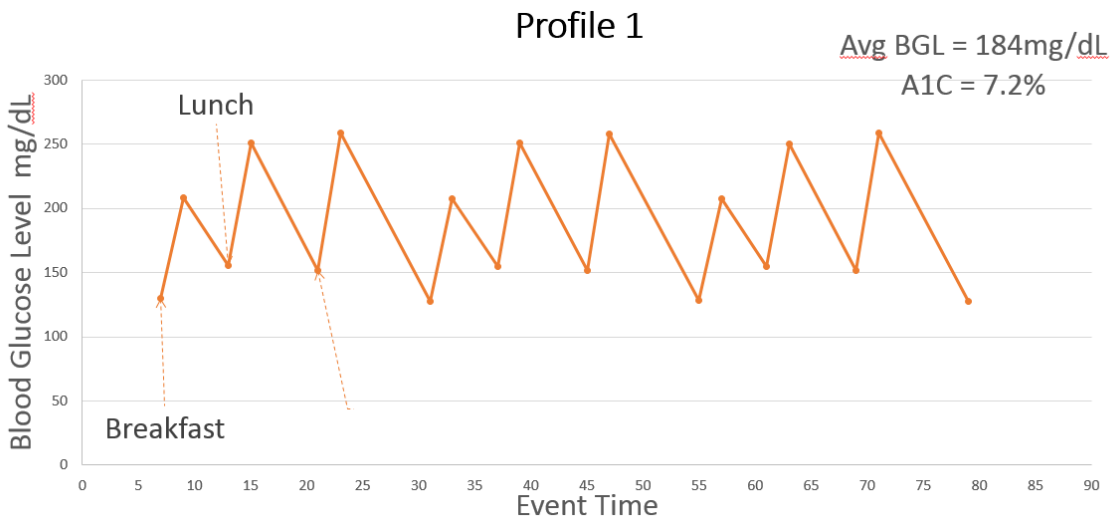

Figure 5 : Profile 1 blood glucose level after different events

Figure 6 : Profile-1 BGL before and after of each events for reduced diet

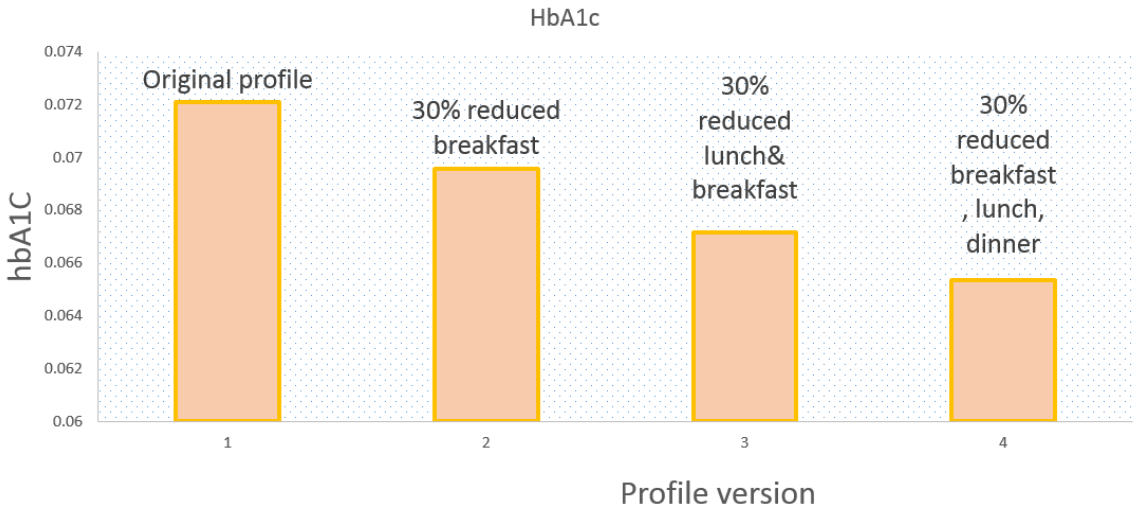

Figure 7 : Profile-1 HbA1C value with different reduction of diet

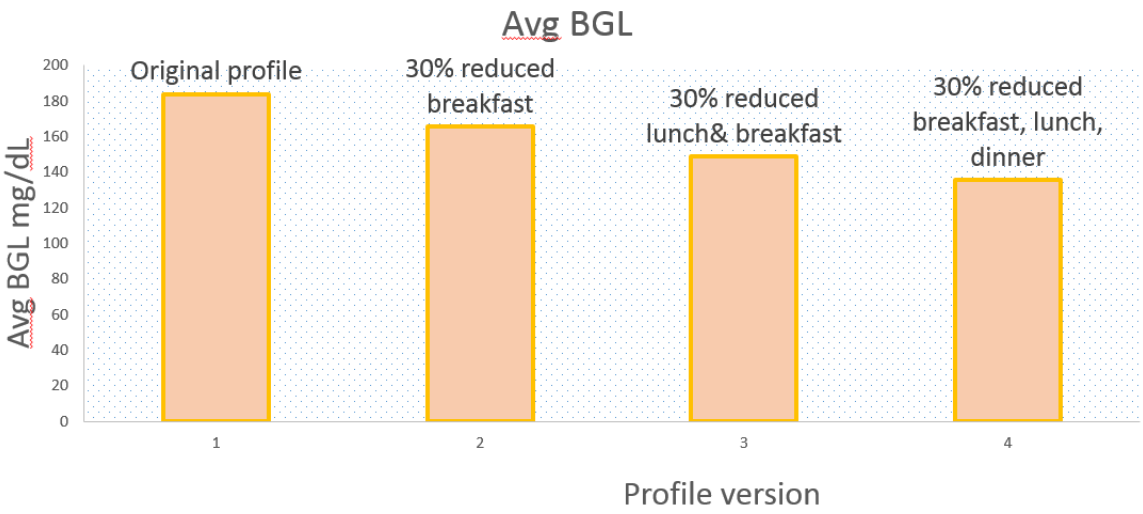

Figure 8 : Profile-1 average BGL for different reduction of diet

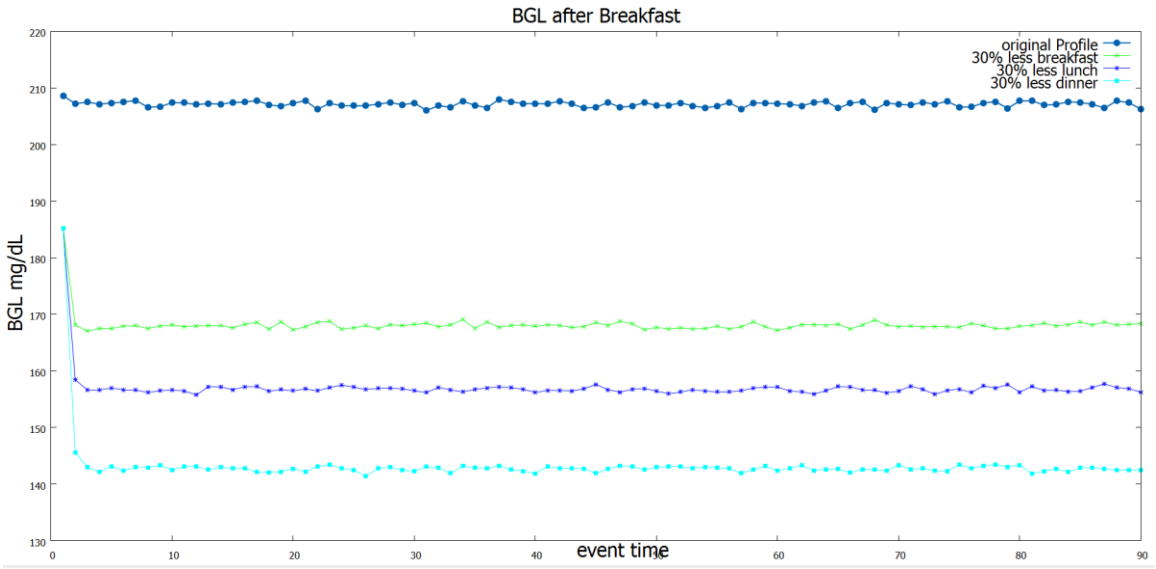

Figure 9 : Profile-1 BGL after breakfast for reduced food

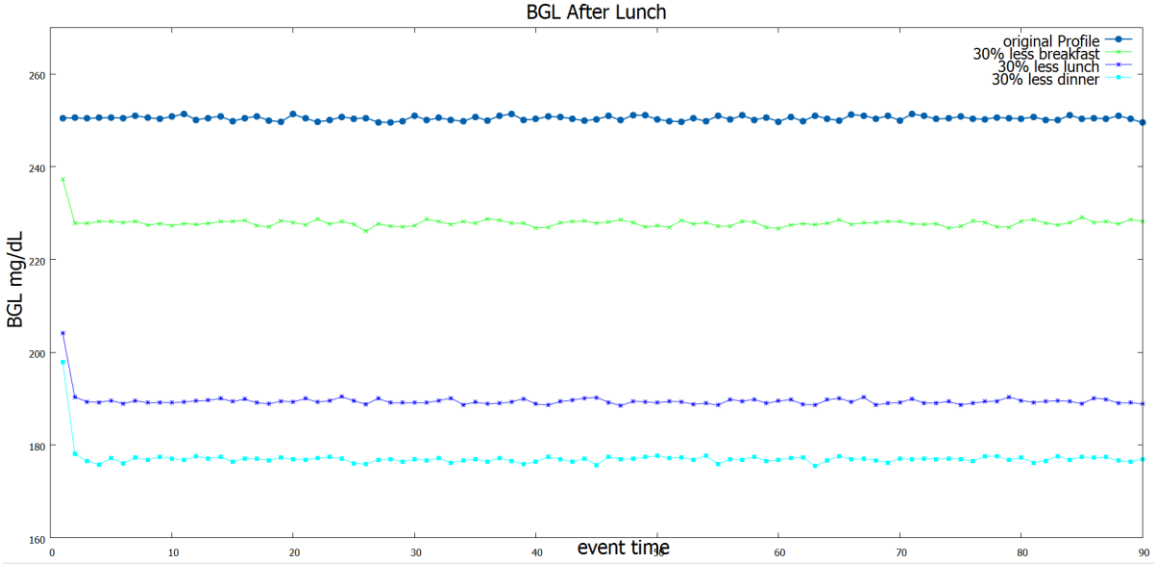

Figure 10 : Profile-1 BGL after lunch for reduced diet

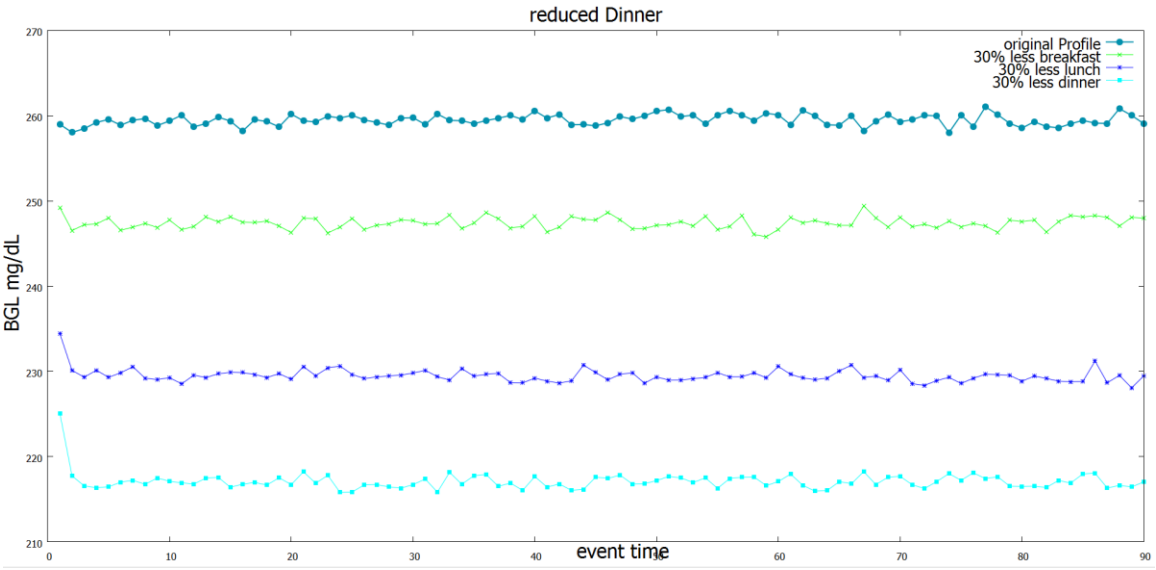

Figure 11 : Profile-1 BGL after dinner for reduced diet

4.2 Profile 1.2

This profile is a variant of profile 1 where the person adds one exercise event before dinner in his diet/exercise habit (figure 12). This exercise event linearly decreases his blood glucose level by 0.60 mg/dL per minute. Figure 12 shows that his blood glucose falls to 124mg/dL which was 155mg/dL in original profile just before the dinner event. Table 3 shows the metabolic rate and other profile parameters for profile 1.2.

Table 3 : profile1. 2 metabolic rate

Meal	Rate per minute
Breakfast	0.67
Lunch	.80
Dinner	.90

Exercise	.60

If this person continues with this modified profile for 90 days his HBa1C value after 90 days becomes 6.9% and his average BGL becomes 165 mg/dL. Without exercise this person's average BGL was 184 and A1C value was 7.4 % (Figure 12). In addition to new exercise event, if he also reduces breakfast amount by 30%, his average BGL and A1C value become 140 mg/dL and 6.5% respectively. In addition to new exercise event and reduced breakfast, if he also reduces his lunch by 30%, his average BGL and A1C value become 112 mg/dL and 6.2% respectively. In addition to new exercise event and reduced breakfast/lunch, if he also reduces his dinner by 30%, his average BGL and A1C value become 103 mg/dL and 6.01% respectively (Figure 13, 14, 15). Figures 16 and 17 show blood glucose levels 2 hours after lunch and dinner respectively over 90 days for various interventions.

Figure 12 : Profile 1.2 BGL after adding exercise before dinner

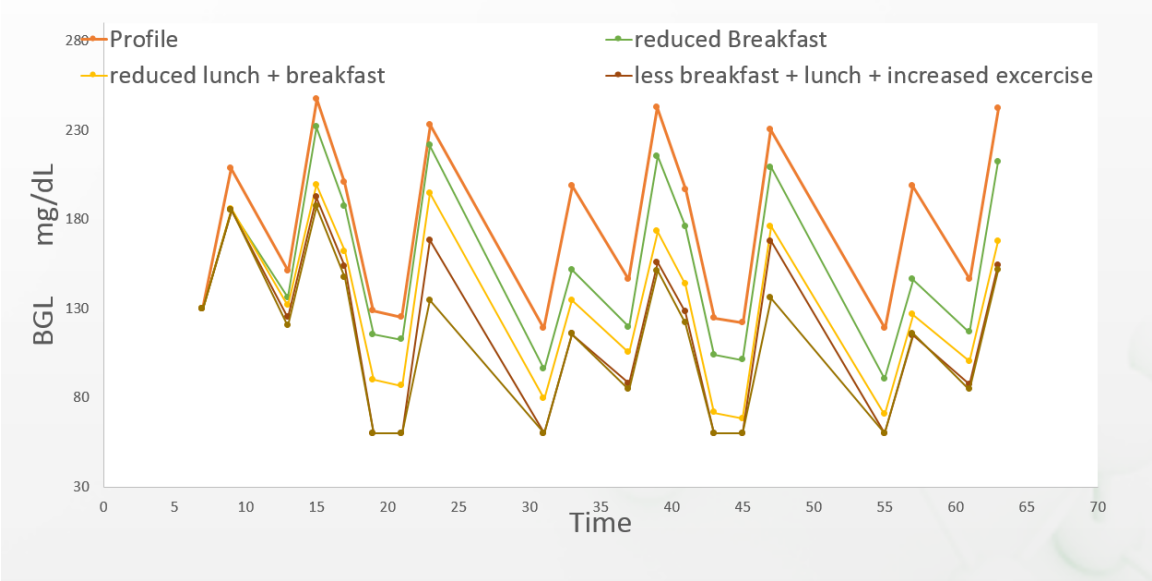

Figure 13 : Profile 1.2 reading of BGL before and after every events after adding exercise

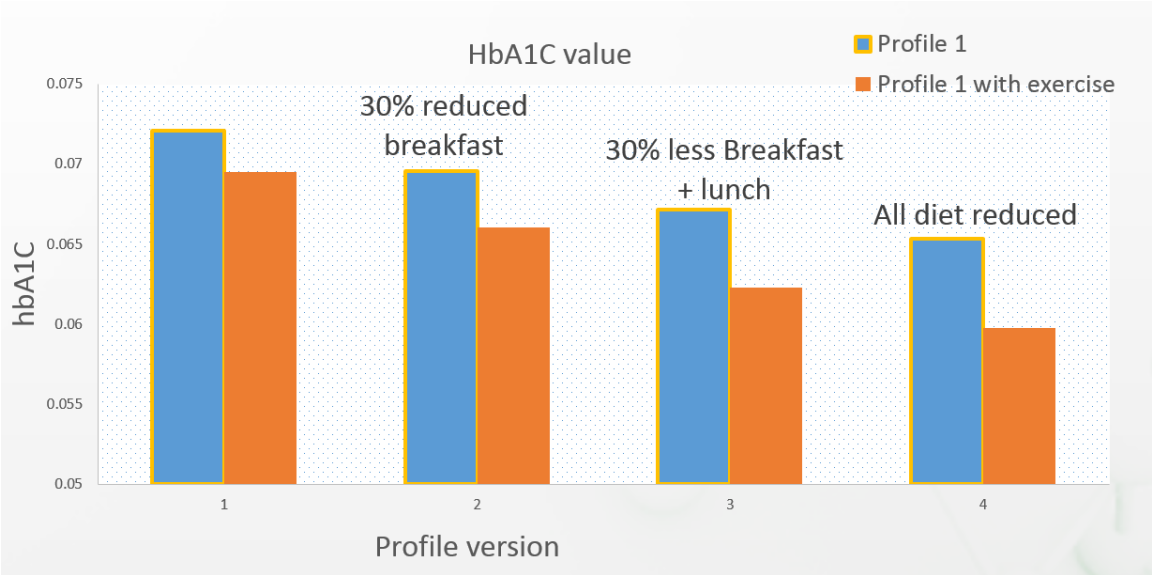

Figure 14 : Profile 1 HbA1C vs. Profile 1.2 HbA1C

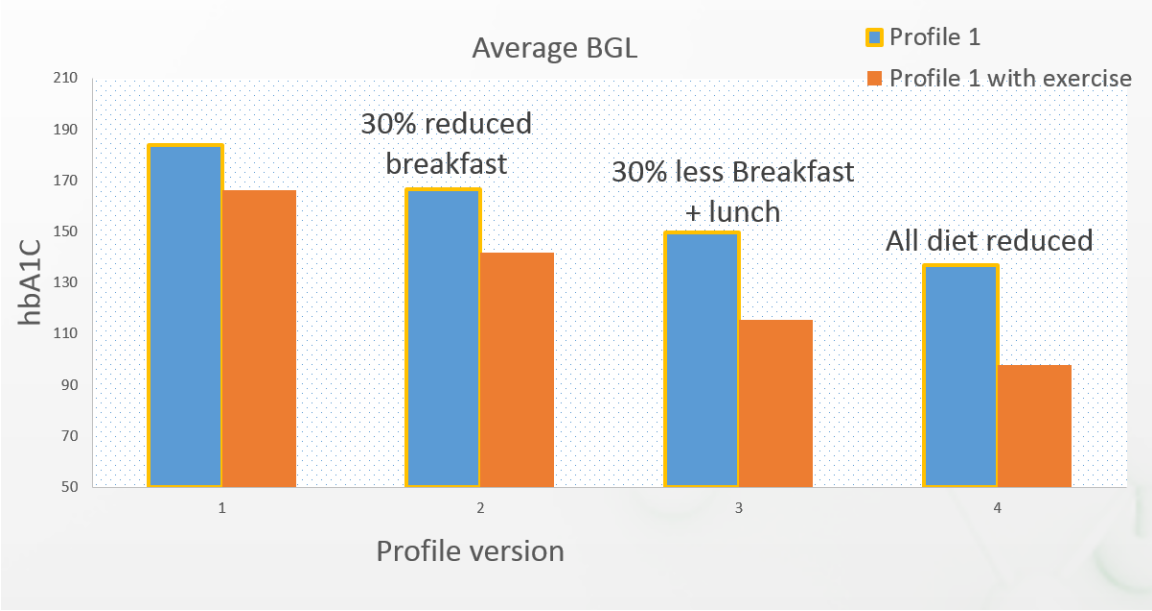

Figure 15 : Profile 1 average BGL vs. Profile 1.2 Average BGL

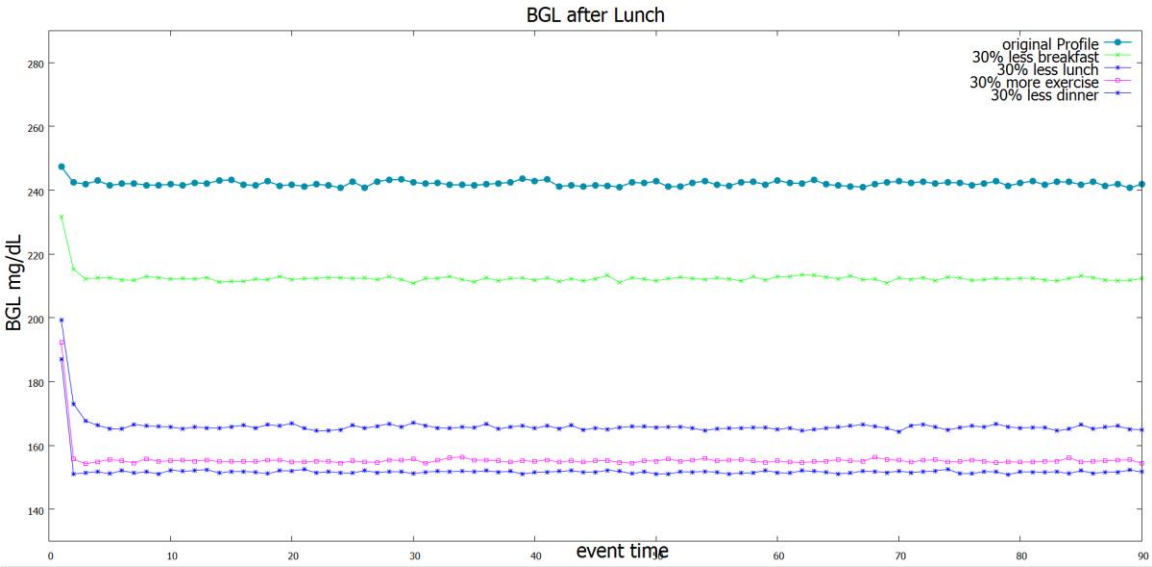

Figure 16 : Profile 1.2 BGL after Lunch

Figure 17 : Profile 1.2 BGL after dinner

4.3 Profile 2

Our 2nd profile is that of a type-2 diabetic person who does not do any exercise and takes breakfast, lunch and dinner as daily food. This person has initial fasting BGL 160 mg/dL. Table 4 shows the linear rate of BGL change per minute due to each meal intake. The simulator assumes that each meal intake affects BGL for 2 hours. For example, if BGL of this person before lunch is 140 mg/dL, the peak BGL after lunch (achieved 2 hours after lunch) will be 140 + 1.10 * 120 = 272 mg/dL. Table 5 shows sample impact of each type of meal on BGL. After that, the BGL starts to decrease as per the rates associated with rest/sleep shown in Table 6.

Table 4 : profile 2 metabolic rate

Meal	Rate per minute mg/dL
Breakfast	0.7
Lunch	1.1
Dinner	1.05

Table 5 : Blood Glucose reading after different event

Event	Before mg/dL	After mg/dL
Breakfast	160	244
Lunch	173	305
Dinner	167	293

Table 6 shows the decrease in BGL per minute during different hours of rest/sleep.

These rates involve a geometric reduction in value with time.

Table 6 : Decrease in BGL per minute during rest

Hour	Decrease in BGL (mg/dL /minute)
1	0.478406
2	0.318937
3	0.212625
4	0.14175
5	0.0945
6	0.063

7	0.042
8	0.028

Figure 18 shows the changes in blood glucose level over 3 days for this profile. If this person continues with this food habit for 90 days, his HbA1C level would be 7.6% and his average BGL would be 206 mg/dL. If this person decreases his breakfast intake by 30 % his average BGL after 90 days falls to 197g/dL and his HbA1c value becomes 7.3% (Figures 19, 20, 22). In addition to breakfast, if he reduces his lunch intake by 30 % then his average BGL after 90 days falls to 182mg/dL and HbA1c value becomes 7.1 % (Figure 19, 20, 22). Finally if he reduces all breakfast, dinner and lunch by 30% than his average BGL after 90 days falls to 170/dL and HbA1c value becomes 7.01% (Figure19, 20, 22). Figures 21, 23 and 24 show this person's BGL two hours after breakfast, lunch and dinner respectively over 90 days under various interventions.

Figure 18 : BGL after different events for profile 2

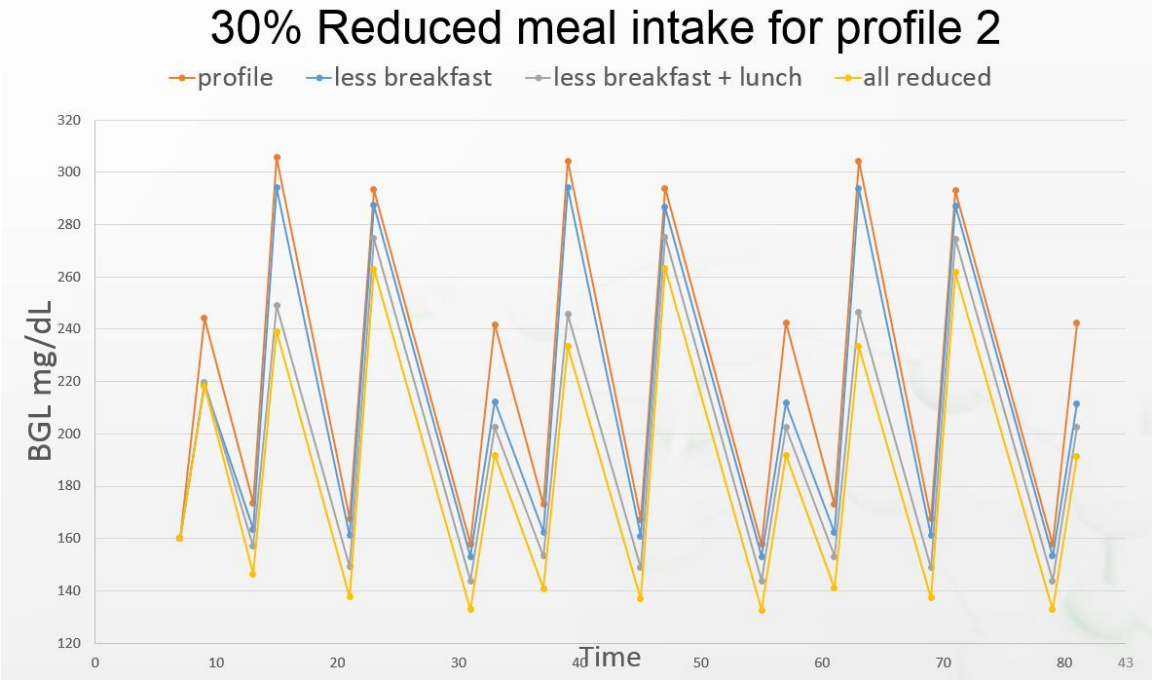

Figure 19: Profile 2 BGL after reduced meal intake

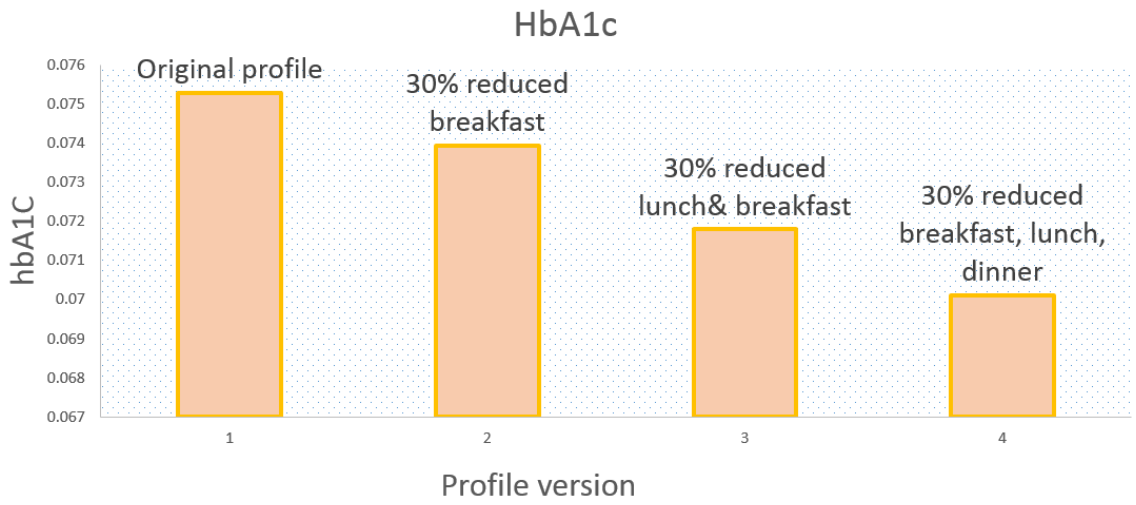

Figure 20 : Profile 2 HbA1C value after modification of meal intake

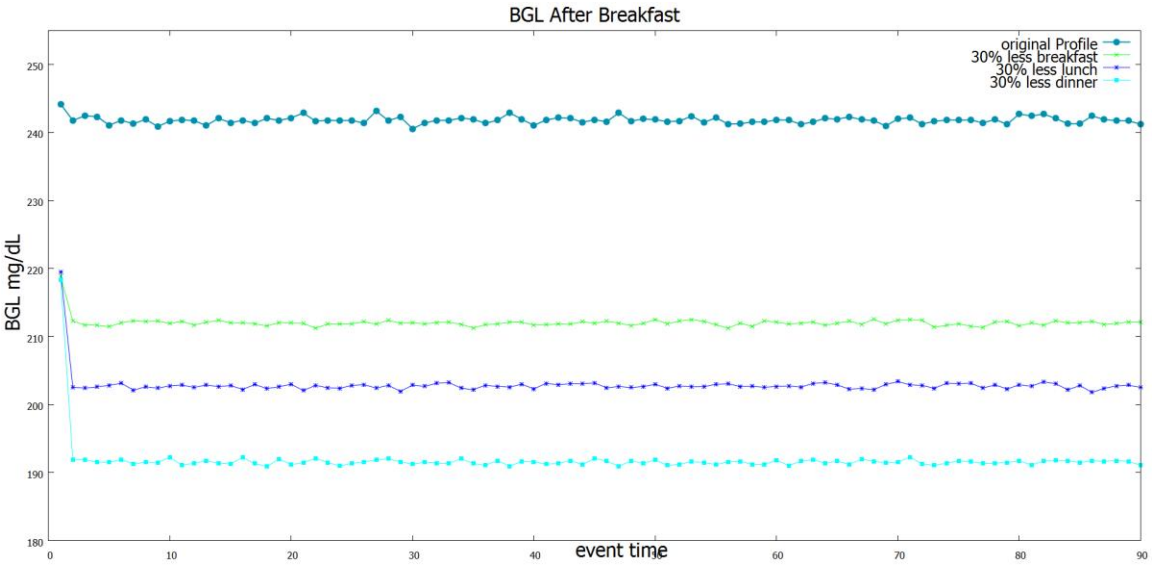

Figure 21 : Profile 2 BGL after breakfast with reduced diet

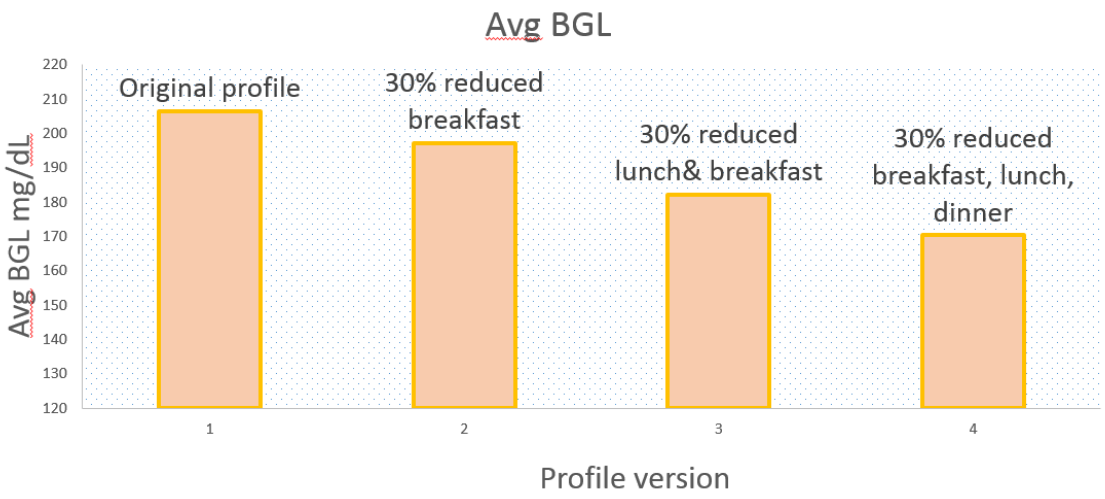

Figure 22 : Profile 2 average BGL changes with diet change

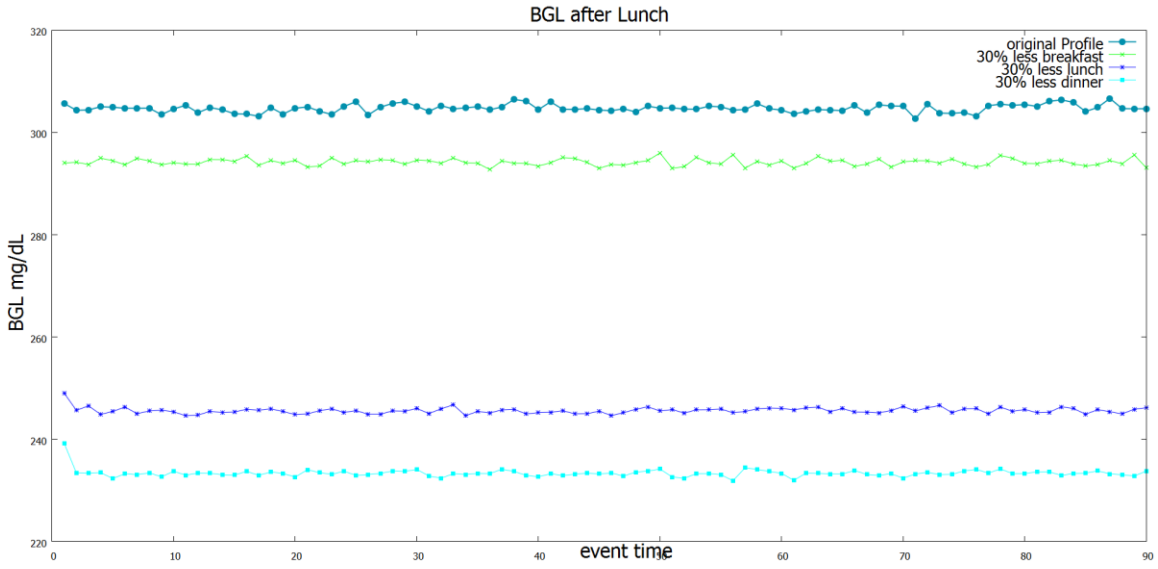

Figure 23 : Profile 2 BGL after lunch with reduced diet

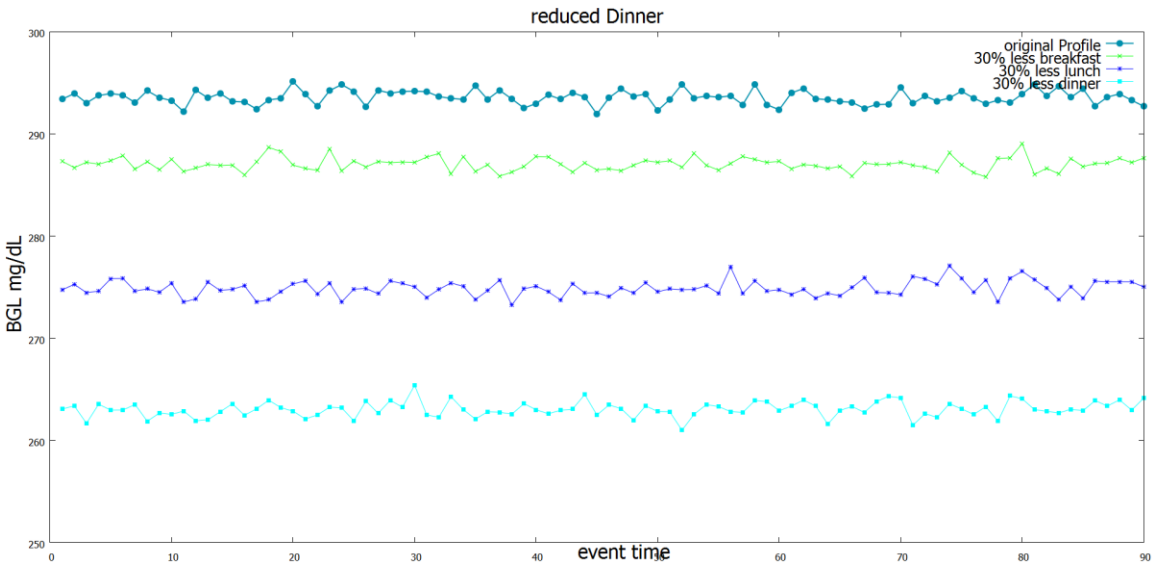

Figure 24 : Profile 2 BGL after dinner with reduced diet

4.3 Profile 2.2

This profile is a variant of profile 2 where the person adds one exercise event before dinner in his diet/exercise habit (figure 25). This exercise event linearly decreases his blood glucose level by 0.70 mg/dL per minute. Figure 25 shows that his blood glucose falls to 131 mg/dL which was 167mg/dL in original profile just before the dinner event. Table 7 shows the metabolic rate and other profile parameters for profile 2.2

Table 7 : Profile 2.2 metabolic rate

Meal	Rate per minute
Breakfast	0.666667
Lunch	1.02
Dinner	0.750000

Exercise	0.7

If this person continues with this modified profile for 90 days his HBa1C value after 90 days becomes 7.26% and his average BGL becomes 188 mg/dL. Without exercise this person's average BGL was 206 and A1C value was 7.6 % (Figure 25). In addition to new exercise event, if he also reduces breakfast amount by 30%, his average BGL and A1C value become 176 mg/dL and 7.1% respectively. In addition to new exercise event and reduced breakfast, if he also reduces his lunch by 30%, his average BGL and A1C value become 157 mg/dL and 6.8% respectively. In addition to new exercise event and reduced breakfast/lunch, if he also reduces his dinner by 30%, his average BGL and A1C value become 144 mg/dL and 6.6% respectively (Figure 26, 27, 28). Figures 29, 30 and 31 show blood glucose levels 2 hours after breakfast, lunch and dinner respectively over 90 days for various interventions.

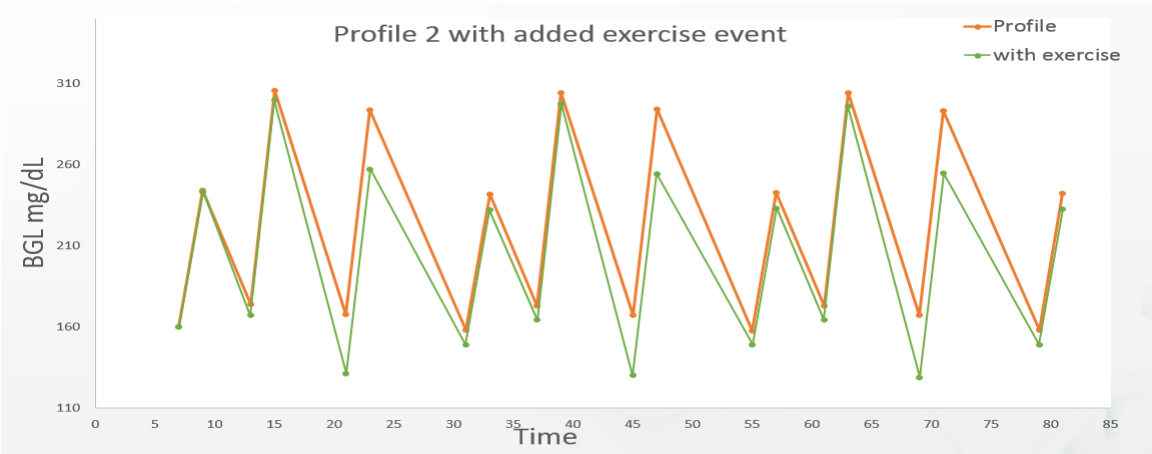

Figure 25 : Profile 2.2 BGL reading after adding Exercise

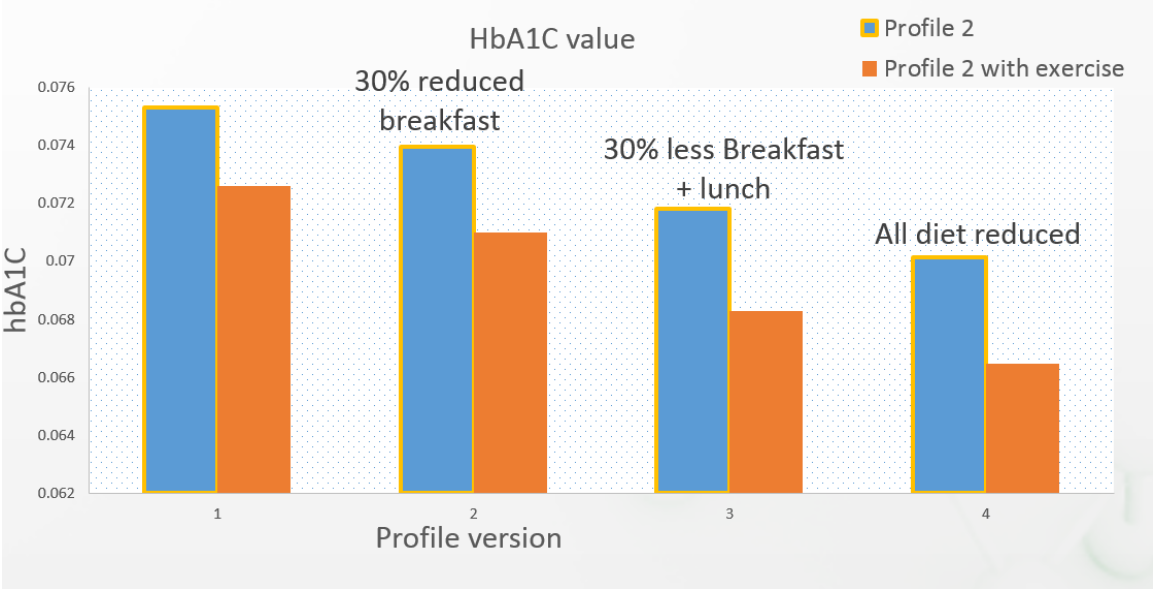

Figure 26 : Profile 2.2 A1C value with exercise event and reduced diet

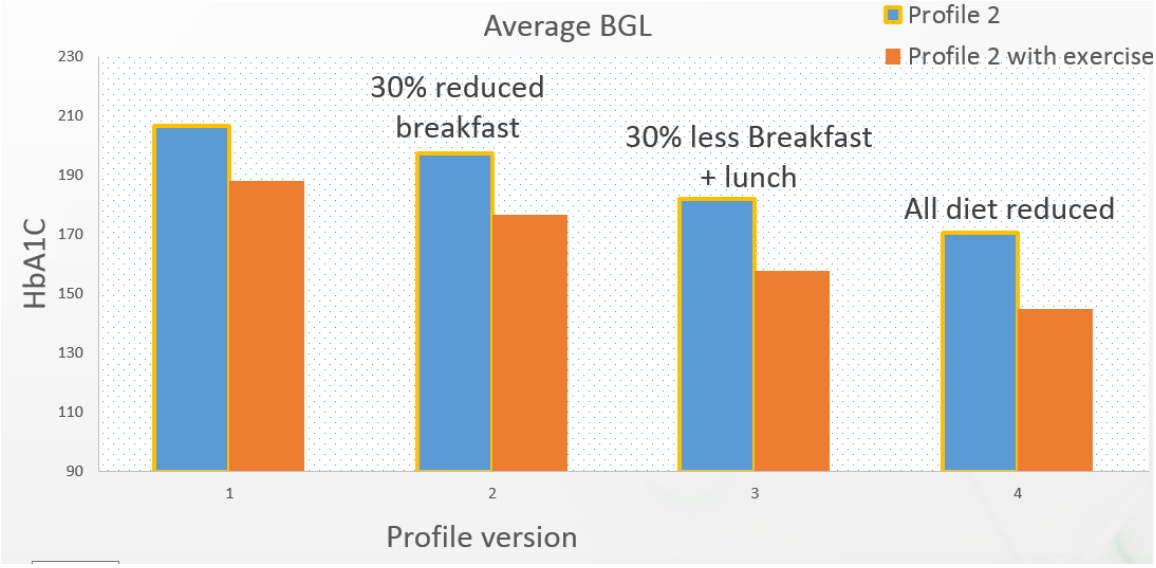

Figure 27 : Profile 2.2 average BGL after adding exercise events with reduced meal

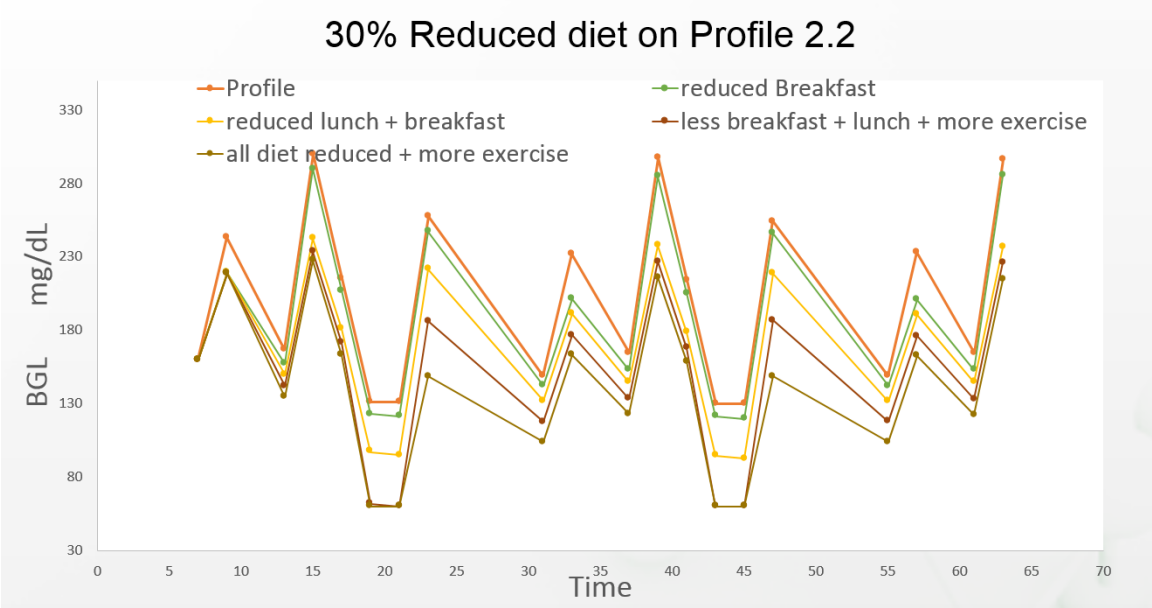

Figure 28 : Profile 2.2 BGL reading after reduced diet/exercise events.

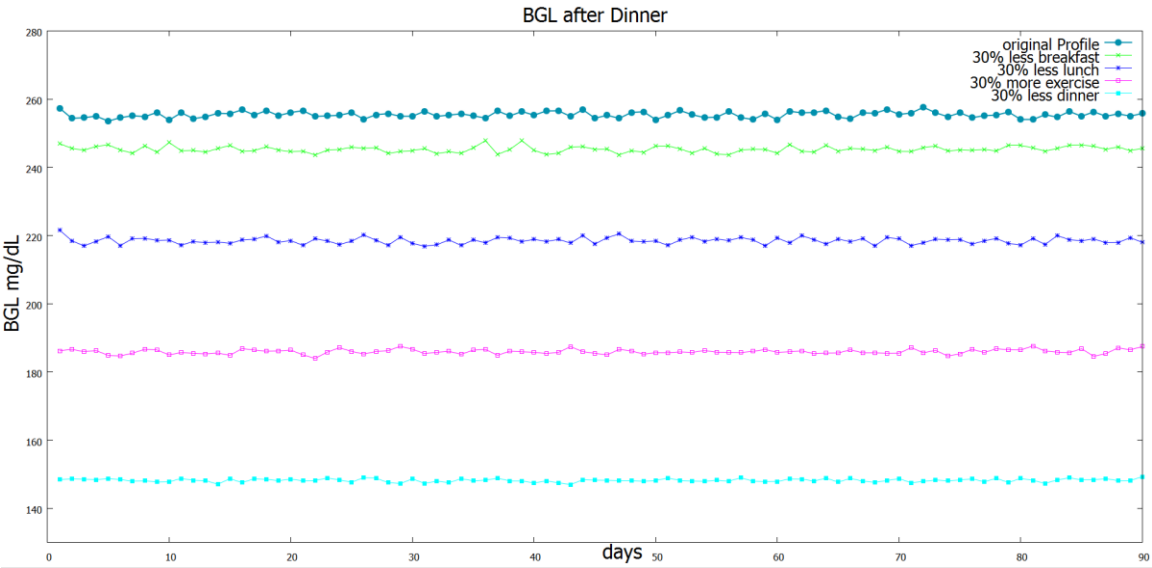

Figure 29 : Profile 2.2 BGL after breakfast for 90 days with reduced diet

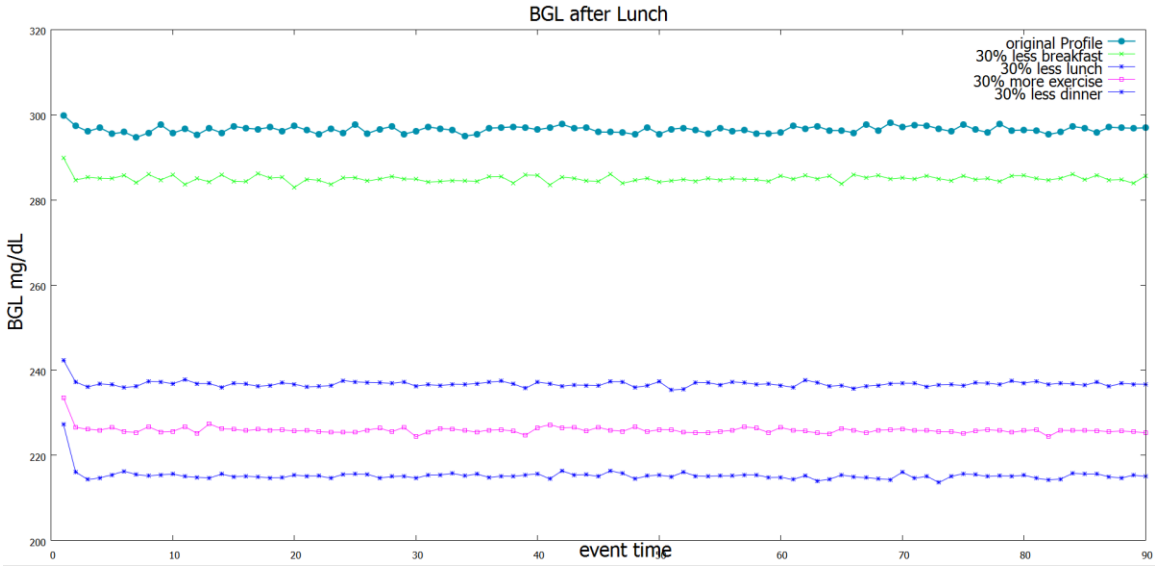

Figure 30 : Profile 2.2 BGL after lunch with reduced diet

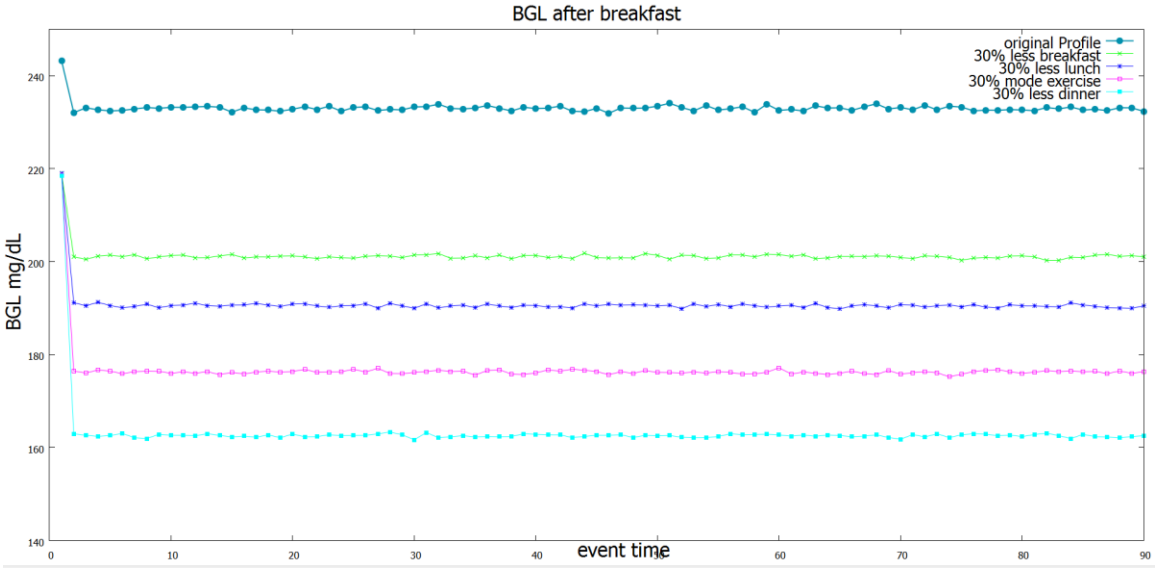

Figure 31 : Profile 2.2 BGL after breakfast for 90 days with reduced diet

4.5 Profile 3

Our 3rd profile is that of a type-2 diabetic person who does not do any exercise and takes breakfast, lunch and dinner as daily food. This person has initial fasting BGL 110

mg/dL. Table 8 shows the linear rate of BGL change per minute due to each meal intake. The simulator assumes that each meal intake affects BGL for 2 hours. For example, if BGL of this person before lunch is 140 mg/dL, the peak BGL after lunch (achieved 2 hours after lunch) will be 140 + .65 * 120 = 218 mg/dL. Table 9 shows sample impact of each type of meal on BGL. After that, the BGL starts to decrease as per the rates associated with rest/sleep shown in Table 10.

Table 8 : Profile 3 metabolic rate

Meal	Rate per minute mg/dL
Breakfast	0.55
Lunch	.65
Dinner	0.70

Table 9 : Profile 3 sample BGL reading before and after events

Event	Before mg/dL	After mg/dL
Breakfast	110	176
Lunch	116	194
Dinner	111	195

Table 10 shows the decrease in BGL per minute during different hours of rest/sleep. These rates involve a geometric reduction in value with time.

Table 10 : Decrease in BGL per minute during rest

Hour	Decrease in BGL (mg/dL /minute)
1	0.44809
2	0.263582
3	0.155048
4	0.0912049
5	0.05365
6	0.0315588
7	0.018564
8	0.01092

Figure 32 shows the changes in blood glucose level over 3 days for this profile. If this person continues with this food habit for 90 days, his HbA1C level would be 6.5% and his average BGL would be 136 mg/dL. If this person decreases his breakfast intake by 30 % his average BGL after 90 days falls to 129 mg/dL and his HbA1c value becomes 6.4% (Figures 33, 34, 35). In addition to breakfast, if he reduces his lunch intake by 30 % then his average BGL after 90 days falls to 120mg/dL and HbA1c value becomes 6.3 % (Figure 33, 34, 35). Finally if he reduces all breakfast, dinner and lunch by 30% than his average BGL after 90 days falls to 112mg/dL and HbA1c value becomes 6.1% (Figure 33, 34, 35). Figures 36, 37 and 38 show this person's BGL two hours after breakfast, lunch and dinner respectively over 90 days under various interventions.

Figure 32 : Profile 3 BGL level before and after every events for 3 days

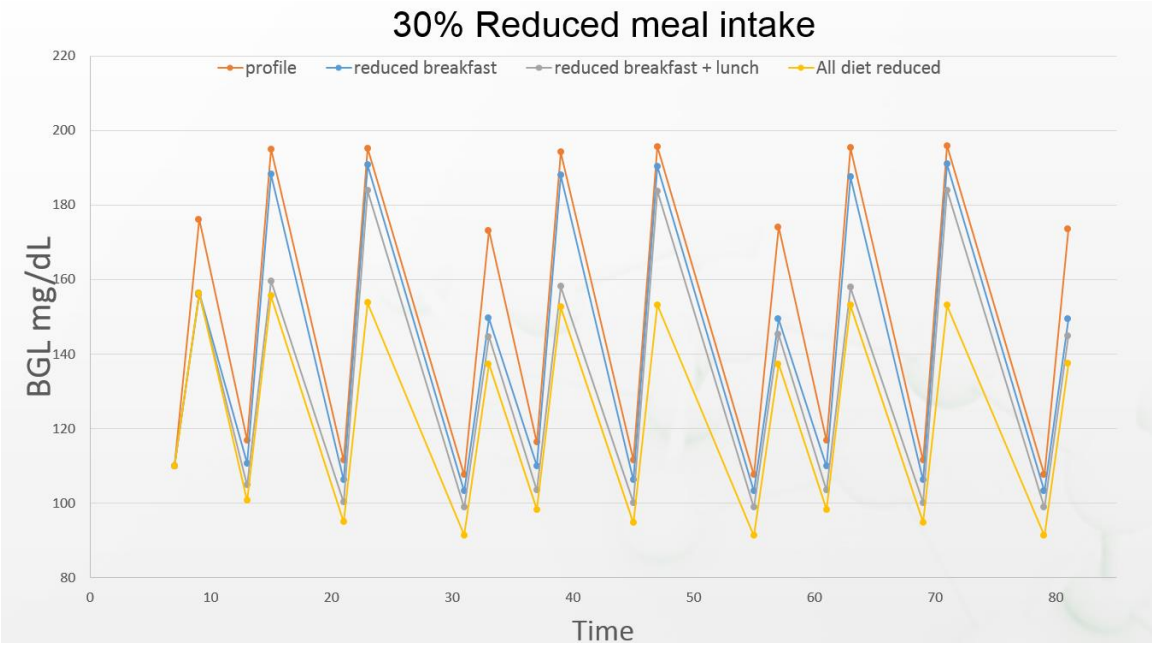

Figure 33 : Profile-3 BGL level after every event with reduced diet for profile 3

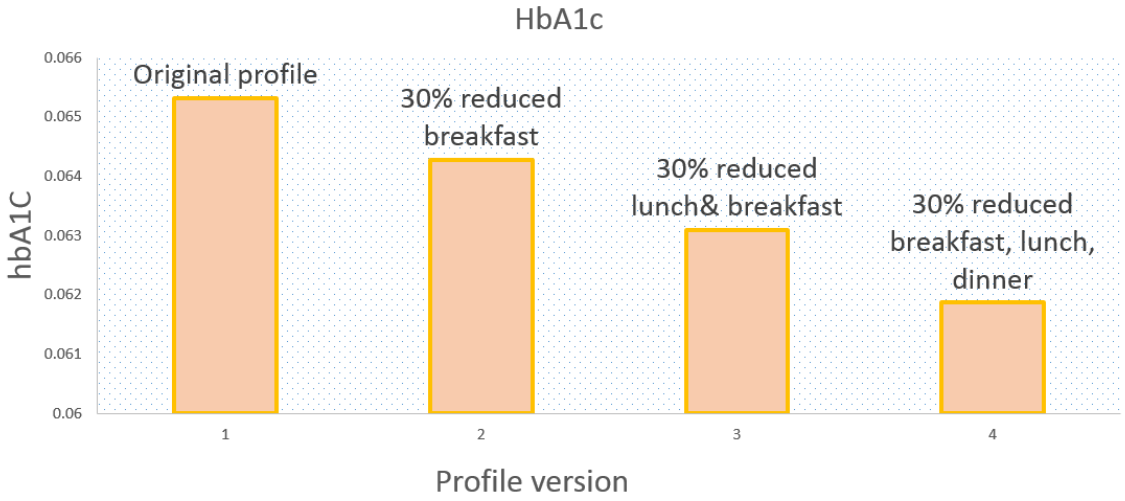

Figure 34 : Profile-3 HbA1C value with reduced meal intake

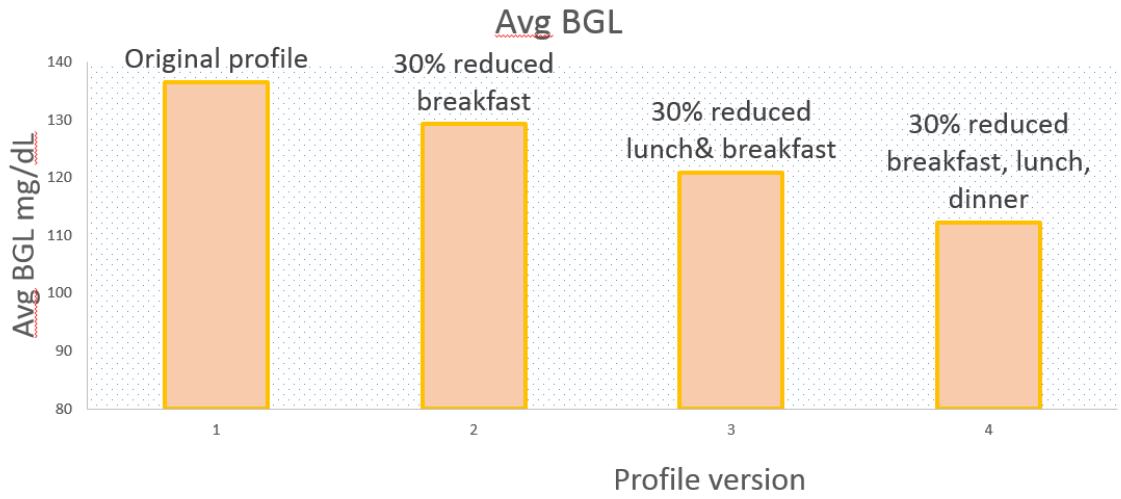

Figure 35 : Profile-3 average BGL with reduced meal intake

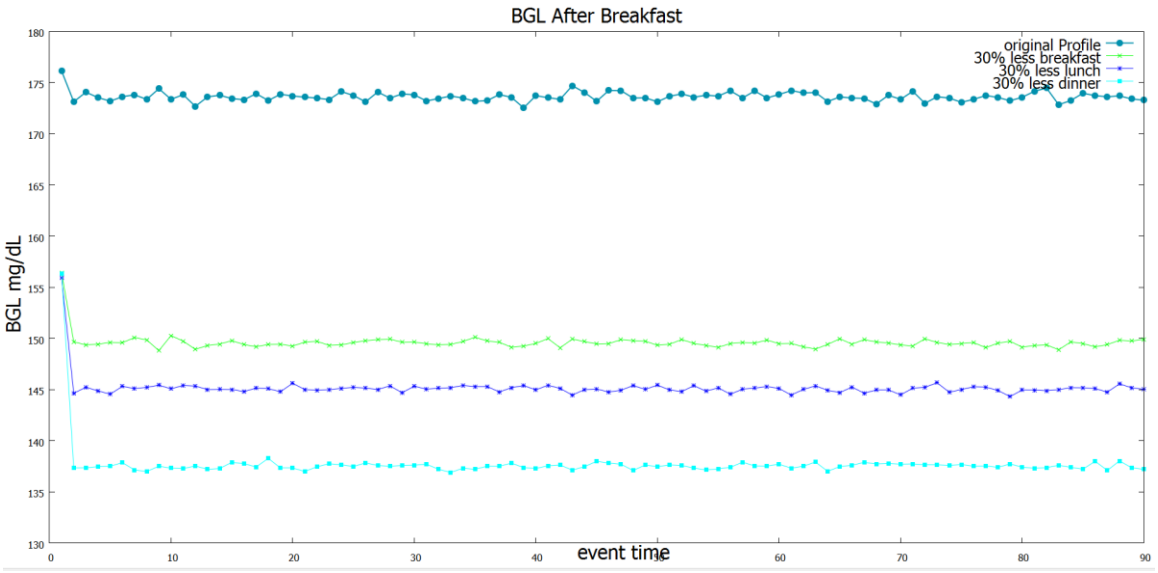

Figure 36 : Profile-3 BGL after breakfast for 90 days with reduced diet

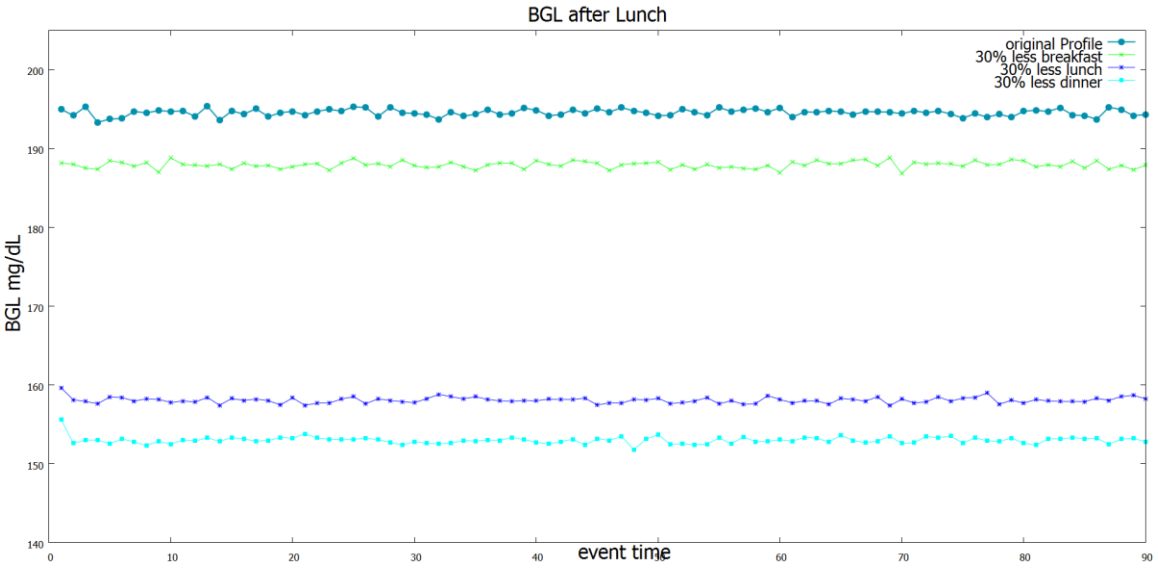

Figure 37 : Profile-3 BGL after lunch for 90 days with reduced diet

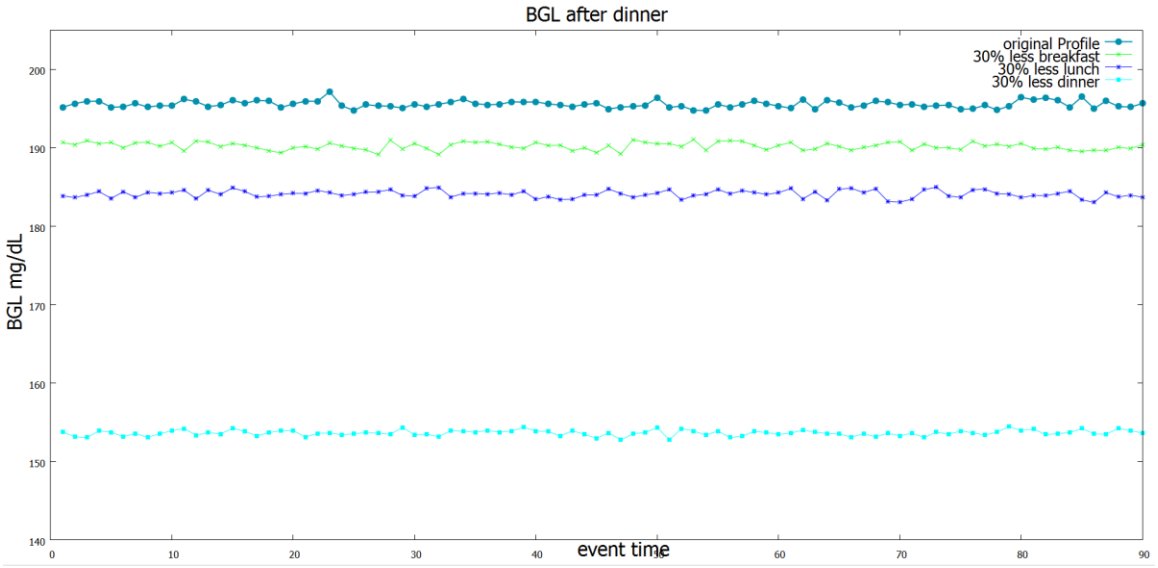

Figure 38 : Profile-3 BGL after dinner for 90 days with reduced diet

4.6 Profile 3.2

This profile is a variant of profile 3 where the person adds one exercise event before dinner in his diet/exercise habit (figure 39). This exercise event linearly decreases his blood glucose level by 0.45 mg/dL per minute. Figure 39 shows that his blood glucose falls to 79mg/dL which was 111 mg/dL in original profile just before the dinner event. Table 11 shows the metabolic rate and other profile parameters for profile 3.2.

Table 11 : Profile 3.2 Metabolic rate with added exercise event

Meal	Rate per minute
Breakfast	0.55
Lunch	.65
Dinner	0.70

Exercise	-0.45

If this person continues with this modified profile for 90 days his HBa1C value after 90 days becomes 6.34% and his average BGL becomes 121 mg/dL. Without exercise this person's average BGL was 136 and A1C value was 6.53 % (Figure 40 and 41). In addition to new exercise event, if he also reduces breakfast amount by 30%, his average BGL and A1C value become 114 mg/dL and 6.21% respectively. In addition to new exercise event and reduced breakfast, if he also reduces his lunch by 30%, his average BGL and A1C value become 105 mg/dL and 6.08% respectively. In addition to new exercise event and reduced breakfast/lunch, if he also reduces his dinner by 30%, his average BGL and A1C value become 98 mg/dL and 5.95% respectively (Figure 42, 40, 41). Figures 43 and 44 show blood glucose levels 2 hours after breakfast and lunch respectively over 90 days for various interventions.

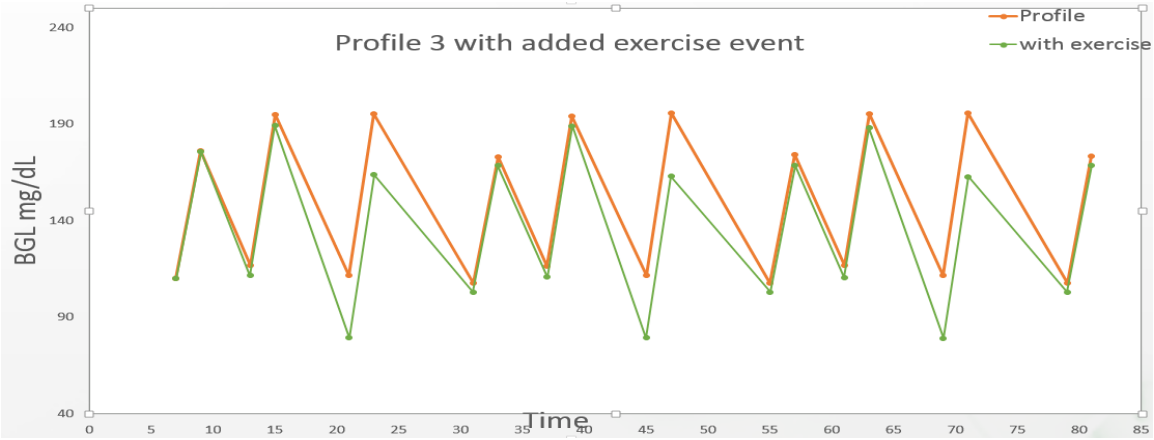

Figure 39 : profile 3.2 generated from profile 3 after adding exercise event

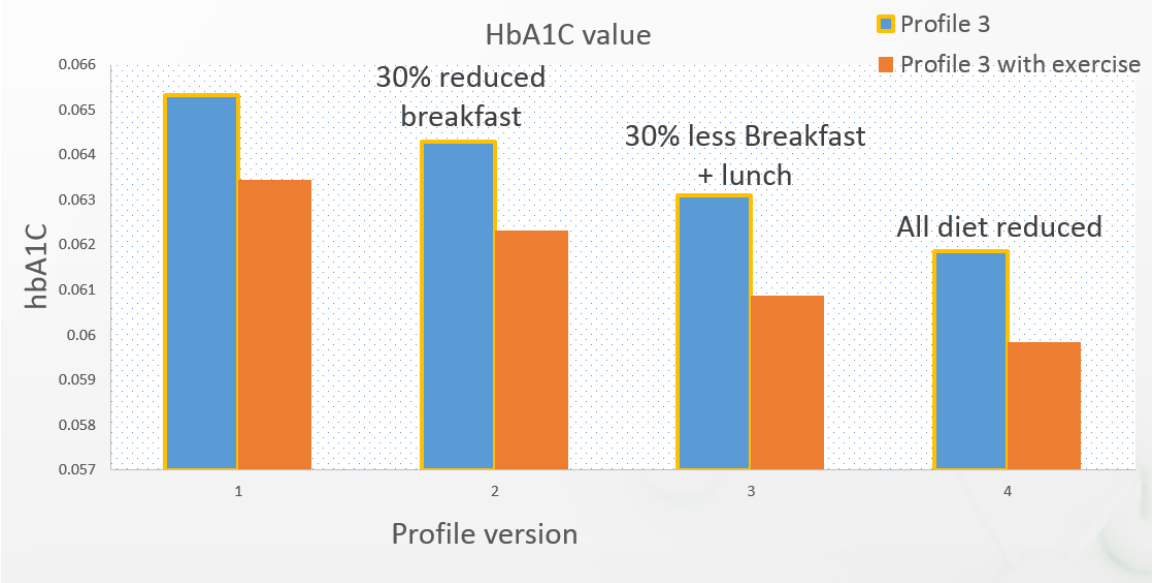

Figure 40 : Profile 3 HbA1C vs. Profile 3.2 HbA1C

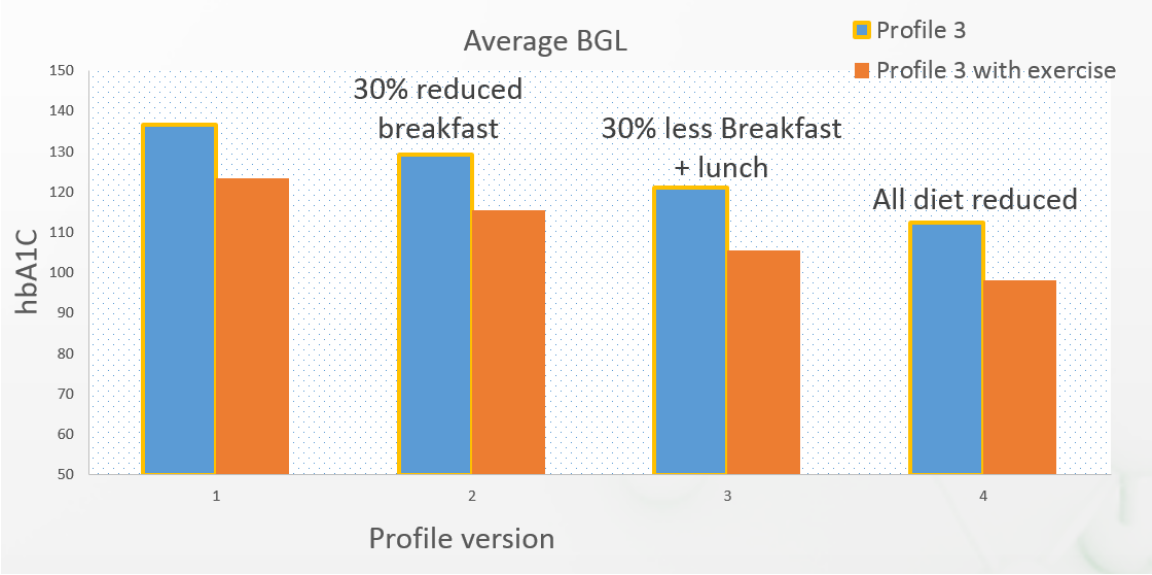

Figure 41 : Profile 3 vs. Profile 3.2 average BGL

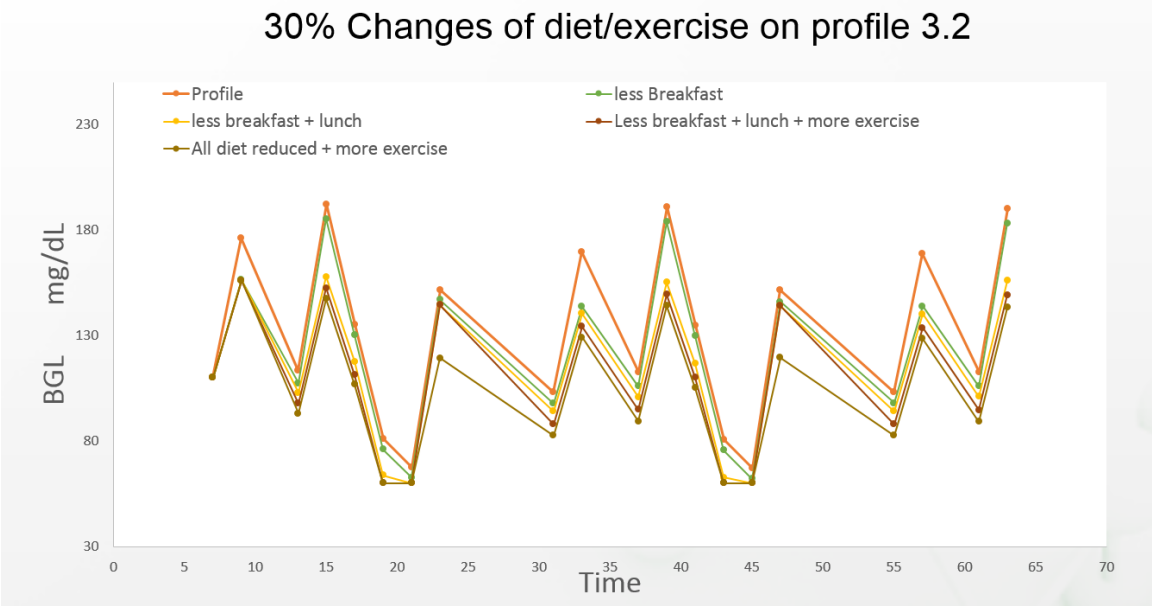

Figure 42 : Profile 3.2 BGL before and after every event with reduced meal and increased exercise

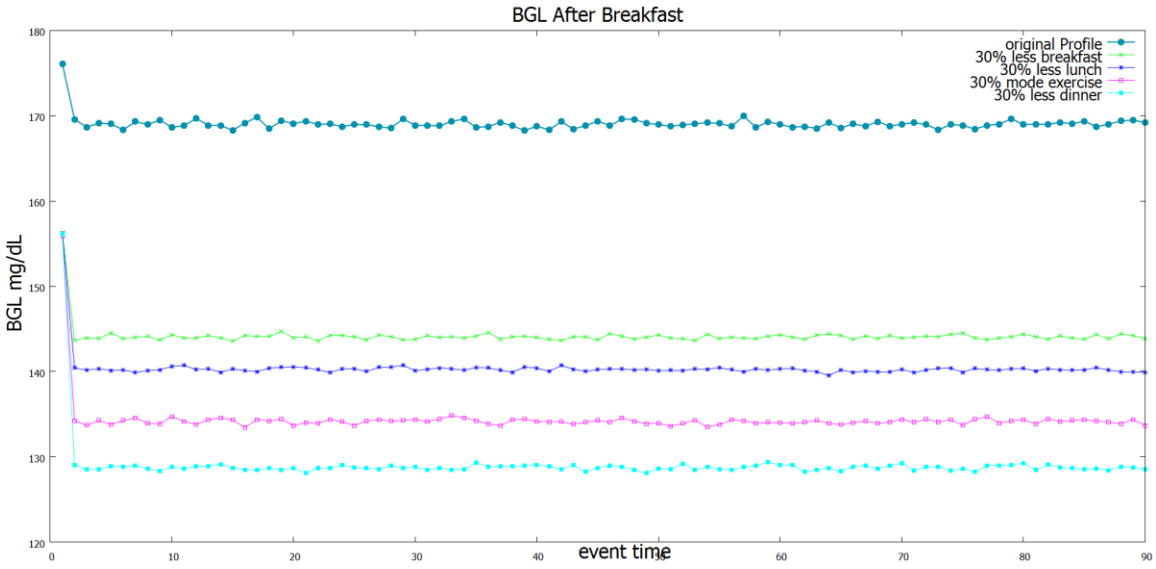

Figure 43 : Profile 3.2 BGL after breakfast with reduced diet for 60 days

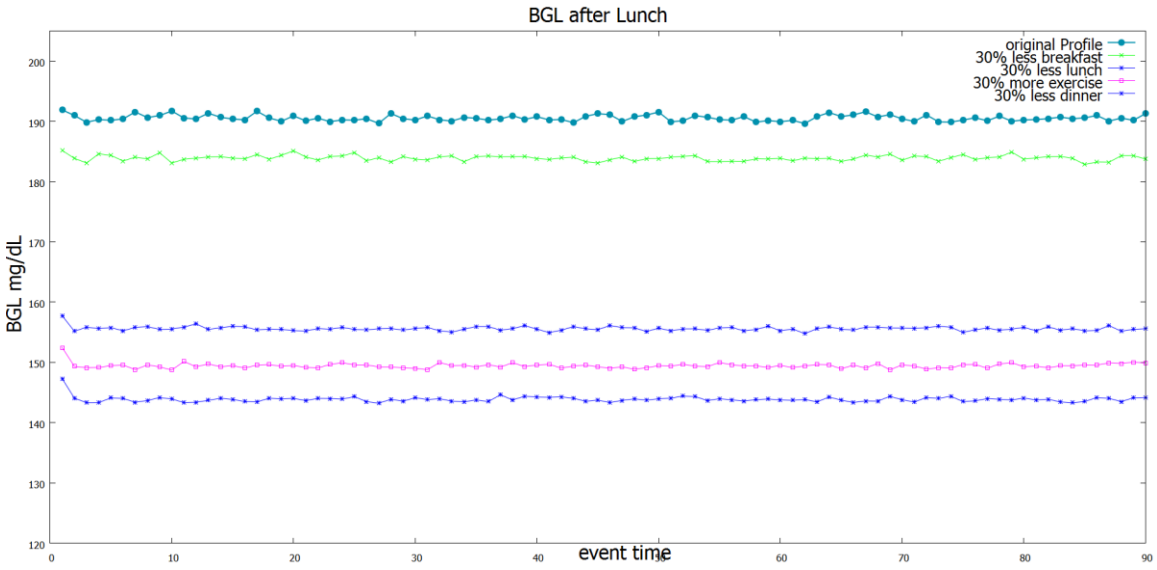

Figure 44 : Profile 3.2 BGL after breakfast for 90 days with reduced diet

4.7 Profile 4

Our 4th profile is that of a type-2 diabetic person who does not do any exercise and takes breakfast, lunch and dinner as daily food. This person has initial fasting BGL 125 mg/dL. Table 12 shows the linear rate of BGL change per minute due to each meal intake. The simulator assumes that each meal intake affects BGL for 2 hours. For example, if BGL of this person before lunch is 140 mg/dL, the peak BGL after lunch (achieved 2 hours after lunch) will be 140 + .50 * 120 = 200 mg/dL. Table 13 shows sample impact of each type of meal on BGL. After that, the BGL starts to decrease as per the rates associated with rest/sleep shown in Table 14.

Table 12 : profile-4 metabolic rate on different meal intake

Meal	Rate per minute
Breakfast	0.50
Lunch	0.53
Dinner	0.63

Table 13 : profile 4 blood glucose level after events

Event	Before mg/dL	After mg/dL
Breakfast	100	160
Lunch	110	172
Dinner	101	177

Table 14 shows the decrease in BGL per minute during different hours of rest/sleep. These rates involve a geometric reduction in value with time.

Table 14 : Decrease in BGL per minute during rest

Hour	Decrease in BGL (mg/dL /minute)
1	0.346845
2	0.23123
3	0.154153
4	0.102769
5	0.0685125
6	0.045675
7	0.03045

8	0.0203

Table 15 : profile-4 BGL reading before and after each events

Figure 45 shows the changes in blood glucose level over 3 days for this profile. If this person continues with this food habit for 90 days, his HbA1C level would be 6.39% and his average BGL would be 126 mg/dL. If this person decreases his breakfast intake by 30 % his average BGL after 90 days falls to 120mg/dL and his HbA1c value becomes 6.29% (Figures 48, 46, 47). In addition to breakfast, if he reduces his lunch intake by 30 % then his average BGL after 90 days falls to 112mg/dL and HbA1c value becomes 6.19 % (Figures 48, 46, 47).). Finally if he reduces all breakfast, dinner and lunch by 30% than his average BGL after 90 days falls to 104mg/dL and HbA1c value becomes 6.07% (Figures 48, 46, 47).). Figures 49, 51 and 51 show this person's BGL two hours after dinner, breakfast and lunch respectively over 90 days under various interventions.

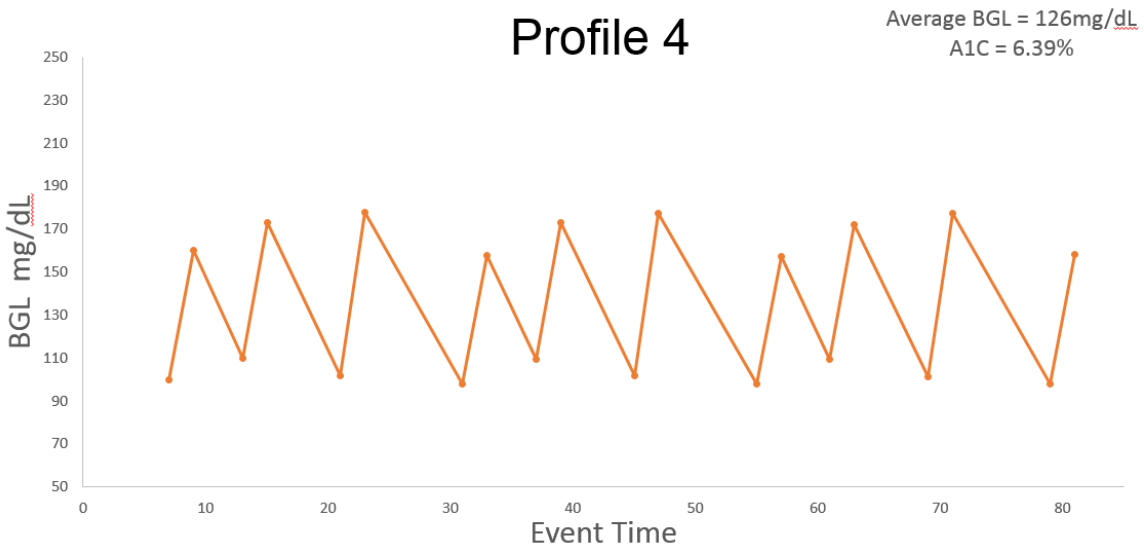

Figure 45 : profile-4 BGL reading before and after each events

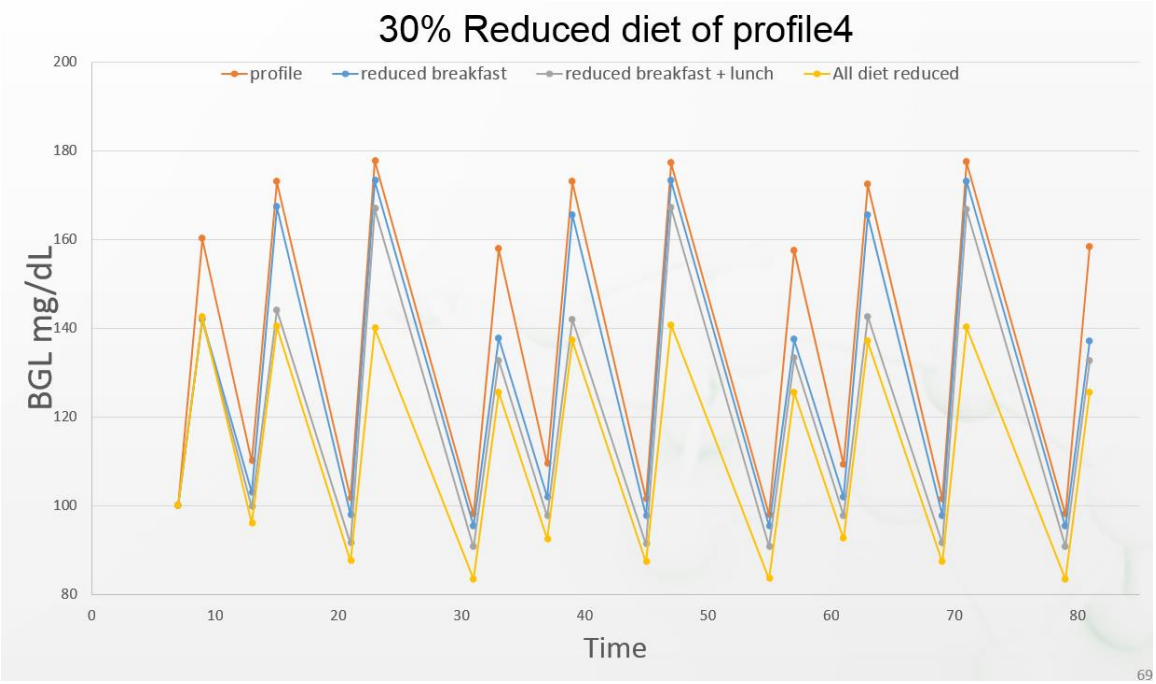

Figure 46 : profile-4 BGL reading before and after each event with reduced meal

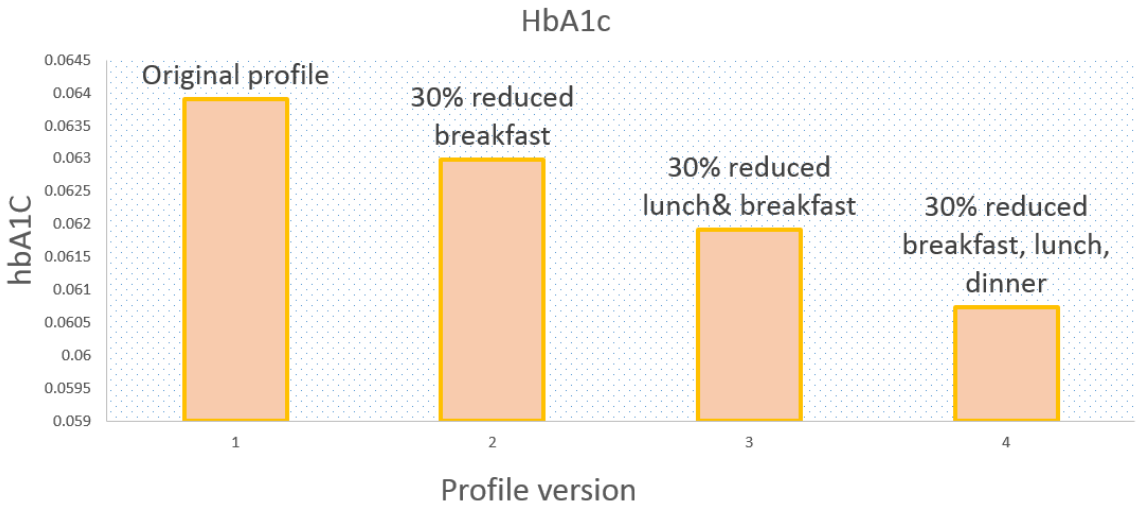

Figure 47 : profile-4 average BGL after meal intake reduction

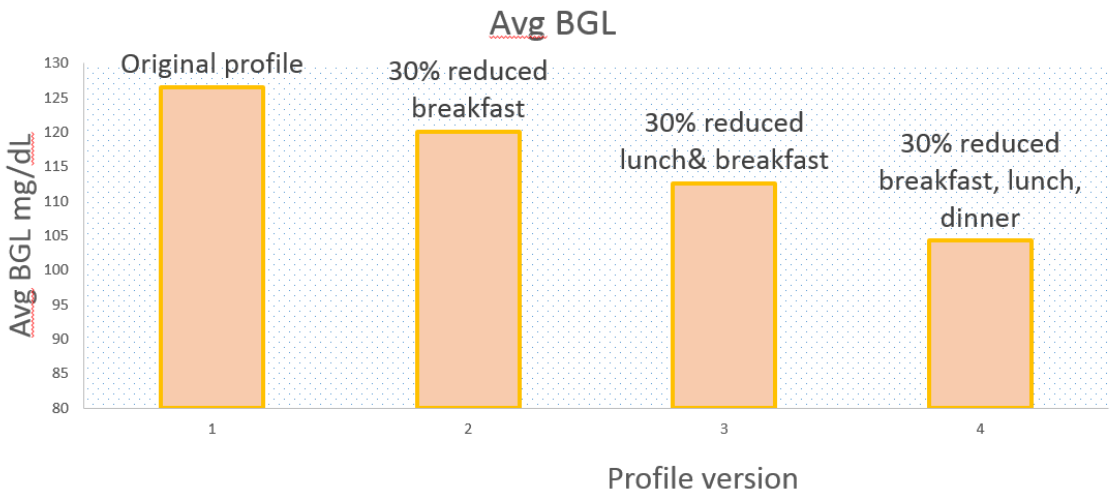

Figure 48 : profile-4 A1C value after meal reduction

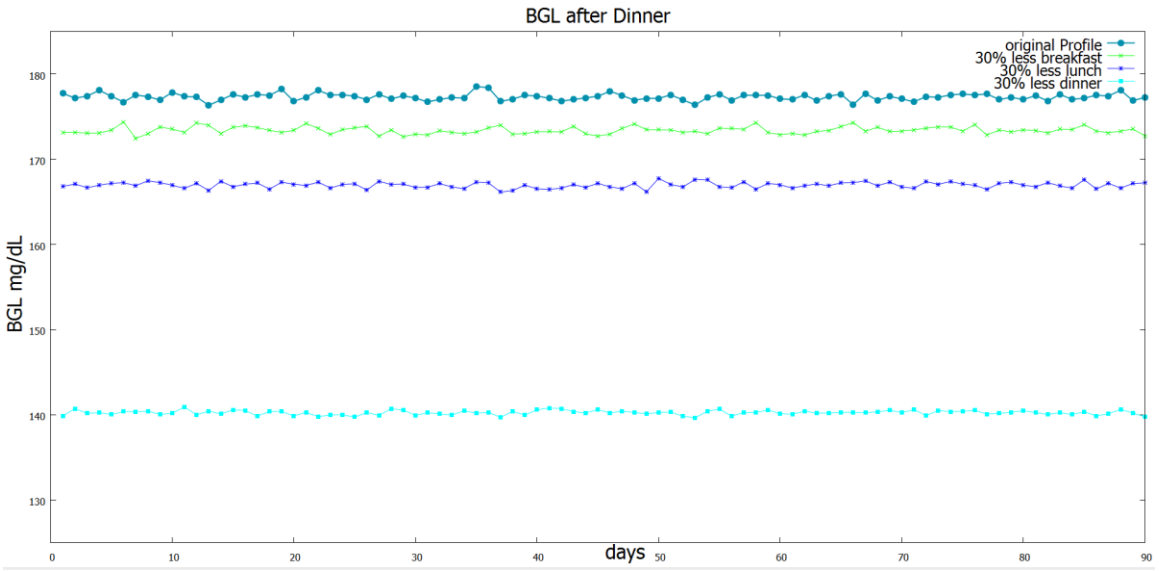

Figure 49 : profile-4 BGL after dinner with reduced diet

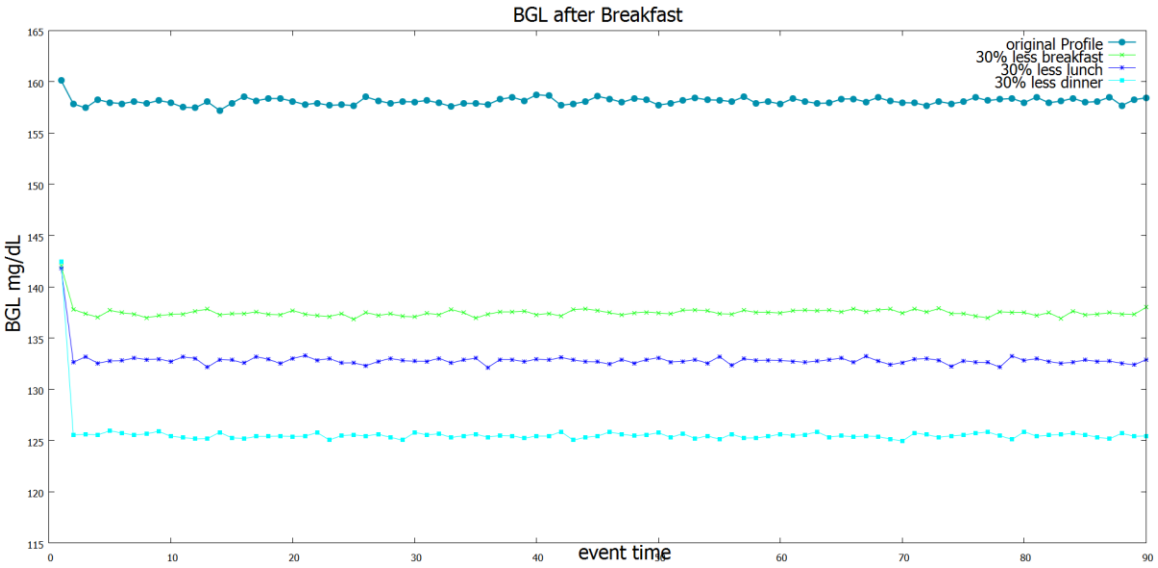

Figure 50 : profile-4 BGL after breakfast with reduced diet

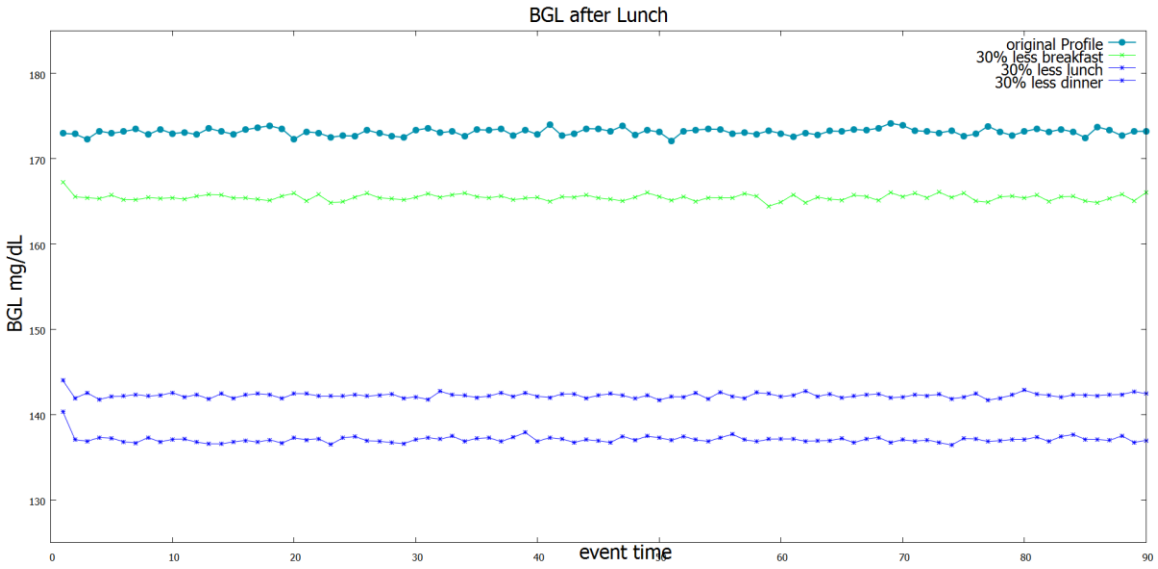

Figure 51 : profile-4 BGL after lunch with reduced diet

4.8 Profile 4.2

This profile is a variant of profile 4 where the person adds one exercise event before dinner in his diet/exercise habit (figure 52). This exercise event linearly decreases his blood glucose level by 0.35 mg/dL per minute. Figure 52 shows that his blood glucose falls to 74 mg/dL which was 101mg/dL in original profile just before the dinner event. Table 16 shows the metabolic rate and other profile parameters for profile 4.2

Table 16: Profile-4.2 metabolic rate with added exercise event

Meal	Rate per minute
Breakfast	0.666667
Lunch	1.02
Dinner	0.750000
Exercise	.35

If this person continues with this modified profile for 90 days his HbA1C value after 90 days becomes 6.26% and his average BGL becomes 117 mg/dL. Without exercise this person's average BGL was 136 and A1C value was 6.39 % (Figure 53, 54). In addition to new exercise event, if he also reduces breakfast amount by 30%, his average BGL and A1C value become 109 mg/dL and 6.14% respectively. In addition to new exercise event and reduced breakfast, if he also reduces his lunch by 30%, his average BGL and A1C value become 100 mg/dL and 6.01% respectively. In addition to new exercise event and reduced breakfast/lunch, if he also reduces his dinner by 30%, his average BGL and A1C value become 92 mg/dL and 5.90% respectively (Figure 53, 54, 55). Figures 56 and 57

show blood glucose levels 2 hours after breakfast and lunch respectively over 90 days for various interventions.

Figure 52 : profile 4.2 generated from profile 4 after adding exercise event

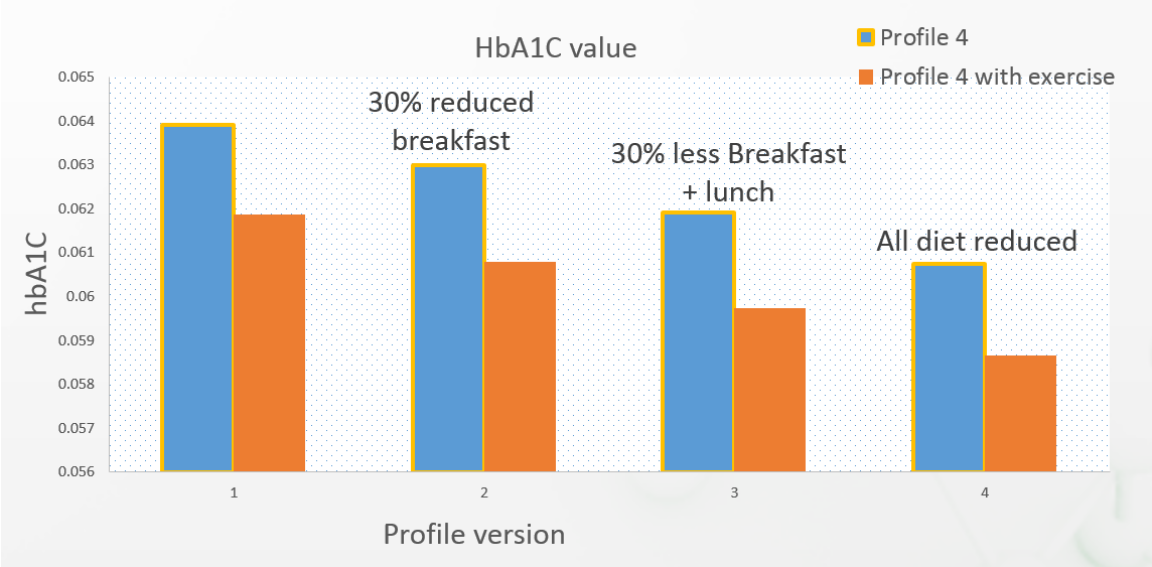

Figure 53 : Profile 4 vs Profile 4.2 HbA1C value

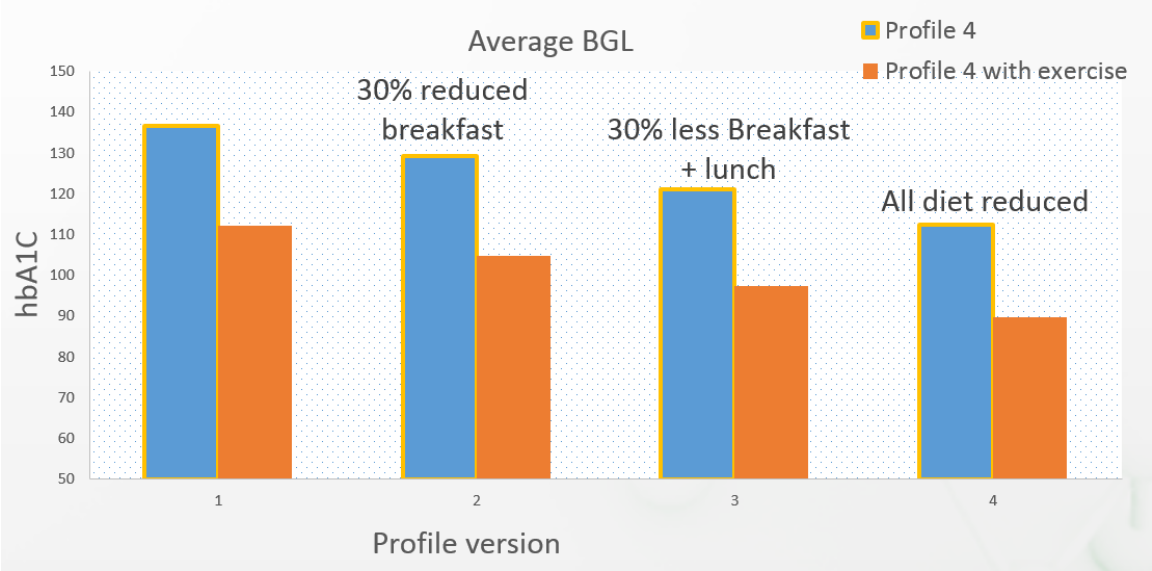

Figure 54 : Profile 4 vs Profile 4.2 average BGL

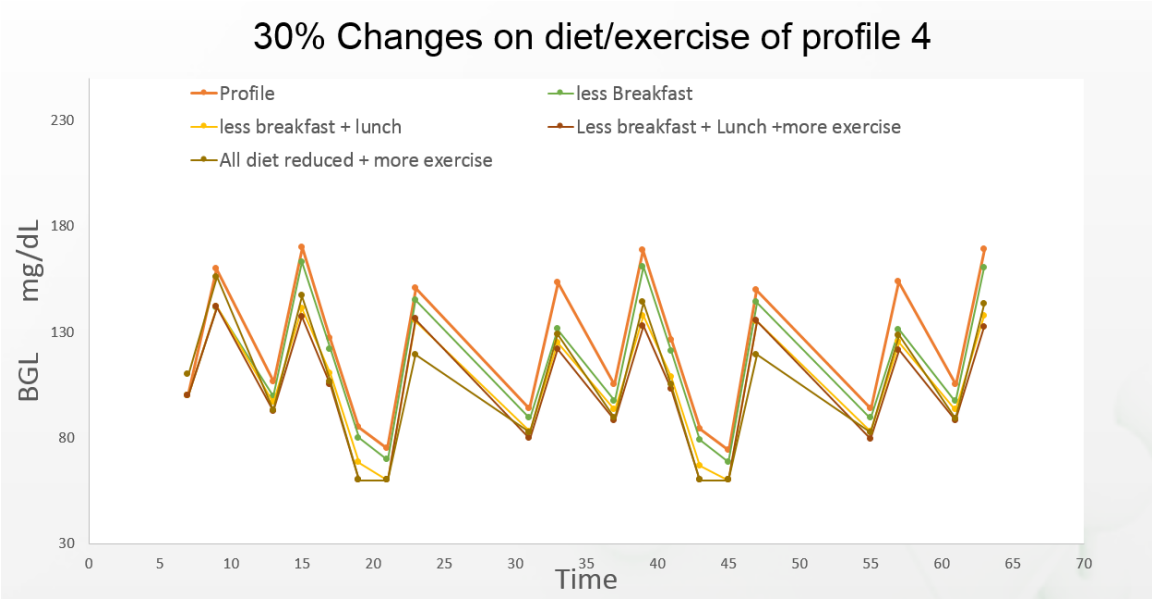

Figure 55 : Profile-4.2 BGL before and after each events with added exercise and with reduced diet

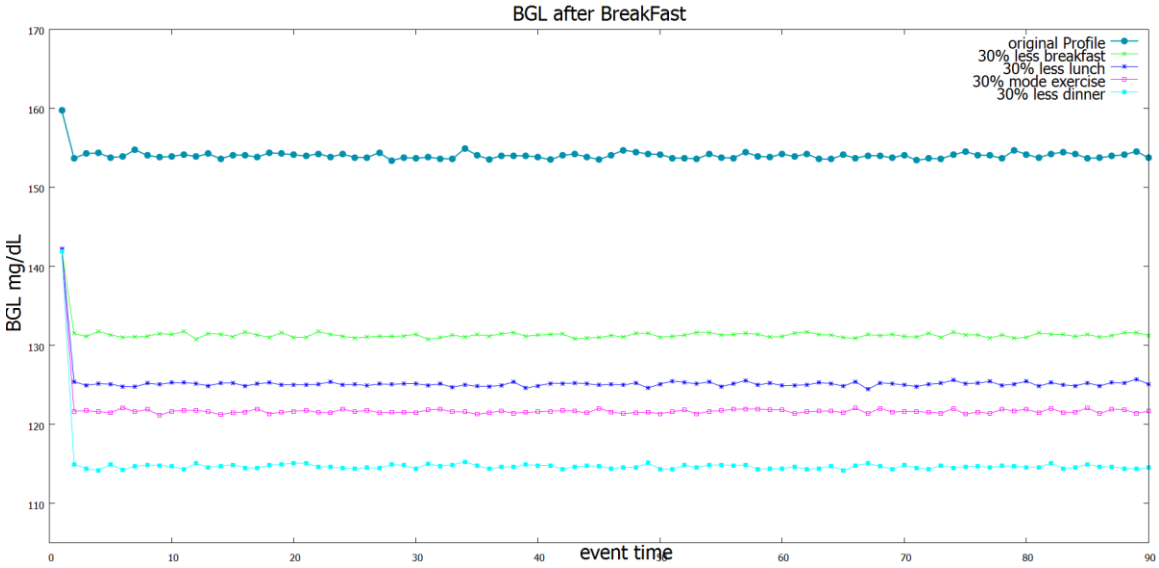

Figure 56 : Profile-4.2 BGL after breakfast with reduced diet

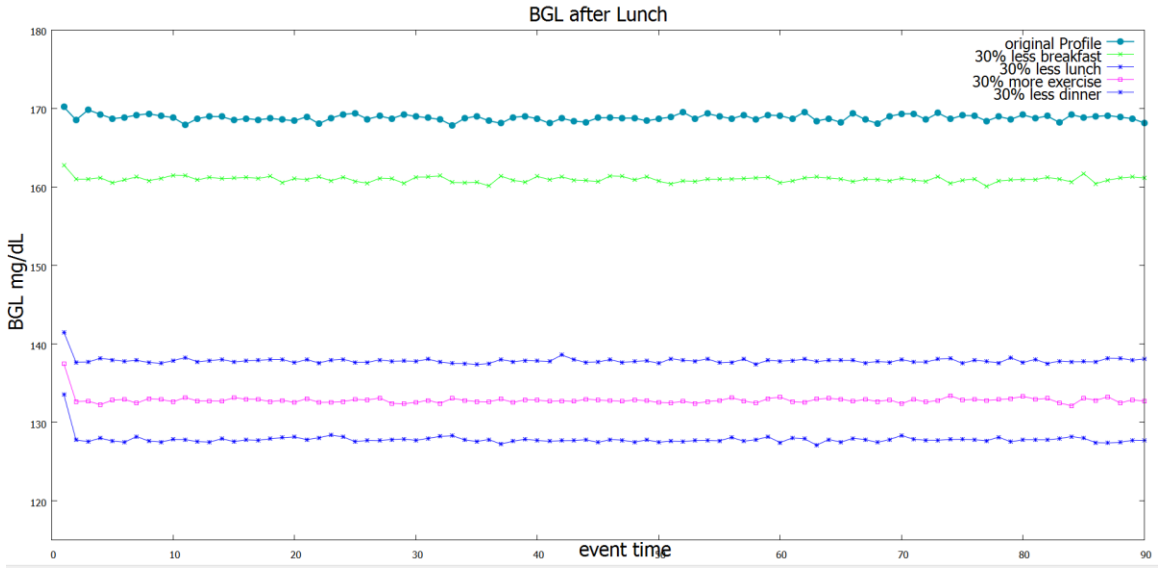

Figure 57 : Profile-4.2 BGL after lunch with reduced diet

5. Conclusion and Future Work

In this work, we designed and implemented a discrete-event simulator to track the blood glucose level and HbA1c level of a diabetic person over several months. We also demonstrated the ability of the simulator to quantify the impact of a change in diet/exercise routine on a person's average blood glucose level and HbA1c level. This simulator currently makes a number of simplifying assumptions. A diet/exercise activity currently has a linear impact on the blood glucose levels. More importantly, the impact of a diet/exercise activity does not last beyond the occurrence of the next activity. The future work will involve allowing for more sophisticated ways for a diet/exercise activity to impact the blood glucose level. Another modification will allow a lifetime distribution to be associated with erythrocytes (rather than having a fixed life time for each erythrocyte). With these modifications, this simulator will evolve into a powerful tool to realistically simulate how blood glucose level varies for a diabetic person as she goes through her daily life. This capability will be immensely useful for diabetes research.

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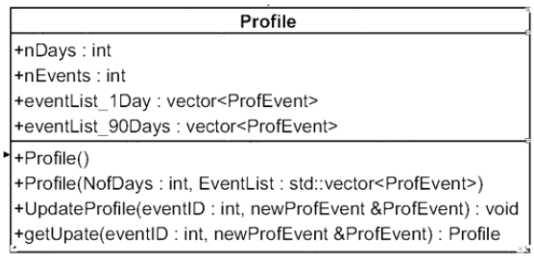
Appendix

Class diagrams detailed level design

Class Name: **Profile Generator**

Attributes List:



Name: nProfile

Type: int

Accessibility: public

Description: number of total profile for the simulation.

Name: nProfVariation

Type: int

Accessibility: public

Description: number of total profile version of each profile.

Name: nProfile

Type: int

Accessibility: public

Description: number of total profile for the simulation.

Name: nSimDays

Type: int

Accessibility: public

Description: no day's simulation will run for each profile

Name: profileList

Type: profile vector

Description: keeps array of profiles

Name: simConf

Type: SimConfig pointer

Description: Keeps the pointer of global simulation configuration instance

List of Operations

Name: ProfileGenerator

ParamIn : simConff ; type : SimConfig *&

Return Type: No return type (constructor)

Description: Profile generator read global configuration files, which contains number of profile, profile variation, human body information. Using configuration data it generates required number of required profile, generates profile variation and also generates consistent event list.

Name : WriteConfigFile

ParamIn : filename , type : char*

Return value: return integer 1 on success, o on failure

Description: WriteConfigFile files writes number of different configuration file for the simulator to run. Simulator needs event change rate in every minute. These files provides those change rates values.

Name : genEventList

ParamIn: nEvents , which tells number of events for a particular profile

ParamIn: ProfEvent; type : vector

Return value : void

Description: this function will generate food exercise event list for generating different profile.

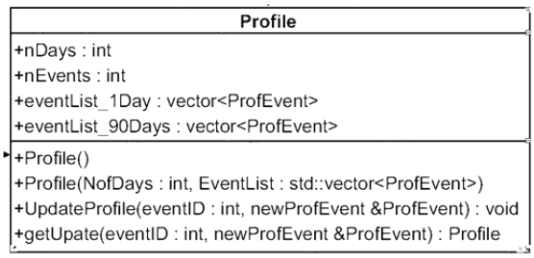
Class Name: Profile

Attribute List:

Name: eventList_1Day

Type: ProfEvent

Description: keeps record of the event list for a single day for the profile.



Name: eventList_1Day

Type: ProfEvent

Description: keeps record of the event list for 90days for the profile.

List of Operations

Operation Name	**Parameters In**	**Parameters Out**	**Return type**	**Description**
Profile	NofDays : number of Events for the profile EventList : list of events for a single day	NA	NA, constructor	Constructs a new profile with given events list
UpdateProfile	eventId : event Id to be updated newProfEvent : Updated eventList	NA	void	Update profile with given Id and updated event

getUpate	eventId : event Id to be updated newProfEvent : Updated eventList	NA	Profile * : return a new updated profile	Constructs a new profile from the existing profile with given ID and updated event list

Class Name: HumanBody

List of Attributes

Attribute Name	**Type**	**Description**
AgeBins	Array of RBCBin	Keeps new and glycated RBCs
Bin0	Int	Initial agebins Index
rbc_birth_rate	Int	rate of RBC cells generations in every minutes

glycation_prob_slope	Double	Adjusted probability slope of finding glycated RBCS
glycation_prob_const	Double	Adjusted probability slope constant of finding glycated RBCS
BGL	Double	Keeps current blood glucose level during simulation
minBGL	Double	Minimum blood glucose level restricted during simulation
maxBGL	Double	
Rate	Double	Current rate of changes in blood glucose level after an event and until next event
AvgBGL	Double	Average blood glucose level after 90days simulation

List of Operations

Operation Name	**Parameters In**	**Parameters Out**	**Return type**	**Description**
Humanbody	NA	NA	NA ;constructor	Constructs a new Humanbody

				Instance with initial configurations
updateBGL	NA	NA	void	Update current blood glucose level after every minute during simulation with the current BGL update rate
set_rbc_birth_rate	Rate : rate of RBC birth in every minute	NA	Void	set rate of Birth of RBC in every minute for humanbody Instance
set_glycation_prob_slope	probSlope : probability slope	NA	void	Set probability slope for humanbody

				instance
set_glycation_prob_const	probConst : probability const of Humanbody	NA	void	Set probability const for Humanbody instance
set_min_bgl	minBGL : minimum level of BGL	NA	void	Set minimum blood glucose level constrain during simulation
set_max_bgl	mxBGL : minimum Blood Glucose Level	NA	void	Maximum blood glucose level constrain for the simulation
changeRate	newRate : set new change rate for new	NA	void	Set new BGL change rate for a new event

	event			occurred during simulation time
SetAvgBGL	NA	NA	void	Initialize avegerage BGL level reading before simulation
UpdateAvgBGL	Amount : currnt BGL Time : total simulation time before that event	NA	void	Update Average BGL reading in every minute by adding new BGL reading with previous AVG and dividing by total time
GetAvgBGL	NA	NA	double	Return Average BGL

				after simulation
GlucoseLabel	NA	NA	double	Return current BGL during simulation time