CLASSIFIED

NEW CONCEPTS FOR MANAGING DIABETES MELLITUS

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ABSTRACT

Title: New concepts for managing Diabetes Mellitus.

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Key terms: Simulation; Human energy system; CHO counting; GI; ets; Equivalent teaspoons sugar; Blood sugar response prediction; Insulin response prediction; Insulin requirement calculation; Human energy system control; Blood glucose simulation; Diabetes regime calculator.

Preface

Biotechnology is generally considered to be the wave of the future. To facilitate accurate and rapid development of medication and treatments, it is critical that we are able to simulate the human body. One section of this complex model would be the human energy system.

Pharmaceutical companies are currently pouring vast amounts of capital into research regarding general simulation of cellular structures, protein structures and bodily processes. Their aim is to develop treatments and medication for major diseases. Some of these diseases are epidemics like cancer, cardiovascular diseases, stress,

obesity, etc. One of the most important causes of these diseases is poor blood glucose control.

Current management methods for insulin dependent diabetes are limited to trial and error systems: clearly ineffective and prone to errors. It is critical that better management systems be developed, to ease the diabetic epidemic.

The blood glucose control system is one of the major systems in the body, as we are in constant need of energy to facilitate the optimum functioning of the human body. This study makes use of a developed simulation model for the human energy system to ease the management of Diabetes mellitus, which is a malfunction of the human energy system.

This dissertation is presented in two parts: The first part discusses the human energy simulation model, and the verification thereof, while the second presents possible applications of this model to ease the management of Diabetes.

The human energy system simulation model

This section discusses the development and verification of the model. It also touches on the causes, and current methods, of managing diabetes, as well as the functioning of the human energy system.

The human energy model is approached with the conservation of energy in mind. A top down model is developed, using data from independent studies to verify the model.

Application of human energy simulation model

The human energy simulation model is of little use if the intended audience cannot use it: people suffering from malfunctioning energy systems. These include people having trouble with obesity, diabetes, cardiovascular disease, etc. To facilitate this, we need to provide a variety of products useable by this group of people.

We propose a variety of ways in which the model can be used: Cellular phone applications, Personal digital assistants (PDAs) applications, as well as computer software.

By making use of current technology, we generate a basic proof-of-concept application to demonstrate the intended functionality.

SAMEVATTING

Titel: Nuwe konsepte vir die beheer van Diabetes Mellitus

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Sleutelwoorde: Simulasie; Menslike energiestelsel; Tel van CHO; GI; ets; Ekwivalente teelepel suiker; Bloedsuiker respons; Bloedsuiker reaksie; Bloedsuiker voorspelling; Insulien reaksie voorspelling; Insulien vereistes sirmulasie; Menslike energiestelsel beheer; Bloedsuiker simulasie; Diabetes roetine berekening.

Inleiding

Biotegnologie speel daagliks 'n groter rol in elk van ons se lewe. Die impak van verbeterde mediese tegnologie raak ons almal op een of ander manier. Om akkurate en vinnige ontwikkeling van medikasie en behandeling moontlik te maak is dit belangrik dat ons die menslike liggaam kan simuleer. Een van die subdele van hierdie komplekse model is die simulasie van die menslike energiestelsel.

Farmaseutiese maatskappye is op die oomblik besig om baie geld te spandeer op die simulasie van selstrukture, proteïen strukture en liggaamlike prosesse. Die doelwit is duidelik die ontwikkeling van medikasie, en behandeling, vir wydverspreide siektes.

Hierdie siektes sluit epidemies soos kanker, hardvatsiektes, spanning, oorgewig, ens in. Een van die belangrikste oorsake van hierdie siektes is swak bloedsuiker beheer.

Huidige bestuursmetodes vir insulien afhanklike diabete is beperk tot lukraak metodes. Hierdie tipe metodes is inherent oneffektief, en geneig tot foute. Dit is duidelik nodig dat beter bestuurstelsels ontwikkel word om die behandeling van diabetiese pasiënte te vergemaklik.

Die bloedsuikerbeheerstelsel is een van die belangrikste stelsels in die menslike liggaam sedert ons 'n konstante vloei van energie nodig het om gesond te bly. Diabetes mellitus is 'n abnormale werking van die energiestelsel. Hierdie studie maak gebruik van 'n ontwikkelde simulasiemodel vir die menslike energiestelsel, om die behandeling van Diabetes mellitus te vergemaklik. Moontlike implementasies van die model word voorgelê.

Die studie word in twee dele voorgelê. Die eerste deel behandel die menslike energiestelsel, en die kontrolering daarvan. Die tweede deel lê weer moontlike toepassings van hierdie model voor. Die doel van die toepassings is om die behandeling van Diabetes mellitus te vergemaklik.

Die menslike energiestelsel simulasiemodel

Die eerste deel van die studie behels die simulasiemodel van die menslike energiestelsel. Hierdie deel bespreek die ontwikkeling en kontrolering van die model. Daar word ook geraak aan die werking van die menslike energiestelsel, die oorsake van diabetes, en huidige metodes vir behandeling van diabete,

Die menslike energiestelsel model word benader met die behoud van energie in gedagte. 'n Oorsigtige model, asook die kontrolering van die model se akkuraatheid, word bespreek.

Toepassing van die menslike energiestelsel simulasiemodel

Die simulasiemodel van die menslike energiestesel is van min nut indien die geteikende verbruikers dit nie kan gebruik nie: daardie mense wat probleme het met

energiestelsels wat foutief werk. Dit sluit mense in wat probleme het met gewig, diabetes, hardvatsiektes, ens. Daar word moontlike implementasies van die model voorgelê wat die bestuur van hierdie siektes kan vergemaklik.

Aan hand van die simulasiemodel word daar 'n paar moontlike implementasies bespreek: Sellulêre telefoon programme, persoonlike digitale assistente (PDAs) programme, asook rekenaar sagteware.

Deur gebruik te maak van huidige tegnologie word daar 'n program geskryf vir gebruik op 'n sellulêre telefoon, om die basiese funksionaliteit te demonstreer.

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NOMENCLATURE

LIST OF ABBREVIATIONS

BMI	Body Mass Index
ETS	Equivalent Teaspoons Sugar
GI	Glycaemic Index
GL	Glycaemic Load
IDDM	Insulin Dependant Diabetes Mellitus
IR	Infra-red
GPRS	General Packet Radio Service
GUI	Graphical User Interface
NIDDM	Non Insulin Dependant Diabetes Mellitus
PDA	Personal Digital Assistant
RDA	Recommended Dietary Allowance
WAP	Wireless Application Protocol

GLOSSARY

Autoimmune response	An immune response by the body against one of its own tissues, cells, or molecules.
Blood glucose level	Blood glucose concentration measured in mmol/l or mg/dl. Also known as blood sugar level.
Blood glucose monitor	Device measuring blood glucose level.
Blood glucose test strip	Strip on which a blood sample is placed for blood glucose measurement with a blood glucose monitor.

Body mass index (BMI)	A measurement of the relative percentages of fat and muscle mass in the human body, in which weight in kilograms is divided by squared height in meters and the result used as an index of obesity.
Carbohydrates	Any of a group of organic compounds that includes sugars, starches, celluloses, and gums. Serves as a major energy source. These compounds are produced by photosynthetic plants and contain only carbon, hydrogen, and oxygen, usually in the ratio 1:2:1.
Diabetes	Disease wherein the body cannot produce sufficient amounts of insulin or the insulin produced is not effective in its function causing blood sugar levels to stay elevated.
Digestive system	The alimentary canal and digestive glands regarded as an integrated system responsible for the ingestion, digestion, and absorption of food.
Endocrine system	The bodily system that consists of the endocrine glands and functions to regulate body activities. The system of glands that produces endocrine secretions that helps to control bodily metabolic processes.
Glucagon	A hormone produced by the pancreas that stimulates an increase in blood sugar levels, thus opposing the action of insulin. Triggers the conversion of glycogen to glucose.
Glucose	A monosaccharide sugar, $C_6H_{12}O_6$. It is the principal circulating sugar in the blood and the major energy source of the body.

Glycaemic control	Blood sugar control
Glycogen	A polysaccharide, $(C_6H_{10}O_5)_n$, that is the main form of carbohydrate storage and occurs primarily in the liver and muscle tissue. It is readily converted to glucose as needed by the body to satisfy its energy needs.
Hormone	A substance produced by one tissue and conveyed by the bloodstream to another to effect physiological activity, such as growth or metabolism.
Hyperglycaemia	The presence of an abnormally high concentration of glucose in the blood.
Hypoglycaemia	An abnormally low level of glucose in the blood.
Insulin	A hormone secreted by the Islets of Langerhans in the pancreas and functioning in the regulation of the metabolism of carbohydrates and fats, especially the conversion of glucose to glycogen, which lowers the blood glucose level.
Insulin Dependant Diabetes Mellitus (IDDM)	Diabetes that requires insulin administration for long-term survival.
Islets of Langerhans	Irregular clusters of endocrine cells scattered throughout the tissue of the pancreas that secrete insulin and glucagon.
Long-acting insulin	Insulin with a long onset time and relative low prolonged activity level. Also referred to as basal insulin.
Non-Insulin Dependant Diabetes Mellitus (NIDDM):	Diabetes that does not require insulin administration for long-term survival.

Operating system (software)	Software designed to control the hardware of a specific data-processing system in order to allow users and application programs to make use of it.
Pancreas	A gland lying behind the stomach that secretes pancreatic juice into the duodenum and insulin, glucagon, and somatostatin into the bloodstream.
Short-acting insulin	Insulin with a short onset time, peak activity 2-4 hours after injection and activity time of less than 8 hours.
Type I diabetes	Occurs when pancreas produces very little or no insulin. People with Type 1 diabetes are insulin dependent and require daily insulin injections to survive. Previously referred to as Insulin Dependent Diabetes Mellitus.
Type II diabetes	Occurs when the pancreas can still produce insulin but not enough to meet the present demand of the body. Patients can survive without insulin on the long term but are often given insulin to improve glycaemic control. Previously referred to as Non Insulin Dependent Diabetes Mellitus.

SYMBOLS

AUC	Area under the curve
AUC_I	Area under the insulin concentration curve over time
BS	Blood sugar level
$BS_{current}$	Current blood sugar level
$BS_{predicted}$	Predicted blood sugar level
$BS_{control}$	Desired blood sugar or control set point for blood sugar level
$BS_{prior\ insulin}$	Blood sugar level prior to insulin injection

$BS_{post\ insulin}$	Stabilized blood sugar level a while after insulin injection
BS_{excess}	Difference between predicted and desired blood sugar levels
BS_{rise}	Absolute increase in blood sugar level
BS_{fall}	Absolute decrease in blood sugar level
$BS_{t=x\ min}$	Blood sugar level measured at time x minutes
CHO	Carbohydrate
E	Energy
E_{CHO}	Carbohydrate energy content in food
E_{RDA}	Recommended dietary allowance of energy for an individual
$E_{teaspoon\ sugar}$	Energy in a teaspoon sugar
ETS	Equivalent Teaspoons Sugar
ets_{RDA}	Recommended dietary allowance of equivalent teaspoons sugar
ets_{meal}	*ETS* content in meal
ets_{needed}	Additional *ETS* needed to raise blood sugar to desired level
f	Conversion factor
$f_{insulin}$	Blood sugar decrease per unit insulin injected
$f_{exercise}$	Conversion of ets expended to resultant blood sugar decrease
$f_{expended}$	Relationship between ets needed for energy expended by person
I	Insulin measured in U (units)
$I_{secreted}$	Insulin secreted by pancreas also quantified in U
I_{long}	Long-acting insulin
I_{short}	Short-acting insulin
$I_{units\ test}$	Short-acting insulin units injected during insulin sensitivity test
$I_{units\ left}$	Active insulin units from previous short-acting insulin injection left in blood
$I_{units\ injected}$	Short-acting insulin units injected

$I_{units\ needed}$	Short-acting insulin units needed to lower blood sugar to desired level
m_{CHO}	Mass of carbohydrates in food

UNITS

ETS	Equivalent Teaspoons Sugar
g	Grams
h	Hours
kCal	Kilocalories
kJ	Kilojoules
kg	Kilograms
l	Liter
m	Meters
min	Minutes
mmol	Milli-mol
U	INSULIN UNIT

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CHAPTER 1 INTRODUCTION

This chapter provides an overview of the dissertation, as well as some background on the subject field.

1.1 PREAMBLE

Biotechnology has been defined as "using a combination of life sciences, high technology, and innovative research to drive progress and profits in health care" [1].

Today 14 pharmaceutical giants are listed in the top 60 most valuable companies in the world [2], resulting in a highly competitive field. Traditionally simulation is one of the most versatile and valuable engineering tools, and coupling simulation with biotechnology should provide a pharmaceutical company with a competitive edge.

The use of simulation in the medical field has been limited: Partly due to the complexity of the subject material, and partly due to the background of medical practitioners.

Diabetes is a disease that widely affects a large section of the populous [12],[13],[9]. Current methods are insufficient for accurate control: Resulting in poor control. Good blood glucose control in people with diabetics leads to fewer complications in the long term, improving the life quality of all people affected [6].

1.2 BACKGROUND

The following sections provide a background on the human energy system and deviations from the norm. This will provide the reader with the basic background for the next section.

1.2.1 The human energy system

The human body needs energy to maintain its functions. This energy is obtained from sugar transported in the blood. In general the human body functions much as a machine, or engine, does [3]. As such it converts input energy (fuel) to mental and physical energy, enabling the normal functioning of the body. This input energy is obtained primarily from the ingestion of food [4].

The energy is contained in, and transported by, the blood circulation system, in the form of glucose (blood sugar). The flow of energy via the blood circulation system is

mainly accomplished by endocrine regulation and concentration imbalance between the different components [6].

Much has been learned of the requirements for performance, excess build-up, and malfunctions in the regulatory systems, but there still remains a lot to be learned and understood with regards to the human system [6]. The constant interaction between all systems and components in the body provides a truly high level of complexity.

The prediction of the glycaemic response is, however, not a simple operation. It requires knowledge of many variables and there exist some debates in the literature pertaining as to which methods are better to use [17]. The important fact, though, is that ingested food has the most noteworthy effect on blood sugar levels [6].

Due to the rise in blood sugar levels, diabetic patients need to inject insulin for regulatory control. The method of CHO counting assists the person in estimating the required insulin dose corresponding to the amount of CHO ingested [16],[6]. Some success has been obtained, but some limitations have been found concerning this method.

An alternative method has been presented, and also enjoys wide spread acceptance. This method makes use of the impact each food type has on the blood glucose, by comparing a specific mass of each with the same mass of glucose [17], [18], [19]. The system of glycaemic indexing (GI) has its own weaknesses though.

1.2.2 Diabetes mellitus

Blood glucose levels in the body are regulated by two mechanisms to keep the balance within optimum levels [7]. These mechanisms continuously monitor the levels of blood glucose, and react to any disturbances in the levels [8]. We will refer to these mechanisms as the regulation and counter regulation systems [8].

These systems function as follows: Whenever the blood glucose levels drops below a specific set point, the counter regulation system is activated, and attempts to correct the blood glucose level by triggering the secretion of certain hormones into the blood circulation system. These hormones activate the energy storage system in the body to

release glucose into the blood circulation system, and thereby restore the blood glucose level to its previous status [6].

On the other hand, we have the occasions where the blood glucose levels rises above another set point. In this case the regulation system also triggers the secretion of specific hormones (Insulin, among others) into the bloodstream, triggering the uptake of glucose by cells. This absorption of blood glucose from the blood circulation system reduces the blood glucose levels, and restores the balance [9].

As in any machine or engine, malfunctions invariably occur. We will be considering the case called diabetes mellitus. Diabetes is defined as the condition where the pancreas either fails to produce insulin (Type 1), or the person has built up a resistance to insulin (Type 2). Type 2 diabetics thus have slower regulation and counter regulatory reactions, due to the dampening factor of the insulin resistance [6]. Type 2 diabetes is also referred to as non-insulin dependent diabetes mellitus (NIDDM).

The lack of insulin in Type 1 diabetes is usually a result of an autoimmune response, wherein the white blood cells within the body attacks the Islets of Langerhans within the pancreas. These islets are responsible for the generation of insulin, and as more of the islets are destroyed, the amount of insulin available to the body decreases, until the patient is completely dependent upon injected insulin, to maintain their health [6]. Type 1 diabetes is also referred to as insulin dependent diabetes mellitus (IDDM).

Hyperglycaemia is defined as plasma glucose levels larger than 200mg/dL [10]. Frequent high blood glucose levels (hyperglycaemia) have far-reaching implications for the health of diabetics. Alternatively a low blood glucose level (hypoglycaemia) can be even more dangerous, causing loss of consciousness and eventually death.

Diabetics currently make use of manually injected insulin to consciously control their blood glucose levels [6]. To accurately control the blood glucose levels is, understandably, a complex exercise [11].

The disease has reached epidemic proportions. There are currently an estimated 110 million diabetics in the world. This number is expected to double by the year 2010

and, if no cure can be found, it can increase to 300 million by 2025 [12],[13]. This rapid increase makes it one of the fastest developing diseases in the world. Of these 110 million diabetics, about 30 million are insulin dependant and have to inject insulin on a daily basis [9].

1.3 PROBLEM STATEMENT AND OBJECTIVES

As previously mentioned, current methods for managing diabetes' blood glucose levels are ineffective, and leave a lot to be desired.

This thesis will attempt to present a more accessible method to proactively control the blood glucose levels of Type 1 and Type 2 diabetics, which is more user-friendly and accurate than current methods. By discussing a method developed by Botha [14], and reviewing possible implementations of this simulation model, we will attempt to achieve our goal. The system has to be easy to use, as this will result in a wider acceptance of the method.

1.4 OVERVIEW OF THESIS

The thesis is presented in two main sections. Section 1 deals with the basic simulation model, and the general background to support the model, while the second section deals with the proposed implementation of the model on a cellular phone.

Section 1 contains chapters 1 to 4, while Section 2 contains chapter 5.

Chapter 1 is provided as a general introduction to the thesis and the subject material. Chapter 2 discusses current diabetes management concepts and methods, as well as the problems inherent to blood glucose control. Chapter 3 discusses the new model, with chapter 4 providing an overview of the model verification.

Chapter 5 proposes a possible implementation of the model on a cellular phone, or other PDA.

1.5 CONTRIBUTIONS OF THIS STUDY

To achieve the objectives stated in Section 1.3 contributions were made in this study:

- This study provides the first practical application of the human energy simulation model developed by Botha [14].

- Secondly, the study lays the ground for further development of cellular applications implementing the above-mentioned model.

- Expanding the field based on an improved model provides a wider base for further research based on the improved model.

- Products developed can eventually make the job of the medical practitioner and dieticians treating diabetes much easier. Diabetics will be able to make important decisions regarding their blood sugar control more independently.

- The study finally provides a functional application for use in estimating insulin dosage, based on the provided datum. This application proves to be a more accurate and effective management method for insulin dependent diabetes mellitus. This provides researchers with more data to base further research on.

- Research and development in this study provides a leap towards easy and accurate blood glucose control. Products are based on empirical models developed by Botha [14]. This study therefore provides concepts of the products to be clinically tested and verified in a future study. It forms the basis of a system that may eventually help millions of diabetics.

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CHAPTER 2 IMPROVEMENTS ON CURRENT DIABETES MANAGEMENT METHODS

This section discusses current methods of managing diabetes, and considers its shortcomings. It also touches on the functioning of the human energy system.

2.1 INTRODUCTION

The literature study of the field had to cover not only the causes of both types of diabetes, but also each of the different management methods. The possible cures as well as new research had to be reviewed, and researched.

Filtering through the mountains of medical research and articles only confirmed the original observation: Current methods of managing diabetes are painfully inaccurate. The danger to the health of diabetics is portrayed as less important, by comparing the inaccurate management systems with no system at all. This comparison invariably favours managing diabetes. The need for an improved system is very clear.

2.2 CURRENT METHODS FOR MANAGING DIABETES

Current methods of treating diabetes are limited to its management. This is done with rigorous diets and exercise regimes – coupled with regular insulin injections and blood glucose measurements [16].

2.3 CURES FOR DIABETES

There are currently no perfect cures for diabetes. The possibility of islet or pancreas surgical transplant does exist [35],[36], but these transplants hold other complications. The risks associated with pancreas transplantation include clinical complications caused by the surgery and chronic immunosuppressive drugs, as well as death. A wide variety of medical complications have been documented [38], making surgical treatment a less attractive option than active management of diabetes.

2.4 PROBLEMS AND SHORTCOMINGS OF CURRENT MANAGEMENT METHODS

The methods currently employed are poor trial and error methods [16]. The problem with current methods is the non trivial problem of predicting the blood glucose levels over the next few hours, as the influence of food taken is delayed by durations that are at times influenced not only by personal characteristics, but also by the type of food

[6], [17], [26]. Couple with this the delayed reaction of insulin, and one is left with a truly hit and miss situation [16].

There are currently two major schools of thought concerning the estimation of glycaemic response. On the one hand is the group of researchers preferring the estimation of blood glucose based on the amount of carbohydrates (CHO) ingested [30],[31]. On the other hand, we have the researchers who favour the concept that the type or "effectiveness" of the CHO ingested is the largest deciding factor in glycaemic response [26].

We will refer to these two well-known methods for predicting the insulin response due to food ingestion, as *CHO counting* and the *glycaemic index* (GI) [27],[28]. However, these methods do not always give the correct response and many people find them difficult to use [17],[29],[19]. Additionally, these methods invariably take a generic approach and therefore do not specifically account for differences between people.

2.5 GROUNDS FOR IMPROVED DIABETES MANAGEMENT METHODS

Due to the immense system of variables involved in the human system, there have been few actual attempts to describe a control system for the human body. This provides an opportunity that cannot be ignored. By approaching the concept with the preservation of energy in mind, we observe one small part of the human body, and simulate it. By using approximation one can obtain a relatively accurate model for the human blood glucose effects.

If one considers that there are currently no simulation models for this human system, one can but improve on current systems. At this point in time even an inaccurate model would be an improvement on current knowledge.

This model can now be used to create a simple, but more accurate, management system for diabetics. This system will do nothing more than make basic predictions of

the blood glucose levels, and advise insulin dosages to the patient. The prediction system needs to be simple to use, and not burden the patient with additional hardware.

2.6 THE PROBLEM OF BLOOD SUGAR CONTROL

2.6.1 Background

The prediction of blood glucose levels is a complicated problem, and a solution has proved to be elusive for some time. A problem with the development of a solution is the variability of the subjects. Different foodstuffs affect people differently.

Every clinician is aware that a diabetic patient on the same insulin regimen and resting in bed, eating at the same time each day a dietician-prescribed standard diet, can have quite different blood glucose readings from day to day [39].

The amount of insulin that is secreted for ingested CHO is not well understood. As mentioned, a practical relationship between insulin response and food is important for diabetics as they either do not produce enough insulin or cannot utilise it efficiently [6].

The influence of exercise is also problematic, since exercise also influences, not only the blood sugar levels, but also the insulin sensitivity. This means that exercise will not only influence the current blood sugar levels, but will continue to do so to a certain extent.

Insulin sensitivity differs from person to person – adding another variable to our equation. This means that the same insulin dose will result in different results in different subjects.

The current method of developing a regime for a diabetic is purely by trail and error. Couple with this a strict set diet, and a strict set exercise routine, and the diabetic can *perhaps* be content with almost normal blood sugar control levels, if there is no change in stress levels [16].

Clearly current methods have a lot of room for improvement. These methods are inherently dangerous, as miscalculations are frequent, and can cause permanent damage to the affected person.

2.6.2 ets: A new concept

To ease the development of the human simulation model, a new concept has been developed. Current methods of quantifying energy input into the human energy system were insufficient: Each was lacking in accuracy where the estimation of actual energy absorbed was considered.

Needing the ability to correlate each of the separate energy flows into, and out of, the body, it became clear that a universal measure would be needed. This measure would enable the comparison of energy flows into, and out of the body. This unit needed to be easily understandable to ease the use of the model by the target audience.

A unit of Equivalent Teaspoon Sugar (ets) was developed. This unit can be considered as the amount of energy available to the human body in one teaspoon of sugar. The unit was also used, in part because of its ease of visualisation, and easy acceptance. The largest advantage of the unit is that it not only incorporates the mass of carbohydrates in the food, but also the GI value of the food: resulting in a unit that more accurately predicts the influence of the food on the blood glucose levels [14].

Measurements with a bomb calorimeter suggest that energy of approximately 4 kCal/g can be released from CHO when it is oxidised in pure oxygen [32]. Obviously the human energy system does not use the same process for energy conversion as a bomb calorimeter. Intuitively it can be suspected that the body converts less energy from ingested carbohydrates than the optimum process. It is therefore necessary to investigate how much energy the human energy system actually does convert.

Due to the complex and integrated processes of the human body, it is difficult to measure this conversion process. However, it is well known that the energy extracted from ingested CHO is converted into useful blood sugar energy [33]. But, it is also fairly difficult to measure the amount of blood sugar energy in healthy people. With healthy blood sugar regulation, insulin enables storing and utilisation of the blood

sugar energy during the conversion process [6]. A possible method would be to integrate the blood sugar response curve over time, account for blood volume and time from ingestion to reaching basal blood sugar again, and hence find a fair approximation of this converted energy.

However, as this is too difficult, a simpler way is proposed in this study. Type 1 diabetics have no, or negligible, insulin secretion. Without insulin, the blood sugar energy released through digestion cannot be stored or utilised during the conversion process [6]. This condition simplifies the measurements by removing one of the variables of the system. The level to which diabetics' blood sugar levels rise should therefore give a good measure of the amount of blood sugar energy converted from the ingested CHO.

Therefore a Type 1 diabetic's blood sugar levels can be measured after ingesting the same amount of two different types of CHO, on two separate occasions. (One of the foods is used as a reference.) As an example the person can ingest an equal amount of glucose and fructose. If all the possible energy (4 kCal/g) is made available from the digestion process, similar blood glucose responses would be the expected result.

However, a series of empirical measurements, shown schematically in Figure 2.1, illustrate a trend that is different from this expected result. Blood sugar response to glucose, and thus the conversion of glucose into blood sugar energy, is approximately four times more efficient than that of fructose. The subsequent question is: How could the energy available after conversion for any other type of carbohydrate be calculated?

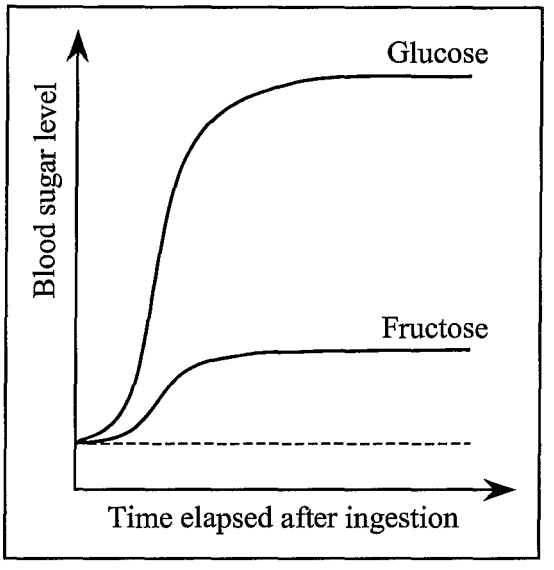

Figure 2.1 – Schematic representation of measurements of blood sugar response when a Type 1 diabetic eats equal amounts of CHO contained in glucose and fructose.

The Glycaemic Index (GI) of glucose, which is the reference food, is 100. This is approximately four times greater than that of fructose, which is only 23 [26]. Therefore, GI actually gives an idea of the energy conversion potential of the carbohydrates under investigation.

However, according to researchers, the definition of GI states that GI is the "rate of absorption" for a CHO into the bloodstream [26]. If this definition were correct (thereby not defining energy) measurements shown schematically in Figure 2.2 would be expected. However, true empirical measurements (Figure 2.1) contradict Figure 2.2. Therefore, a new definition of GI is proposed, namely that GI provides the "energy conversion potential" of carbohydrates.

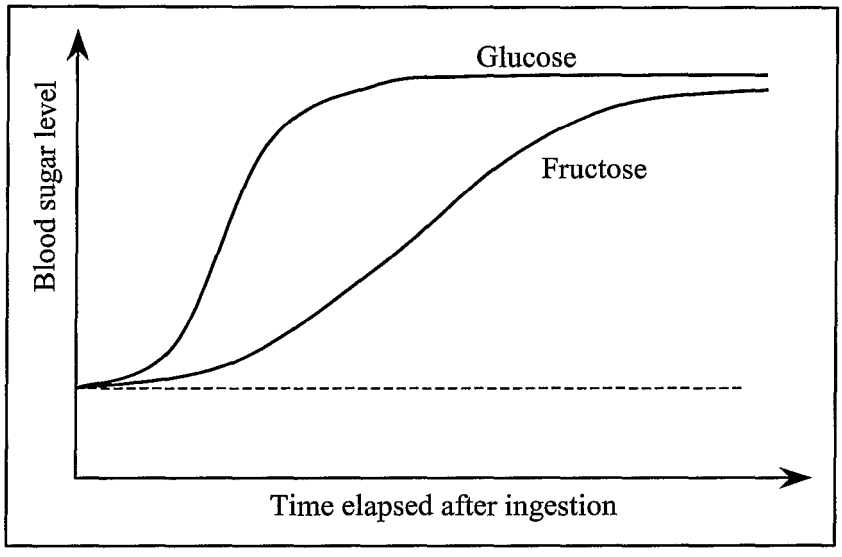

Figure 2.2 – Schematic representation of expected blood glucose response if the correct definition of GI is "rate of digestion": Type 1 diabetic ingesting the same mass of CHO through glucose and fructose.

GI expressed as a percentage (%) can now be used to find the converted CHO energy potential (E_{CHO}, measured in kCal) for a mass (m_{CHO}, measured in g) that is available to the body. Since there are approximately 4 kCal of energy in 1 g of pure glucose, E_{CHO} can be approximated with Equation 2.1 [34].

$$E_{CHO} = 4\frac{GI}{100}m_{CHO} = \frac{GI.m_{CHO}}{25}$$

Equation 2.1

If Equation 2.1 is divided by m_{CHO} throughout, Equation 2.2 is found.

$$\frac{E_{CHO}}{m_{CHO}} = \frac{GI}{25}$$

Equation 2.2

Equation 2.1 can now be used to calculate approximate values for typical energy contents available to the body from ingested carbohydrates. In Table 2.1 a few examples of typical GI values and their corresponding energy contents (E_{CHO}) per mass (m_{CHO}) values are shown.

Food	GI (%)	$\frac{E_{CHO}}{m_{CHO}}$ (kCal/g)
Glucose	100	4
Fructose	23	1
Apple	38	1.5
Table sugar	65	2.6
White bread	75	3
Whole-wheat bread	65	2.6

Table 2.1 – Typical values for E_{CHO}/m_{CHO} *in accordance to corresponding GI values.*

From the table it is clear that what dieticians have been preaching for years is true after all. It is better for weight losers to eat less refined carbohydrates e.g. whole wheat bread, than it is to eat more refined carbohydrates, like white bread, during weight losing diets. This way effectively less energy is absorbed from the same amount of ingested carbohydrates.

2.6.3 The two types of insulin administered by diabetics

Control of blood glucose levels is currently done with injections of two variations of insulin. This combination of insulin is used on a daily basis, to actively control blood glucose levels in insulin dependant diabetes. The first variety is called long acting insulin. As the name suggests, this insulin has a small but almost constant effect on the blood glucose levels. Figure 3.3 shows the insulin concentration profiles for a few long acting insulin variants.

The second variety of insulin is called short acting insulin. Short acting insulin is primarily used to lessen the impact of meals on the blood glucose levels. Figure 2.3 shows the effect of meals on a non-diabetic person. In a Type 1 diabetic the effect of each meal would be cumulative, resulting in a constant high blood glucose level. Short acting insulin is used to decrease the peaks in blood glucose levels.

Long-acting insulin, on the other hand, is used to facilitate the constant energy requirement of the body. This refers to the basic energy needed to keep the critical

systems functioning. These include, for example, breathing, heartbeat, nervous system functioning, etc.

Since insulin is needed by all cells to be able to absorb glucose, there is a constant drop in insulin level within the blood, which constantly needs to be replenished [6]. This is the goal of long acting insulin: replenishing the insulin used by the body in maintaining its critical functions. The level of insulin needed to support these functions is called the basal insulin level.

The plot of blood sugar level in Figure 2.3 shows the effect that a miscalculated long acting insulin dosage will have on the basal insulin level. If Type 1 diabetics thus miscalculate their daily long acting insulin, their short acting insulin regime would be affected, ultimately resulting in an oscillatory control pattern as the short acting insulin dosages vary [16].

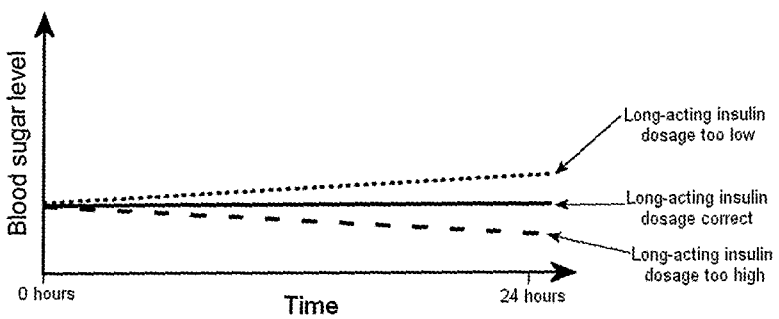

Figure 2.3 – Illustrative fasting blood sugar levels of a Type-1 diabetic to illustrate the effect of incorrect long-acting insulin dosage

2.6.4 Characterisation of patients

Due to the fact that each person differs in various ways, including the reaction to food and insulin, we need to be able to characterise each patient. Botha [14] proposes methods of obtaining two critical characteristics of each person: The insulin sensitivity, and the glucose sensitivity.

The experiment to obtain these figures for a Type 1 diabetic person will be briefly explained: After a fast of roughly six hours, the person tests his/her blood glucose level, and then eats one teaspoon of sugar. The fasting is to insure the stabilising of the blood glucose levels. The blood glucose is then measured at intervals of 15 minutes, until 45 minutes have passed, after which the blood glucose should have stabilized. The increase in blood glucose is defined as ΔBS_{Rise}.

The patient now injects one unit of insulin, and again measures his/her blood glucose levels at intervals of 15 minutes, stopping after 45 minutes. The blood glucose level should have stabilised by now, and the drop in blood glucose is defined as ΔBS_{Fall}. Figure 2.5 shows a schematic representation of the definitions for ΔBS_{Rise} and ΔBS_{Fall}.

These measured values can now be substituted into Equation 2.3 to obtain f_I, the insulin response and ets relationship factor.

$$f_I = \frac{I_{Secreted}}{ets}\frac{\Delta BS_{Rise}}{\Delta BS_{Fall}} = \frac{I_{Injected}}{ets}\frac{\Delta BS_{Rise}}{\Delta BS_{Fall}}$$

Equation 2.3

Figure 2.4 shows a generic visual representation for the above procedure. Each of the important points is highlighted.

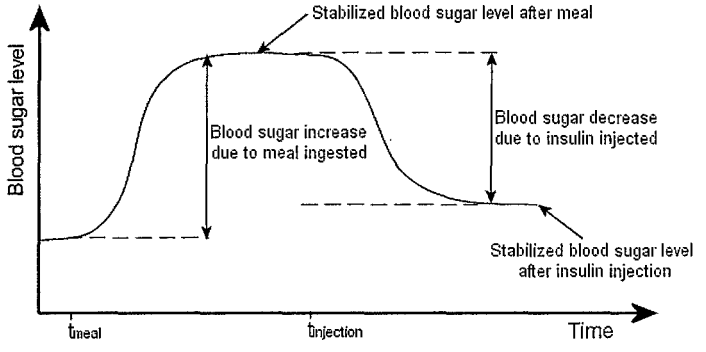

Figure 2.4 – Blood sugar level of Type 1 diabetic during insulin sensitivity test procedure.

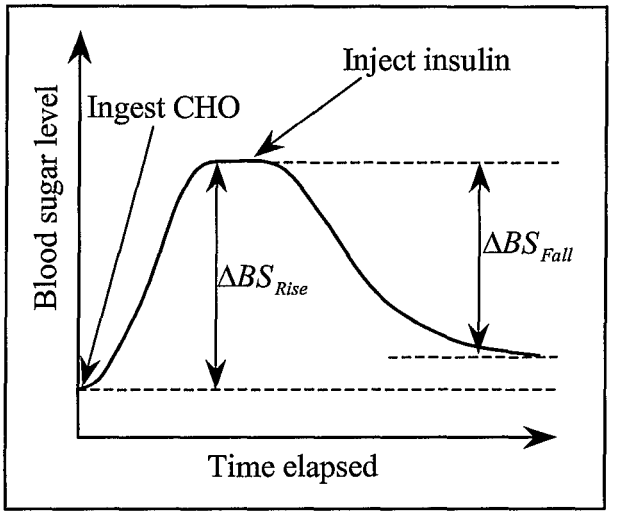

Figure 2.5 – Schematic representation of the definitions of ΔBS_{Rise} *and* ΔBS_{Fall}.

2.6.5 Influence of food intake on blood glucose levels

The effect of digested carbohydrates varies from person to person, as previously discussed. Each person has a specific sensitivity to carbohydrates.

Whenever carbohydrates are ingested as food, the digestive tract, including both the small and the large intestines, breaks down (or hydrolyses) the CHO into the simplest form, namely the monosaccharides (glucose, fructose and galactose). These are then transported to the liver through the portal vein where the monosaccharides are converted to glucose. Some of the glucose is then released into the bloodstream invariably causing the blood sugar level to rise [15].

Figure 2.6 shows the normal blood glucose reaction of a non-diabetic person over a normal day. The peaks clearly show the times at which the person ingested carbohydrates. The figure is also marked to show which areas would be affected by a diabetic's long acting, and short acting, insulin dosages.

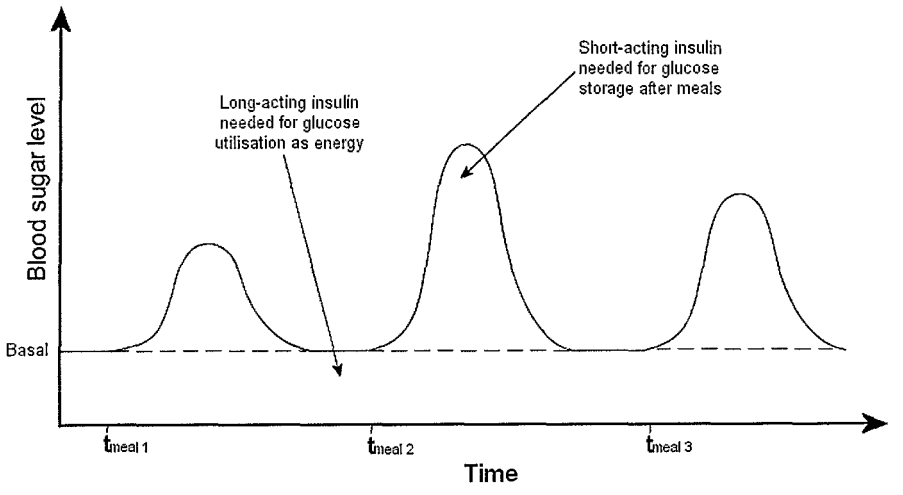

Figure 2.6 – Typical blood sugar profile of a non-diabetic consuming three meals during the day (no carbohydrates in beverages).

Insulin acts as the main regulation agent: Increasing in concentration as the blood glucose level in the blood increases. This results in increased absorption of glucose into tissue, resulting in the storage of the energy. Figure 2.7 shows the correlation between increased blood glucose and insulin concentration.

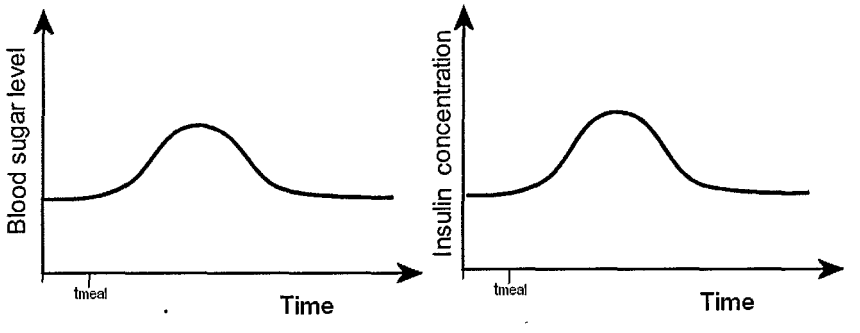

Figure 2.7 – Illustrative blood glucose and insulin concentration curves of a non-diabetic person after ingesting a meal containing carbohydrates.

Figure 2.8 shows the same reaction for a person suffering from Type 1 diabetes mellitus. The result of the absence of insulin can clearly be seen.

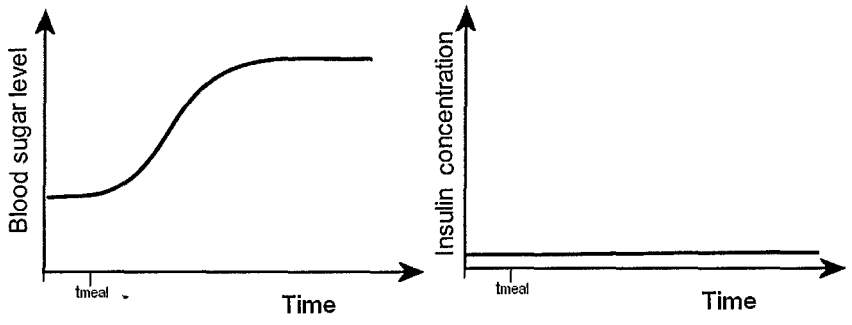

Figure 2.8 – Illustrative blood glucose and insulin concentration of a diabetic person after ingesting a meal containing carbohydrates (not using short-acting insulin).

Making use of the ets concept, as developed by Botha [14], we can link the food intake, energy expenditure, and blood glucose level reaction. Figure 2.9 shows the simplified graphical representation of the energy expenditure link with the blood glucose concentration. The energy expenditure is represented in units of ets.

Figure 2.9 clearly shows that as the amount of energy expended increases, so the blood sugar level decreases. This has the impact that whenever a person with diabetes exercises, their long-term blood glucose level drops, proportional to the amount of energy they expend. This is true to the law of retention of energy.

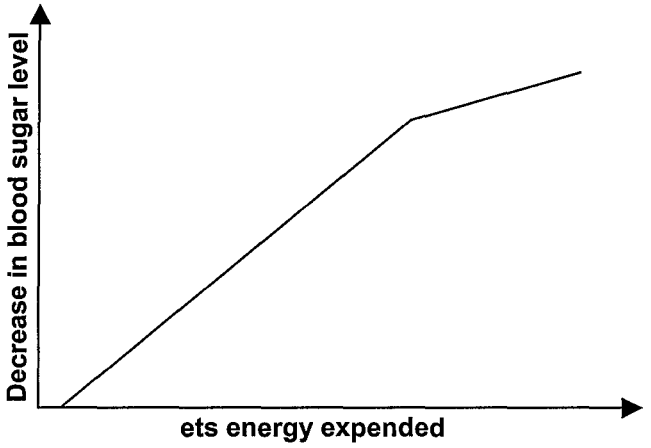

Figure 2.9 – Blood sugar level decrease of Type 1 diabetic as a function of ETS energy expended during exercise.

For Type 1 diabetics we need to be able to calculate a needed insulin dosage to balance the absorption of glucose from the digestive system, and to make possible the absorption of energy from the plasma glucose. This requires models of not only the

ingestion/absorption of foodstuffs, but also an ideal case model for insulin secretion. This ideal model can then be used to calculate the needed insulin dosages needed to balance the level of glucose in the blood.

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CHAPTER 3 A NEW SIMULATION CONCEPT

This section describes the development of the human energy system simulation model.

3.1 SIMULATION MODEL OF ENERGY FLOW IN THE HUMAN BODY

Some idea of the functioning of the human body and its processes is necessary for comprehension of the complete simulation model. A model to predict the glycaemic response is considered, but due to the complex integration of the whole human system it is necessary to be aware of all the energy flow pathways.

It should always be kept in mind that, even though the energy system is discussed and approached in its whole as separate from the rest of the human systems, it is nevertheless a subsystem of a whole and complex system.

For our cursory glance at the model we will only touch on a few main sections of the energy pathways. Figure 3.2 shows a simplified schematic layout of the blood sugar control system in the human energy system.

3.2 ENERGY INPUT

All nutritious food intakes constitute energy sources for the human body [34]. Ingested food is broken down into its absorbable components by digestion processes, after which the components are either converted into, or used for, direct energy supply to the body. Alternatively these components can also be stored for later use. All food is composed of macronutrients, micronutrients, and water [48].

Four basic forms of usable fuel needed by the body in order to maintain metabolism, movements and mental functions were considered. These types are glucose, keto acids, fatty acids and ketones [49]. The central nervous system and brain, for instance, are primarily dependent on a minimum level of blood glucose to stay functional, and healthy [50], while the heart muscle prefers ketones as its primary fuel [51].

A schematic layout of the integrated human energy system simulation model is given in Figure 3.1. Each of the energy components (digestion system, bloodstream, etc) as well as the connection lines and control components have been modelled [14]. Most

of the details fall beyond the scope of this study, and will therefore not be discussed, except where it is of key importance to the comprehension of specific sections.

As seen in Figure 3.1, glucose flows from the digestive system into the bloodstream. From here it can either be utilised in the energy expenditure component ($\dot{G}_{Exercise}$), or it can be stored in the storage component ($\dot{G}_{Store-IN}$).

For both of these flows a regulation hormone is needed. If such a hormone is not available, the glucose will simply remain in the bloodstream and result in glucose build-up. This results in hyperglycaemia, and as previously mentioned holds a variety of dangers. This is usually the case with Type 1 diabetics. As their systems have no insulin at their disposal (insulin being the regulation and storage hormone [54]), the glucose keeps building up in the bloodstream.

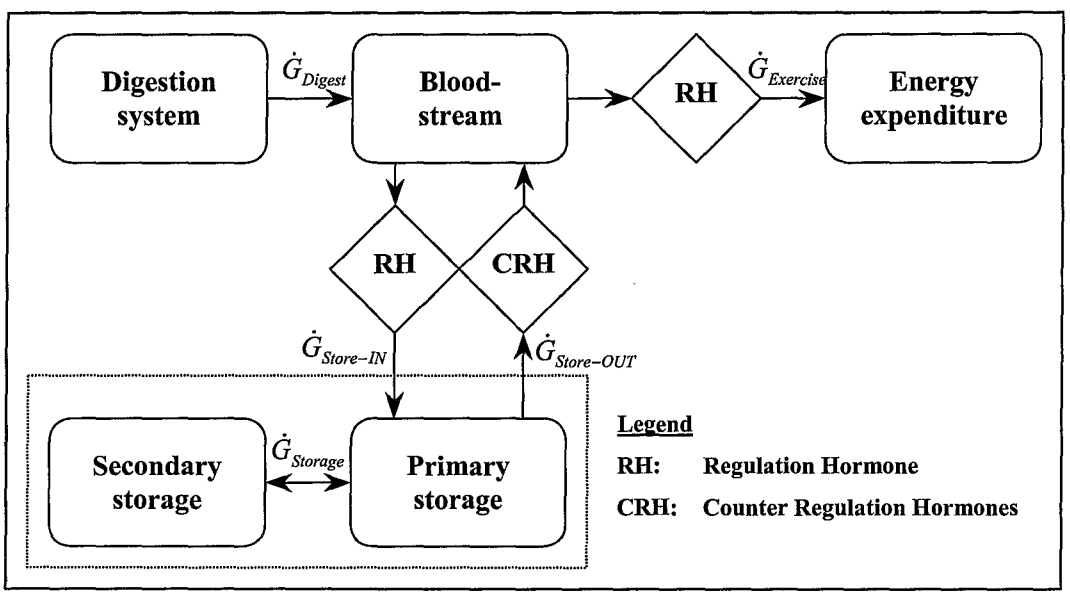

Figure 3.1- Schematic layout of the integrated human energy simulation model.[14]

The basic preservation of energy principle is used to derive a function for the amount of blood glucose. This equation is shown as Equation 3.1.

$$G_{Blood(t)} = G_{Blood(t-1)} + \left(\dot{G}_{Digest} + \dot{G}_{Store-Out} - \dot{G}_{Store-In} - \dot{G}_{Exercise}\right)_{(t)}$$

Equation 3.1

We also obtain Equation 3.2 from the same principle. There are only two main energy-consuming sections. These are

- The glucose energy required for keeping the vital organs alive. This also includes the energy needed to perform normal daily activities. This is referred to as the basal energy requirement ($\dot{G}_{Basal}$).

- The glucose energy flow required for performing exercises other than those performed during normal daily activities ($\dot{G}_{Movement}$). This is mainly required for muscle function.

$$\dot{G}_{Exercise} = \dot{G}_{Basal} + \dot{G}_{Movement}$$

Equation 3.2

Equation 3.3 is used to calculate short acting insulin dosages, and Equation 3.4 to calculate long acting insulin dosages [14].

$$I_{Injected} = f_I ets$$

Equation 3.3

$$I_{Injected(Long)} = \frac{f_I}{f_{Expended}} E_{Expended(RDA)}$$

Equation 3.4

f_I is calculated from Equation 3.5 [14].

$$f_I = \frac{I_{Secreted}}{ets}\frac{\Delta BS_{Rise}}{\Delta BS_{Fall}} = \frac{I_{Injected}}{ets}\frac{\Delta BS_{Rise}}{\Delta BS_{Fall}}$$

Equation 3.5

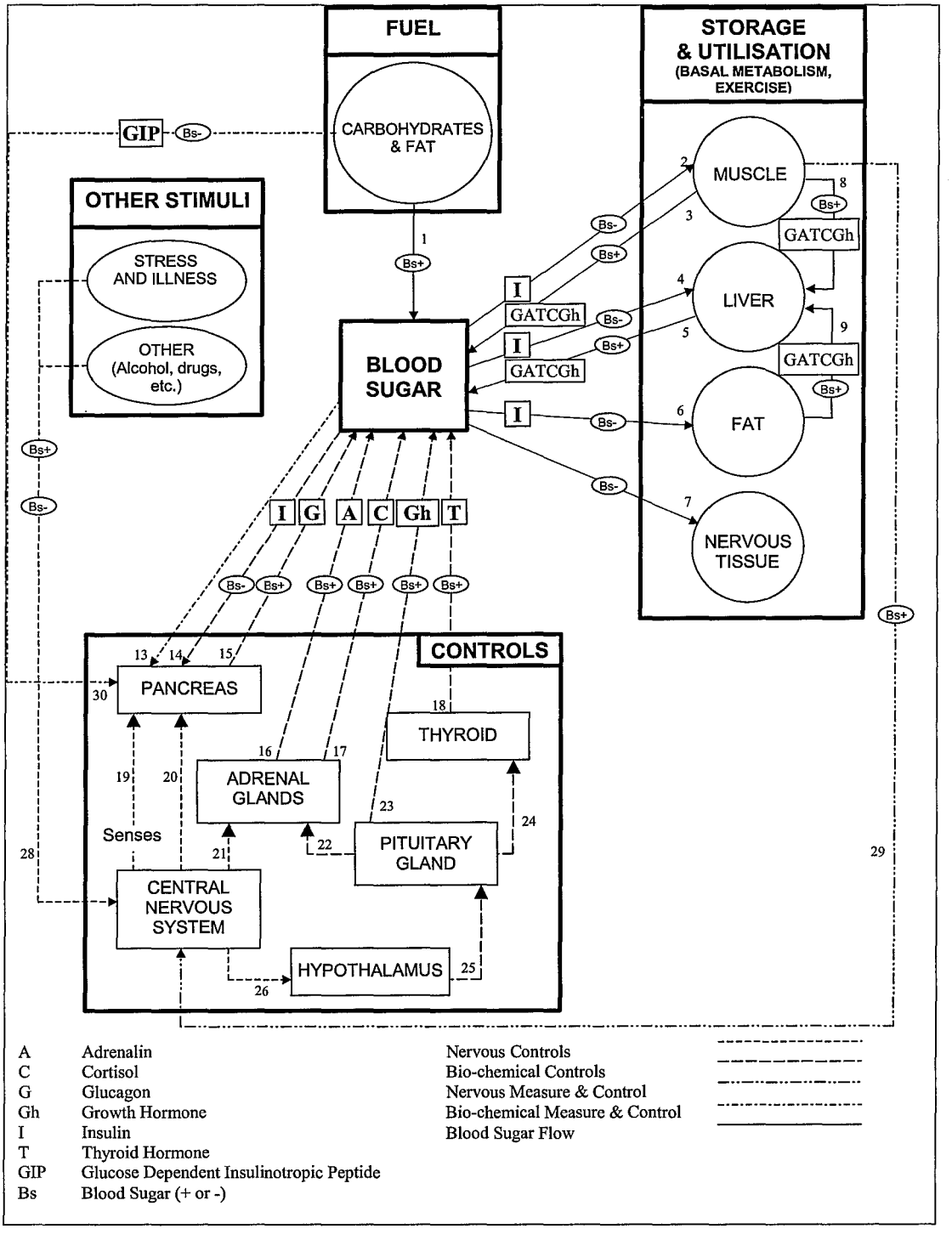

Figure 3.2 - Simplified schematic layout of the blood sugar control system in the human energy system.[14]

To calculate $f_{Expended}$ we can make use of the following procedure: After a suitable fasting period (6 hours) we inject a known amount of glucose directly into the blood stream of the subject, and we measure the maximum blood glucose response over time back to the basal level. After another suitable fasting period the subject should

then eat the same amount of pure glucose as was injected in the first section of the procedure. Again we measure the blood glucose response. We define f_{CHO} as the fractional areas under the curves (AUC) of the two measured responses. This relationship is shown in Equation 3.6.

$$f_{CHO} = \frac{AUC_{Ingested}}{AUC_{Injected}}$$

Equation 3.6

Now we use f_{CHO} substituted in Equation 3.7 to obtain $f_{Expended}$ [14].

$$f_{Expended} = 65 f_{CHO}$$

Equation 3.7

Equation 3.4 is however only applicable for a single exercise for which the energy expenditure is represented with $E_{Expended}$.

A possible procedure to measure $E_{Expended}$ is suggested: The method involves finding the precise amount of chemical energy released by the process of carbohydrate oxidation in the body. This requires measurement of both VO_2 (the amount of oxygen utilised in the body) and RQ (the respiratory quotient) of the athlete while he or she is exercising [52]. The exercise should be performed at event pace, but in a laboratory under controlled circumstances.

The values obtained from the measurements can then be substituted into Equation 3.7. This Equation was developed by Nishi in order to find $E_{Expended}$ and expressed it in Watt [52].

$$E_{Expended} = 352(0.23RQ + 0.77)VO_2 \text{ Watt}$$

Equation 3.8

Fortunately normal every-day living can also be seen as continuous exercise, and we can directly assume that the amount of energy expended during this continuous exercise is equal to the total amount of recommended energy throughout the day. This

is called the recommended daily energy allowance ($E_{Expended(RDA)}$), and was substituted for $E_{Expended}$ in Equation 3.3

3.3 INFLUENCE OF LONG ACTING INSULIN ON DIABETICS

Insulin is key to the control of the energy model. Without the insulin to provide counter control the model results in clipped values. Insulin injections result in a reduced blood glucose level, as the energy is absorbed into the tissue.

Figure 3.3 shows the plasma insulin concentration effect of each of three different long acting insulin variants. As seen, the closest insulin to the ideal, among the insulin variants shown, is Lantus®. Lantus is thus the best variant of insulin to function as basal insulin in Type 1 diabetics [14].

Correct long acting insulin dosage calculations are critical to correct short acting insulin dosage calculations, as the release effect of insulin into the blood stream is calculated for each time step throughout the solving process. As every type of insulin has a different response [53], it is critical that the correct type be used: Both in practice and in the simulation model.

As Lantus provides the best release profile it is advisable for people with Type 1 diabetes to make use of Lantus, as their long acting insulin.

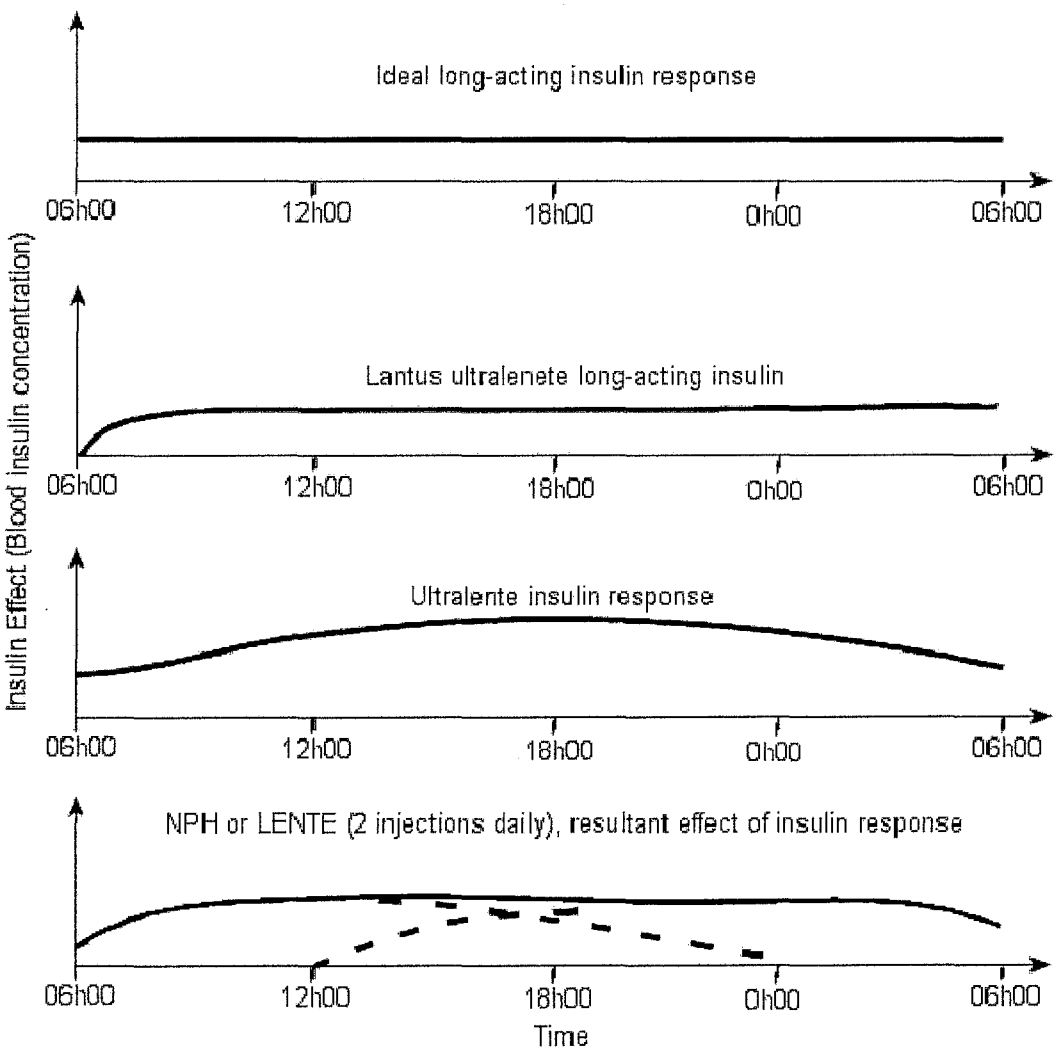

Figure 3.3 – Long-acting insulin profiles showing the difference in activity levels during the day.

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CHAPTER 4 VERIFICATION

This section gives an overview of the verification of the simulation model, with the data from the Wolever and Bolognesi trials.

4.1 VALIDATION WITH INDEPENDENT DATA

The model was verified with, among other data, experimental data provided by Dr. Wolever. In total 532 data points were recorded and compared.

Figure 4.1 shows a thick diagonal line representing the optimum accuracy. The more accurate the simulation values are, the closer to the line the data points are. Two thin lines adjacent to the optimum line represent the 1 mmol/L error band.

Accuracy of the simulations was defined as the amount of data points that fell within a certain error band when compared with the measured data. For a whole day the 1.0 mmol/L error band was considered acceptably accurate, and therefore the simulations regarded as 71% accurate, as calculated from the fraction of points within the error band.

Table 4.1 shows the Pearson's R^2-values for the datasets on which the model was tested [14]. The Pearson's R^2-values show the correlation between the normalised insulin response integral (AUC_I) and the CHO, GI, and ets values. The average R^2-values for the different methods decisively show ets to be the preferred insulin predictor.

Compartmental models can offer powerful tools for understanding, predicting and controlling processes. Figure 4.2 shows the observed blood glucose values shown against the predicted values obtained with a compartment model of glucose-insulin interaction [29],[63]. It is apparent that the error of this model leaves somewhat to be desired. This simple plot communicates a large volume of data to other researchers, about the model used by the AIDA system. The AIDA system is a computer program that started its life attempting to be an automated insulin dosage advisor [64],[65],[66].

As can be seen from Figure 4.2 there is a considerable scatter in the data. Data such as this led researchers to realise, some years ago, that such compartmental models were not reliable enough for making glycaemic prediction or thereby deriving any clinical therapeutic decisions for individual patients [67].

Table 4.1 – Pearson's R^2-values for correlations between CHO, GI and ets values.

Test subject	Mass of carbohydrates (CHO)	Glycaemic index (GI)	Equivalent teaspoons sugar (ets)
1	0.345	0.451	0.734
2	0.380	0.395	0.803
3	0.408	0.506	0.805
4	0.456	0.521	0.882
5	0.430	0.398	0.710
6	0.226	0.718	0.631
7	0.628	0.237	0.745
8	0.624	0.355	0.877
9	0.792	0.378	0.874
10	0.603	0.558	0.929
11	0.718	0.377	0.915
12	0.834	0.228	0.848
13	0.745	0.186	0.736
14	0.622	0.403	0.826
15	0.614	0.226	0.784
Average R^2	**0.562**	**0.396**	**0.807**
% standard deviation / average R^2	**32**	**36**	**10**

Figure 4.1 shows the measured blood glucose values against the values obtained via the simulation model developed by Botha [14].

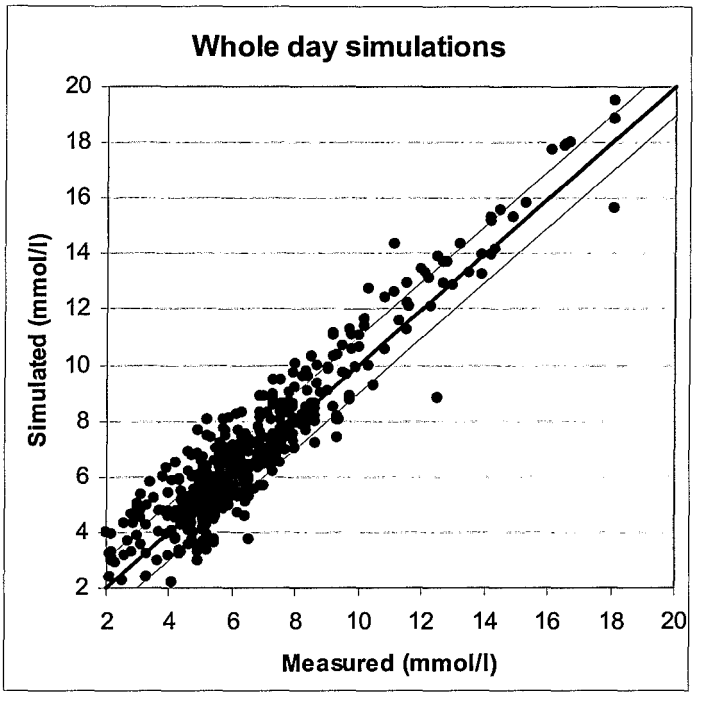

Figure 4.1 - Simulated versus measured blood sugar values using the ETS human energy simulation model.

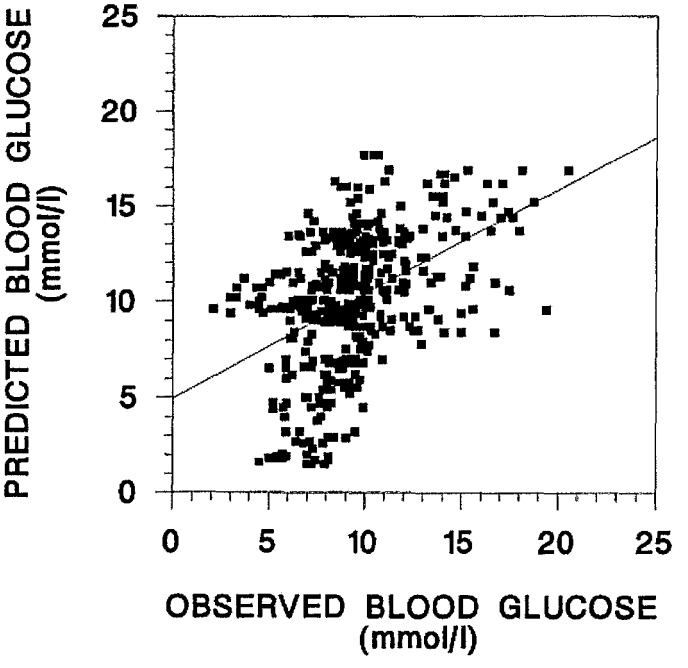

Figure 4.2 - Observed versus predicted blood glucose values for a compartment model of glucose-insulin interaction in diabetes [29],[63]

It is clear from the presented data that the new model is not only easier to use, and simpler, but more accurate as well. [14],[29],[63].

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CHAPTER 5 APPLICATION

We reviewed the human energy system in the previous section. In this section we will cover a few possible application of this new model.

5.1 POSSIBLE APPLICATIONS OF THIS NEW MODEL

By using the experiment previously described one can obtain characterization figures for each person, resulting in values useable for designer medication (f_I, f_{CHO}, etc).

Designer medication can be made possible by our ability to predict the exact influence of sugar on the person that has been characterised.

Health assistant software for a variety of electronics is also made possible by being able to configure each application for a specific person. Cellular phones, PDAs and computers are all rich environments for applications of this type.

5.2 CELLULAR PHONE

This section covers the design and implementation of a demonstration of concept application for a cellular phone.

A "diabetic companion" product can be developed to help the diabetic with his/her control regime. To reach the largest target group an application for a cellular phone was decided on. The product is a software implementation of an exercise and food logbook, in future coupled with an add-on blood glucose monitor, and the ets/human energy system simulation-model to predict blood glucose levels.

5.2.1 Design

Cellular phones are equipped with input and output interfaces sufficient for our purposes. Cellular phones are also quite powerful, and becoming increasingly so. The wide variety of cellular phones is ever increasing, and becoming even more affordable by the year. Resources available on the cellular phones are also becoming more accessible by applications, and easier to develop for.

There are a variety of software development kits provided by the cellular telephone manufacturers: Resulting in a more rapid time to market of applications. These

applications are also increasing in quality, as the testing of applications on more powerful systems is more rapid and thus more extensive than before.

A variety of systems can currently be integrated with cellular systems. Most cellular phones entering the market at the moment has an interpretive language called "Java for Micro Devices" (J2ME) included with the embedded operating system (OS). J2ME is a layer of software lying on top of the cellular phone OS, providing hooks into the lower levels of the cellular phone.

A cellular phone was selected with J2ME capabilities. A J2ME application was designed for the cellular phone, simulating the obtaining of input from the user, as well as the blood glucose monitor. The simulation model uses this data to predict and track the diabetic's blood glucose level. The application can be extended to implement safety features: Alerts, automated emergency help requests, etc.

This unit can be expanded, by constructing a small, modular, blood glucose monitor that clips on to the cellular phone. The largest components in current blood glucose monitors are their batteries and displays. By using these components of the cellular phone, the blood glucose monitor can be reduced to a unit smaller than 1cm across, 1cm high, and 4cm wide. This will enable the diabetic patient to carry along a blood glucose monitor that is much less obtrusive, and bulky, than current models.

For test purposes a Nokia cellular telephone, model 3410, was used. The telephone was configured for WAP, and the application downloaded via WAP.

5.2.2 Programming

The application was written in a basic text editor (conTEXT), and compiled with "Wireless toolkit" provided by SUN Microsystems. The "Wireless toolkit" was obtained from Sun Microsystem's website: http://java.sun.com/j2me/index.jsp

The cellular telephone makes use of over the air download capabilities to download the application to the cellular telephone. The cellular telephone's wireless application

protocol (WAP) configuration needed to be configured for access to the Internet with the WAP.

The application was designed along the lines of a basic tree structure, leading the user through menus to the goal of adding a specific foodstuff to their daily ets sum, and subtracting where exercise is involved.

The main menu is shown in Figure 5.4. The user can choose between

- Configuring the application, to characterise the application for him/her,
- Measuring their blood glucose level with a blood glucose monitor plugged into the serial port of the cellular telephone,
- Calculating their insulin dosage,
- Adding a food item to the amount of ets eaten,
- Or adding to the amount of daily exercise.

The totals can be manually changed, and a dosage can be calculated whenever needed. The dosage calculation makes use of the ets-intake, ets-expended, insulin sensitivity, ets-sensitivity, and target blood glucose level, to calculate a dosage. A negative dosage answer has to be converted into ets, which the user has to ingest, in order to reach the target blood glucose level.

5.2.3 Testing

The application was compiled into a package, resulting in two files: one ".jar" file (Java archive file), and one ".jad" file (Java application description file). These two files where uploaded to a web server, and the web server MIME types augmented to handle ".jad" and ".jar" files.

This was done by adding the file shown in Figure 5.1 to the root folder of the folder in which the ".jad" and ".jar" files where copied. The file is named ".htaccess", and was a plain text file.

```
AddType text/vnd.sun.j2me.app-descriptor jad
AddType application/java-archive jar
```

Figure 5.1- Listing of the .htaccess file used to configure the apache web server.

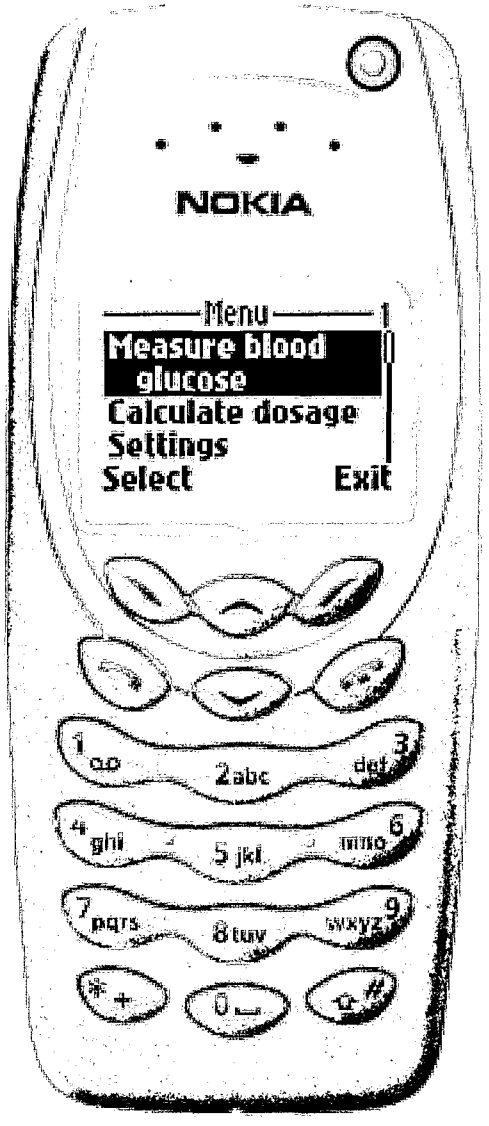

Figure 5.2- Image of the application running on a Nokia 3410 cellular telephone. The image shows the main menu.

Figure 5.2 to Figure 5.5 show examples of the menus and prompt screens of the application running on a Nokia 3410 cellular telephone.

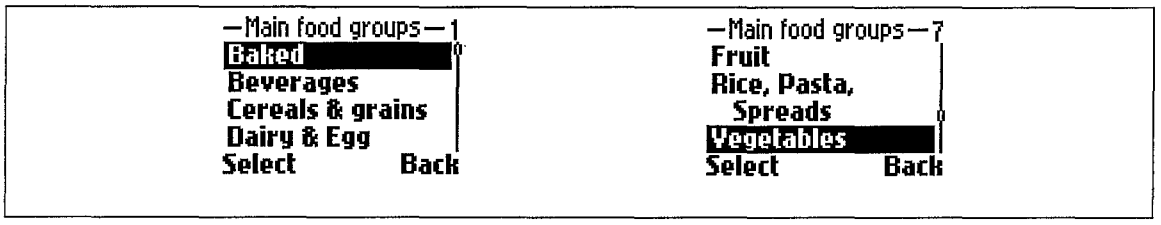

Figure 5.3- These images shows most of the main food groups submenu, as selected from the main menu.

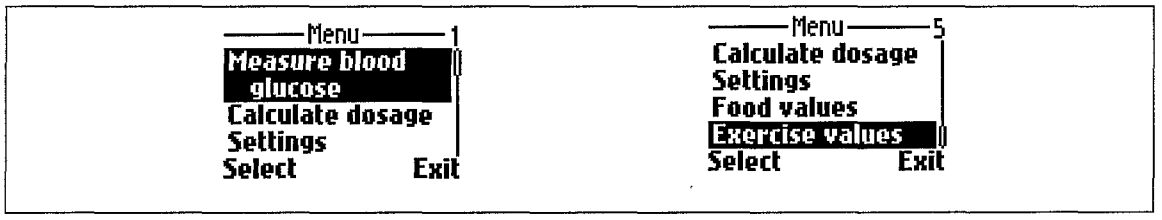

Figure 5.4- These images shows the main menu options.

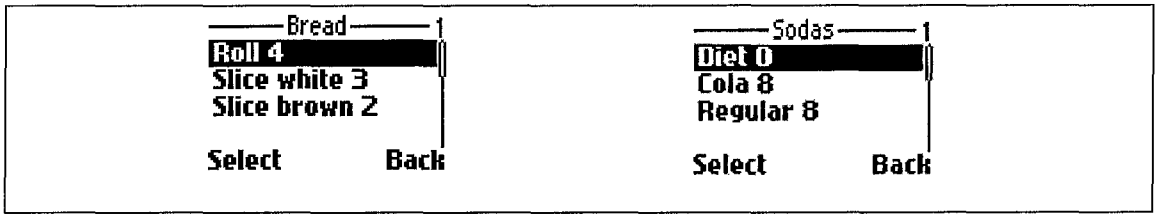

Figure 5.5- These images show examples of the food type submenus. The menu items show the ets value of each item.

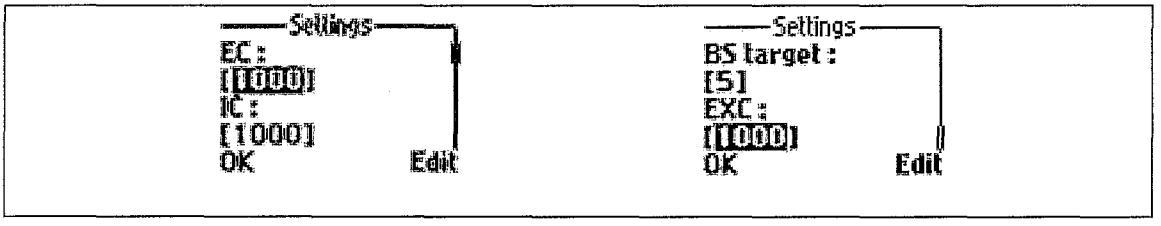

Figure 5.6 - These images show the screen for settings and configuration.The settings for insulin sensitivity, exercise sensitivity, ets-sensitivity, and target blood glucose level are shown.

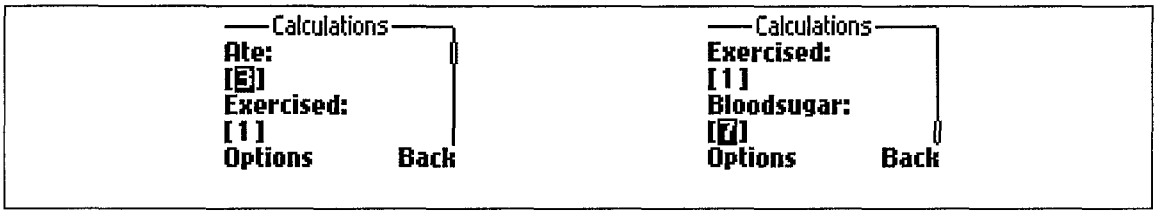

Figure 5.7- These images show the screen where the energy input, output, and blood glucose level can be customized.

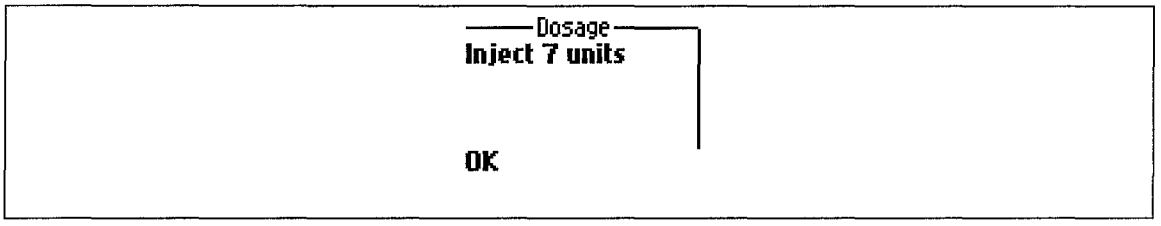

Figure 5.8 - This image shows the dosage calculation result, advising the patient to either inject the specified units of insulin, or eat the specified amount of ets.

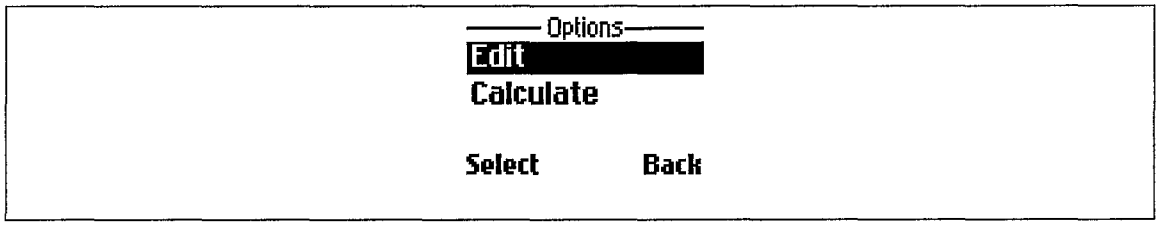

Figure 5.9 - This image shows the options given for the settings shown in Figure 5.6.

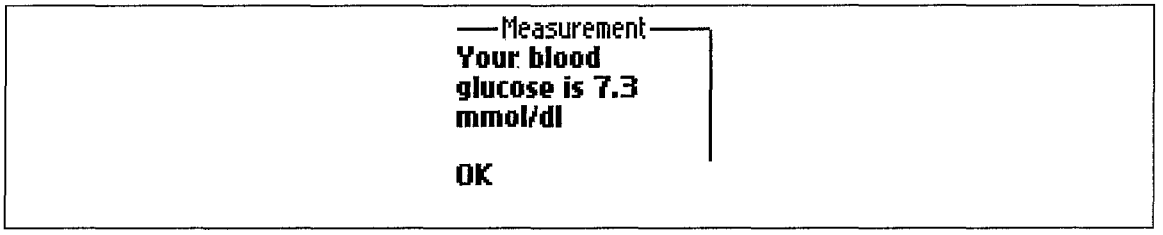

Figure 5.10 - This image shows a possible representation of a screen showing the blood glucose level measurement, as measured by conceptual modular blood glucose monitor.

The code for the demonstration application is presented in Appendix C.

5.2.4 Discussion

The application, coupled with a blood glucose monitor, will enable diabetics to monitor their blood glucose levels, and calculate their insulin dosages. The application on the cellular phone will enable diabetics to reduce the amount of blood glucose measurements currently needed for accurate control. This will have a multitude of long-term benefits, as the possible medical complications of diabetes are legion.

5.2.5 Obstacles to implementation

Current specifications for the J2ME implementation on the cellular phones only mention support for communication with the serial port of the cellular phone as an option. Very few implementations of Java on available cellular phones support serial port communications. None of Nokia's cellular phone models support this ability.

The specification provides for one method of connectivity, and the manufacturers immediately embraced the http connectivity option. This is mostly due to the fact that manufacturers have already developed the needed layers for http, providing the WAP ability of phones.

A test application was written to test the theoretical support for the serial port under the MIDP 2.0 specification. The Wireless Toolkit supports the complete MIDP 2.0 specification, as provided by Sun Microsystems. Using a null modem cable and an application that tests the serial port connectivity, a trial was run.

The trial was coded to purely receive characters from the serial port, and display them on the cellular telephone screen. HyperTerminal was used to transmit characters to the serial port, from another serial port. HyperTerminal is an application that comes with Microsoft Windows 98, and emulates different terminals. The theoretical viability of the concept was thus proven.

A possible workaround for this problem is dependent on the new Symbian OS being shipped with some new cellular phone models. Symbian OS is an operating system for small devices, and most manufacturers are actively using Symbian as the platform for their phones.

It is possible to program a Symbian application that communicates with the cellular phone serial port. Symbian applications will have access to all the hardware of the phones. The application can be adapted to enable a separate Java application to use the serial port, via the Symbian application. In effect a serial port "server" application can be programmed, for use by a Java "client".

Due to the relatively high prices associated with new phones the development of such a device was not attempted. The target market for a diabetic companion application needs to be able to easily, and inexpensively, obtain a platform for the application.

Current prices make the goal of developing an inexpensive glucose monitor, that connects to the cellular phone unobtainable, but market trends in electronic equipment points to an inexpensive model with the needed capabilities by the end of the year 2005 (at the latest).

5.2.6 Blood glucose monitor for cellular phone

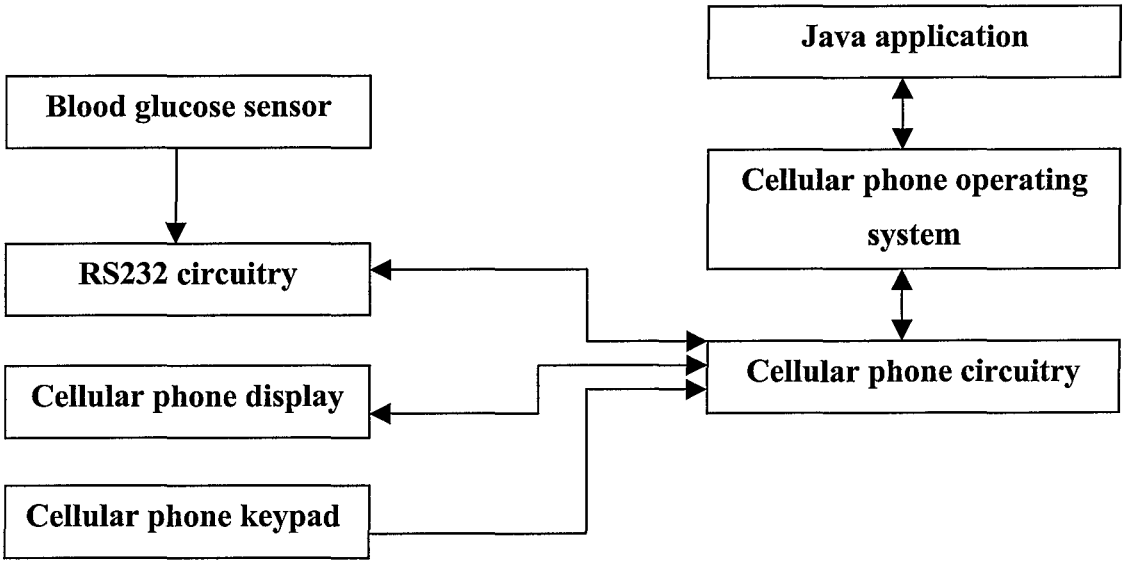

Figure 5.11 - Block diagram of cellular blood glucose monitor components.

Implementation of a modular blood glucose monitor, for use in cellular telephones, is a simple matter. A block diagram showing the main components of the system is shown in Figure 5.11. By making use of the cellular phone display and keypad, the blood glucose monitor system can be greatly reduced in size.

By coupling a glucose sensor with a basic RS232 circuit, for communication with the serial port of the cellular phone, a simple glucose monitor can be constructed. The

unit need not be intelligent, as all calculations and calibration can be done via the application on the cellular phone.

An advanced module can be created with a micro controller on the module itself, instead of using the resources of the cellular phone for data processing. It is even possible to integrate the actual simulation model, and predictive abilities of the model, on the glucose monitor itself, providing even better protection of the intellectual property involved in the monitor.

A blood glucose monitor for use with the cellular phone was not built, due to the lack of an interface between the monitor and the phone.

5.3 PDA

By implementing the system on a PDA the user has access to all of the advanced diagnostics and predictive functionality of the model, without having to use a simplified model.

Modern PDAs provide a powerful platform for calculation of model parameters, and solving of equations a normal person would find bothersome to calculate. PDAs provide a small and simple implementation of the model. The mobility of PDAs are crucial, as patients are active, and would not make frequent use of a solution that is invasive, and additional trouble.

The PDA implements a basic logbook of food eaten, exercise, and insulin injected. Using this data, the model calculates the predicted blood glucose levels, and can advise an insulin dosage at the needed time, to maximise the blood glucose control.

The logbook application should make use of a general menu structure, and a prompting flow of questions to obtain all the needed data. Ease of use is critical, as well as accessibility, as diabetic patients have a wide variety of ailments. The most obvious in this case would be the degradation of eyesight [6],[75], prompting the designer to make use of large, easy to read fonts where applicable.

5.4 BEDSIDE GLUCOSE MONITORING AND CONTROL

A recent study has shown that the precise control of a diabetic patient's blood sugar in a critical surgery unit can improve a person's chances of survival and rapid recovery [13]. This points to a reduction of surgery deaths where active intensive glycaemic control is exercised. The impact of this result is even larger when one considers that hypoglycaemia is also a problem in non-diabetic surgery patients.

By using an automated glucose monitoring and control system, the patient's blood glucose levels can be precisely controlled. Risk of deep sternal wound infections after coronary bypass graft surgery decreased by 66% when insulin was given to keep the glucose levels between 150mg/dL and 200mg/dL.

Van den Berghe and colleagues also demonstrated that intensive insulin therapy (<110mg/dL levels) in patients fed by total parenteral nutrition (TPN), combined parenteral and enteral, or total enteral feeding, reduced overall ICU mortality from 8% to 4.6%, and from 20.2% to 10.6% in patients requiring more than 5 days of intensive care [74].

This unit would make use of a direct, continuous, monitoring of the patient's blood glucose levels, coupled with an intravenous unit for injecting the needed hormones and glucose for direct control of the patient's blood glucose levels.

Using the proposed model we can predict and control the patient's blood glucose levels by injecting the needed hormones where applicable.

The implementation of this unit is subject to a method of real-time monitoring of a patient's blood glucose levels. This method needs to be as non-invasive as possible, to reduce the trauma to the patient.

The unit can make use of a predefined protocol to test the patient's ets-sensitivity and insulin sensitivity, after which it can actively take over the control of the blood glucose levels of the patient.

This unit has a large array of possible additional functions as well. Real time monitoring of the blood glucose levels of the patient can be coupled with remote monitoring stations, and alarms set for specific levels.

Appendix B shows the complete patent for a unit that function as a bedside glucose monitor and controller.

5.5 REFERENCES

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CHAPTER 6 CONCLUSION

The chapter provides a short discussion on the important aspects of the study, with some recommendations for future work

6.1 DISCUSSION

The model has been proven to be more effective than current methods, providing researchers with the tools they need to move one step closer to complete human system simulation: The holy grail of medicine.

The potential for such a complete simulation is truly gigantic. Rapid prototyping and medical testing, easy diagnosis of diseases, and rapid development of cures are all easier with such a model.

It should be noted that had the equations been derived in a different fashion using the Insulin Index (II) instead of the GI of the foods, even better accuracies could have been expected. This is especially true for mixed meals containing a high percentage of protein and / or fat. GI was however used, due to a larger availability of published values. By employing GI the initial usefulness of the ets concept for everyday application will be enhanced.

The model presented was easily implemented as a cellular phone application, and was easily accessible to patients: Users need only download the application from the Internet. The application is only cursory, and can be further expanded to facilitate a wider variety of functions. The application can be further adapted to predict long-term blood glucose effects, and plot the blood glucose levels of the user.

Commercial potential of such products is large as well: The reader is referred to the size of the market segment (Section 1.2.2). The conclusion is thus reached that further development in this field would not only be lucrative, but also add to our medical knowledge. Improved models would invariably follow, and lead the field for further simulation models of other human systems.

The market segment with cardiovascular diseases immediately comes to mind, providing the field for cholesterol and related systems research.

6.2 CONCLUSION

The model developed by Botha is functional and more accurate than the other models reviewed. Errors within compartmental models are larger than those obtained via Botha's model.

This model was simpler to implement, proving it to be a more useful tool. An implementation was incorporated in a product which is easy accessible to patients. The model was transparently implemented. Good marketing of diabetic products is very important, as a large problem within the diabetic community is a lack of understanding, and knowledge, of the disease and its complications.

The model lends itself well to implementations on small devices, and there is a large addition of value to the community, even with simplified implementations of the model.

There is a lack of interest within the community in research regarding diabetes. This lack of interest has the result that new methods of diabetes management have a delayed, and reduced, impact. It is important for people with diabetes to be able to lead a normal life, uncomplicated by the impact of diabetes. This product moves the diabetic one step closer to this goal.

The bedside glucose controller has an especially important impact. The risks involved in surgery are always high, and any reduction in this risk is invaluable. No surgeon can afford to overlook equipment that will reduce the mortality rate in their patients by more than 60%. There is great potential in equipment along this line.

APPENDIX A

PATENT: CELLULAR PHONE BLOOD GLUCOSE MEASURING DEVICE

BLOOD GLUCOSE MONITOR FOR MOBILE COMMUNICATION DEVICE

FIELD OF INVENTION

This invention relates to a portable communication device including a means for capturing/measuring blood glucose levels of said person and output means for displaying the blood glucose level. Said measuring means can either be implemented in the form of a blood glucose monitor built into and integrated into said mobile communication device (i.e. cellular phone) or be a separate plug in device able of communicating said blood glucose level measured to said mobile communication device. Said portable communication device may also comprise of a processing means controlled by downloadable software to process said measured blood glucose level, manipulate data, store data, calculate values from said measurement and previous measurements.

In this specification, the term 'device' refers to any portable/mobile communication device that is able to support a communication connection with a custom designed measuring means for measuring blood glucose levels.

In this specification, the term 'system' refers to the add-on measuring means of the device. This measuring means incorporates a device for measuring blood glucose with a software application executed by the software platform of the device.

OBJECTS AND ADVANTAGES OF THE INVENTION

The main advantage of this invention is the integration of said mobile communication device with said measuring means for measuring blood glucose level. Therefore said user will have the added convenience of only carrying a single mobile communication device or mobile communication device with a small plug-in accessory. The development cost of said device can be reduced by using internal hardware of said mobile communication device for part of the processing, storing and output of any relevant data.

SUMMARY

This invention relates to a portable communication device including a means for capturing/measuring blood glucose levels of said person and output means for issuing the blood glucose level. Said measuring means can either be implemented in the form of a blood glucose monitor built into and integrated into said mobile communication device (i.e. cellular phone) or be a separate plug-in device able of communicating said blood glucose level measured to said mobile communication device. Said portable communication device may also comprise of a processing means controlled by downloadable software to process said measured blood glucose level, manipulate data, store data, calculate values from said measurement and previous measurements.

BRIEF DESCRIPTION OF DRAWINGS

Figure 1a shows the configuration of the device for blood glucose sensing being fully integrated into said mobile communication device.

Figure 1b shows the configuration of the device for blood glucose sensing being implemented as a separate plug in device to the mobile communication device.

Figure 2 shows the possible hardware block diagram indicating the communication of the measuring means (blood glucose sensing device) with the mobile communication device.

DETAILED DESCRIPTION

This invention comprises of a measuring means (blood glucose sensor) being integrated into a mobile communication device. Said measuring means can be fully integrated into a mobile communication device (Figure 1a) to form a new mobile communication device with a built in blood glucose level sensing device. It can also be implemented as a separate plug in device (Figure 1b) able of measuring blood glucose level and communicating measurement data through to said mobile communication device.

Figure 1a shows the blood glucose level sensing device being fully integrated into mobile communication device. A possible layout is shown is Figure 1a with a slot (3) in said mobile communication device (2) for receiving a blood glucose test strip (4). After the blood glucose measurement has been completed the output means of the mobile communication device is used to indicate the measured data and also any possible relevant data that seems necessary.

Figure 1b shows the external plug-in device configuration for integrating the device for blood glucose sensing with the mobile communication device. External plug in device (6) containing said blood glucose level sensor receives a blood glucose test strip (4) through test strip slot (3) and communicate measured data to mobile communication device (5) through the data ports (7) of said mobile communication device.

The system can be activated by either pressing a button on the device, selecting the software application from the menu of the mobile communication device, inserting a test strip (4) into the Glucose sensor slot (3) or by plugging an external unit that measures blood glucose levels into the data port of the phone/device.

Measured data can be processed and indicated on the output means by a software application controlling the processing means of the mobile communication device and/or the device for sensing the blood glucose level.

Relevant data can be logged over time, date and other data in the storage means of the mobile communication device and/or the device for sensing the blood glucose level.

Relevant data can be communicated to other communication devices and or equipment. Measured data logged with time, date and other data in the storage means of the mobile communication device and/or the device for sensing the blood glucose level can be communicated through by any communication means of the mobile communication device to other devices.

Figure 2 shows the possible hardware block diagram indicating the communication of the measuring means (blood glucose sensing device) with the hardware components of the mobile communication device.

CLAIMS

A portable communication device including capturing means for capturing data relating to the blood glucose levels of a user; and output means for issuing the said data.

A portable communication device according to claim 1 wherein the capturing means include measuring means for measuring the said blood glucose level (BGL) of said person.

A portable communication device according to any of the preceding claims wherein the capturing means is selected from the group consisting of either
a portable communication device with blood glucose monitor built in and integrated into the portable communication device or,
a plug-in blood glucose monitor device for a mobile communication device or accessory for mobile communication device able of communicating and functioning with mobile communication device.

A portable communication device or portable communication device accessory according to any of the preceding claims which includes a processing means and wherein the capturing device includes an input means for entering the said data into the processing means.

A portable communication device according to any one of the preceding claims which is in the form a cellular phone.

A portable communication device according to any one of the preceding claims which is in the form a mobile communication device.

A portable communication device according to any one of the preceding claims wherein the output means is selected from the group consisting of on-screen display, printer output, wireless communication output, and electric wire link output.

A portable communication device according to any one of the preceding claims wherein the processing means is capable of processing said signals measured by said measuring means and

communicating processed data to said portable communication device for storage, further processing, communication with other devices or output of data.

ABSTRACT

This invention relates to a portable communication device including a means for capturing/measuring blood glucose levels of said person and output means for issuing the blood glucose level. Said measuring means can either be implemented in the form of a blood glucose monitor built into and integrated into said mobile communication device (i.e. cellular phone) or be a separate plug in device able of communicating said blood glucose level measured to said mobile communication device. Said portable communication device may also comprise of a processing means controlled by downloadable software to process said measured blood glucose level, manipulate data, store data, calculate values from said measurement and previous measurements.

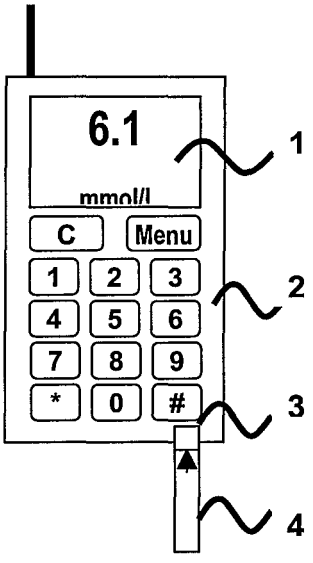


Figure 1(a)

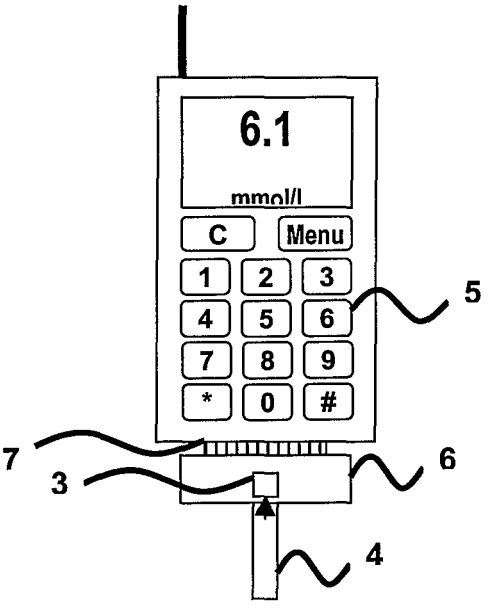


Figure 1(b)

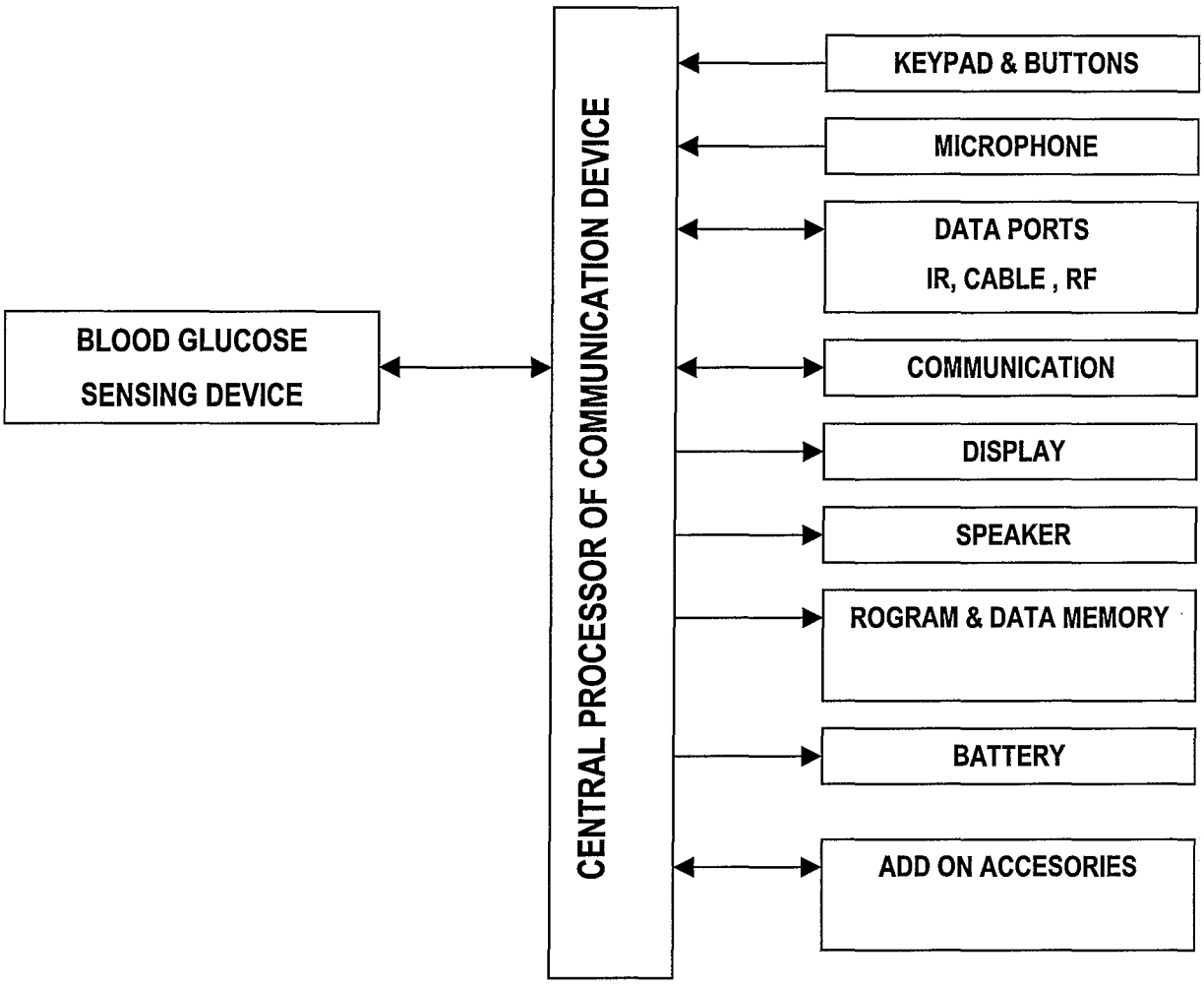

BLOOD GLUCOSE
SENSING DEVICE
CENTRAL PROCESSOR OF COMMUNICATION DEVICE
KEYPAD & BUTTONS
MICROPHONE
DATA PORTS
IR, CABLE , RF
COMMUNICATION
DISPLAY
SPEAKER
ROGRAM & DATA MEMORY
BATTERY
ADD ON ACCESORIES

Figure 2

APPENDIX B

PATENT: BEDSIDE GLUCOSE MONITORING DEVICE

BEDSIDE BLOOD GLUCOSE CONTROLLER

FIELD OF INVENTION

This invention relates to the fields of medical care. It relates in particular to a system able of monitoring and controlling the blood glucose concentration of patients treated.

In this specification, the term Equivalent Teaspoon Sugar (ETS) means an energy unit quantifying energy in food, wherein:

$$ETS = \frac{E_{CHO}}{E_{teaspoon\ \ sugar}} = \frac{GI.m_{CHO}}{325}$$

And wherein:

E_{CHO}	is the energy content available from carbohydrates in the food being quantified and is measured in KJ or kCal.
$E_{teaspoon\ sugar}$	is the energy content in a teaspoon sugar namely 20kCal or 84KJ.
GI	is the Glyceamic Index of the food being quantified.
m_{CHO}	is the mass of the carbohydrate content measured in grams of the food being quantified.
ETS	is energy content of the food being quantified in equivalent teaspoons sugar.

Furthermore, in this specification, the term insulin includes within its scope any blood sugar regulatory substance.

DESCRIPTION OF PRIOR ART

Said invention will control enteral feeding substance rate and also control blood glucose level by the administration of insulin and/or glucose (or other sugar related substance) to a person. The blood glucose level will make use of control algorithms to lower blood glucose levels using insulin and glucose to raise low blood glucose levels of patients. If said patient are not able to eat said invention will control the rate of enteral feeding to supply said person with sufficient nutritional substances to cater for the person's energy requirements. Said device will be of great value to treat diabetics while unconscious in hospital.

The ETS concept is the fundamental principal used by this device. This device is used to calculate the corrective action needed by Type I diabetics to control their blood glucose levels. ETS is a new generic energy unit. ETS is the abbreviation for equivalent teaspoons sugar. This energy unit can be used to quantify energy in food. By quantifying food in ETS the effect that food intake will have on the blood glucose level of a specific person can be predicted. The blood sugar response after a meal will be predicted by using the amount of ETS in the meal and the ETS sensitivity of the diabetic. This is a very practical method to calculate the appropriate insulin dosage for type I diabetics. In general ETS is an innovative energy unit that can be used to relate different energy processes and systems in the human body to each other.

Introduction to the ETS concept

The present invention will be used to configure several products for the individual patient. The primary objective of this invention is to calculate ETS and insulin sensitivities. In order to understand why these measurements are necessary the derivation of the ETS concept is included below.

Insulin response is inter alia influenced by ingested food1. A practical relationship between insulin response and food is important for diabetics as they either do not produce enough insulin or cannot utilise it efficiently2.

Well known methods for predicting insulin response due to food ingestion are CHO counting7 and the glycaemic index8 (GI). However, these methods do not always give

the correct response9,10 and many people find them difficult to use11. Furthermore, these methods do not specifically account for differences between people.

A user-friendly method is theoretically derived. It uses an easy-to-understand measuring unit which is called equivalent teaspoons sugar or ETS. It will be shown that ETS predicts insulin response more accurately than the other two well-known methods. The insulin / ETS equation also includes an efficiency factor called f_{AUCI} which accounts for physiological differences between people. f_{AUCI} could help explain why some people are more prone to Type II diabetes, find it difficult to loose weight and why some athletes become hypoglycaemic when others do not.

The quality of insulin predictions for the CHO and the GI methods are first examined using measurements by Lee and Wolever12. These measurements give insulin response curves for different healthy test subjects ingesting different amounts of CHO (0 to 100 grams) with varying GI values (23 to 100).

The time integrals ($\int BI(t)dt$) of the Lee and Wolever blood insulin (BI) response curves for one subject are normalised and plotted against the amount of CHO consumed (Figure 2) and against the GI (Figure 3) of the ingested foods. Pearson's R^2-values[13] were calculated for linearised trend fits through the plotted data. The R^2-values for the CHO and the GI methods were 0.603 and 0.558 respectively. For the CHO method the worst spread is at 50g CHO, namely a factor 12, while for GI at 65 the factor is close to three.

The need for a better insulin prediction method for CHO is obvious. A successful attempt was by Wolever and Bolognesi[10]. They developed an empirical model based on measurements in seven healthy subjects. Unfortunately the resulting non-linear empirical equations have not found popular use, as they are difficult to use by our target market.

We now propose the easy-to-use ETS method. It is theoretically derived using energy balance techniques[14], namely the ingested CHO / blood sugar energy balance. A

theoretical approach is preferred to an empirical one as theory *inter alia* leads to better insight. The simple linear link between insulin response and ETS is given by Equation (11) and is derived in the methods section.

Let us now investigate the quality of insulin predictions by the ETS method. The Lee and Wolever[12] measurements are used again for the same test subject as in Figures 3a and 3b. The results are given in Figure 4. The linear trend line for the ETS method (Equation (11)) yields an R^2-value of 0.929 which is significantly better than those of the other methods.

More test subjects using the same procedure as for the single subject are investigated. The full dataset of Lee and Wolever[12] as well as another dataset from Wolever and Bolognesi[10] are used. Correlation coefficients for data of the 15 test subjects are presented in Table 1. The average R^2-values for the different methods show ETS to be the preferred insulin predictor.

It should be noted that had the equations been derived in a different fashion using the Insulin Index (II) instead of the GI, even better accuracies are expected. This is especially true for mixed meals containing a high percentage of protein and / or fat. We however used GI due to better availability of published values[15]. This will enhance the initial usefulness of the ETS concept. However, in a future paper we will discuss a less expensive method to measure the II which could quicken the development of II and therefore ETS databases.

ETS was developed as a reference unit because it is an easy concept to comprehend and to use. Firstly, *Equation (11) shows that less ETS in a meal always leads to less insulin, making food and meal choices very easy.* Secondly, ETS values for typical foods and serving sizes are usually less than 10 e.g. tomato = 0.5_{ETS}, can of soda = 7_{ETS}, apple = 2.5_{ETS}. Numbers less than 10 are easy to grasp. Thirdly, in a mixed meal of high CHO content the ETS values of the individual constituents can simply be

added to arrive at the total ETS value for the full meal. Fourthly, it is easy to visualise a teaspoon full of sugar which makes it a practical reference. Fifthly, we will show in a future article that for Type 1 diabetics the numerical ETS value of an ingested meal corresponds remarkable well with the numerical amount of insulin dosage required.

The exact relationship between ETS and insulin is dependant on the physiological characteristics of a person (f_{AUCI} in Equation (11)). If AUC is converted to insulin units it is found that for many diabetics the relevant factor is close to one, which results in an easy-to-remember one unit of short-acting insulin needed for one ETS ingested. This makes diabetic glycaemic management easier than before. Better accuracy, as previously described, and easier application will have an important impact on diabetics.

Figure 3b depicts the spread in f_{AUCI} between the healthy individuals measured in the Wolever, Lee and Bolognesi[10,12] trials. These sensitivity factors can be measured and the procedure will be discussed in a later paper.

We hypothesize that the importance of this sensitivity for endurance events was illustrated by the world's most consistently fast marathoner of all times – Gert Thys[3]. This is interpreted by the measurements by Noakes[3] to suggest that Thys has a very high f_{AUCI} which results in high insulin secretion after large CHO ingestion.

The hypothesis is that this leads to a switch from blood sugar utilisation to storage with resulting hypoglycaemia. Gert Thys only became very successful after he started to consume small amounts of ETS throughout the race with resulting small insulin response[3]. Many people have a similar problems as Gert Thys. We find that our blood sugar is low after a large CHO ingestion. The reason could also be a high f_{AUCI}.

The f_{AUCI} sensitivity is also important for weight watchers, those having CVD and certain cancers as high insulin concentrations and insulin resistance are prevalent in

them[5,6,7]. By accounting for f_{AUCI} (and similar factors for the protein and fat cycles) more correct diets could be designed for a specific patient. It is also hypothesized that through "self preservation" f_{AUCI} will increase when a person are on a "fasting" diet to ensure maximum storage. This can make weight loss a little more difficult than one would expect.

It has also not escaped our notice that f_{AUCI} could help explain why people from poor developing nations are prone to Type 2 diabetes when they change over to high caloric western diets with high ETS (high CHO and high GI). With an evolutionary high f_{AUCI} to ensure maximum storing efficiency they "over react" to the high ETS, resulting in hyperinsulinaemia, weight gain, insulin resistance and eventually Type II diabetes.

The impact of such a predictor as ETS on diabetics, endurance sportspeople, weight watchers and those with CVD and certain cancers or those who want to live a healthy life is obvious. In general all these interest groups strive to minimise insulin response. *Equation (11) shows that the CHO containing food with the smallest ETS will always lead to the smallest insulin response making food choices easy from now on.*

Methods

Wolever & Bolognesi[10] and Lee & Wolever[12] trials. Fifteen healthy patients ingested eight different foods with varying amounts of CHO (0, 25, 50, 75 and 100 grams). The ingested foods and their published GI values[16] were the following: fructose = 23, barley = 25, spaghetti = 41, glucose / fructose mix = 61.5, sucrose = 65, bread = 70, potato = 83 and glucose = 100. The full methods are described in references 10 and 12. Our time integrals ($\int BI(t)dt$) for plasma insulin values (minus the baseline insulin) are similar to the "Area Under the Curve (AUC)" described in reference 10 and 12.

Derivation of equations. Only CHO in a meal is directly converted into blood sugar during digestion[17]. The "*conversion potential*" (η_{CHO}) of CHO estimates the amount of energy which is converted into blood sugar by a typical person. All losses, including energy needed for digestion, incomplete digestion, etc. are accounted for in η_{CHO}. This value can be measured (as discussed later) and is a property of the meal. It depends on many factors including the content of dietary fibre, fat and protein in the meal.

Energy from CHO which can be utilised by a person (E_{CHO}) in the form of blood sugar is then a function of the mass of CHO in the meal (m_{CHO}), the full energy content per mass of the CHO (k_{CHO}) measured outside the body by means of a bomb calorimeter[18] and η_{CHO} of the meal which accounts for how efficient the energy can be extracted inside the body.

Note that historically it was incorrectly assumed in diet planning that the energy content (k_{CHO}) of CHO measured outside the body by a different process (bomb calorimeter) was fully utilised inside the body through another process, namely digestion and absorption. (The same mistake is also made with protein and fat.) The correct equation for CHO energy in a meal which can be utilised inside the body (E_{CHO}) is shown by:

$$E_{CHO} = \eta_{CHO} m_{CHO} k_{CHO} . \quad (1)$$

Efficiency towards converting the effective CHO from a meal (Equation (1)) into blood sugar varies between different people. We represent this personalised CHO efficiency by the term f_{CHO}. (Remember that f_{CHO} is a function of a specific person while η_{CHO} is a function of a meal.) The total energy absorbed in the blood for a specific person is then given by

$$E_{Absorb} = f_{CHO}E_{CHO} = f_{CHO}\eta_{CHO}m_{CHO}k_{CHO}. \quad (2)$$

As E_{Absorb} is the CHO energy converted into blood sugar for a specific person, E_{Absorb} can also be found by means of blood sugar measurements for that specific person. First we have to integrate the response curve for blood sugar concentration ($\int BS(t)dt$) above basal level from time of consumption back to basal level. This time elapsed is described by Δt. The elapsed time is specific to a person's blood sugar response and is *inter alia* dependant on a person's insulin secretion rate and sensitivity, etc.

The integral divided by Δt now gives us the average concentration of blood sugar. We then need to multiply the concentration by the total volume of blood of the person (Vol) to find the total amount of glucose (or energy) in the blood. Finally, E_{Absorb} is then found by multiplying with k_{CHO}, the energy value of CHO.

$$E_{Absorb} = \frac{\int_{t=ingestion}^{t=basal} BS(t)dt}{\Delta t} Vol.k_{CHO} \quad (3)$$

Let us now substitute Equation (3) into Equation (2) to find

$$\frac{\int_{t=ingestion}^{t=basal} BS(t)dt}{\Delta t} = \frac{f_{CHO}\eta_{CHO}m_{CHO}k_{CHO}}{Vol.k_{CHO}}. \quad (4)$$

For a typical balanced meal containing CHO there is a direct relationship between blood sugar response ($\int BS(t)dt$) and the insulin response[19] ($\int BI(t)dt$). Although the best fit to this relationship is not linear[12], a linear relationship with an R^2-value of 0.963 was found through measurements by Lee and Wolever[12] using meals consisting

of mostly CHO. This is deemed acceptable, especially if we want to keep the equations practical. Let us write this fact in equation form:

$$\int_{t=ingestion}^{t=basal} BI(t)dt = f_{IBS} \int_{t=ingestion}^{t=basal} BS(t)dt \quad (5)$$

The insulin / blood sugar relationship varies from one person to the next and we describe this person specific characteristic with the blood insulin factor, f_{IBS}. (IBS is an abbreviation for **I**nsulin **B**lood **S**ugar relationship.)

If we substitute Equation (5) into Equation (4) we find Equation (6) which describes the person specific insulin response to ingested food. (The k_{CHO} values from Equation (4) cancelled each other out.)

$$\frac{\int_{t=ingestion}^{t=basal} BI(t)dt}{\Delta t} = \frac{f_{IBS} f_{CHO} \eta_{CHO} m_{CHO}}{Vol} \quad (6)$$

Equation (6) cannot easily be used by our target market. Let us simplify it. Instead of using m_{CHO} and η_{CHO} in Equation (6) for the meals, let us use an easier measurement unit. We propose that effective CHO in foods and meals be expressed in **e**quivalent **t**easpoons **s**ugar (ETS).

Let us now investigate the properties of a teaspoon full of sugar containing 5g of CHO. What is the η_{CHO} of sugar? We hypothesise that the glycaemic index of a specific CHO (GI_{CHO}) approximates this value. Although the official definition[16] of GI_{CHO} is "*rate of CHO digestion*", GI_{CHO} has more value to us.

GI_{CHO} represents the total amount of blood sugar which can be converted from a meal containing 50g CHO divided by the amount of blood sugar converted from 50g glucose by a specific person. As blood sugar is glucose we can safely assume glucose to have a η_{CHO} of close to 100%. This means that the GI_{CHO} of any meal, referenced to glucose, could be a useful predictor of η_{CHO} of that meal.

Sugar therefore has a η_{CHO} of 65% found from its GI_{CHO} value of 65 using the glucose reference[16]. Substituting these values into Equation (1) leads to Equation (7) for total available energy in a teaspoon sugar:

$$E_{teaspoon\ \ sugar} = GI_{sugar} m_{teaspoon\ \ sugar} k_{CHO} = (65)(5) k_{CHO} = 325 k_{CHO}. \tag{7}$$

Let us relate the effective energy for any CHO back to a teaspoon of sugar. We divide Equation (1) for any meal (substituting η_{CHO} with GI_{CHO} for that meal) by Equation (7) ($E_{teaspoon\ \ sugar} = 325 k_{CHO}$) for one teaspoon sugar to find the **e**quivalent **t**easpoon **s**ugar (ETS) for that meal, as shown in Equation (8)

$$ETS = \frac{E_{CHO}}{E_{teaspoon\ \ sugar}} = \frac{\eta_{CHO} m_{CHO} k_{CHO}}{325 k_{CHO}} = \frac{\eta_{CHO} m_{CHO}}{325} = \frac{GI_{CHO} m_{CHO}}{325}. \tag{8}$$

It can be shown that GI_{CHO} can be substituted with II to arrive at a more accurate value of ETS. The assumptions of linearity between insulin and blood sugar response as well as high CHO content are then not needed. It should also be noted that the ETS / insulin relationship is linear to much higher ETS values (approximately three time higher) than the ETS / blood sugar relationship.

Now that we have established the equation for ETS let us further simplify Equation (6). If we substitute Equation (8) into Equation (6) and substitute the term **A**rea **U**nder the **C**urve (AUC_I) for the integral, we find

$$\frac{\int_{t=ingestion}^{t=basal} BI(t)dt}{\Delta t} = \frac{AUC_I}{\Delta t} = \frac{f_{IBS} f_{CHO}}{Vol} GI_{CHO} m_{CHO} = \frac{f_{IBS} f_{CHO}}{Vol} 325\ ETS$$

$$\therefore \frac{AUC_I}{\Delta t} = \frac{325 f_{IBS} f_{CHO}}{Vol}\ ETS \tag{9}$$

By defining a new person specific factor, f_{AUCI}, we can further simplify Equation (9). f_{AUCI} accounts for the person specific factors f_{CHO}, f_{IBS}, Vol and Δt. ($AUCI$ is an abbreviation for "**A**rea **U**nder the **C**urve of **I**nsulin response".) f_{AUCI}, is *inter alia* a function of CHO metabolic efficiency, size, insulin resistance which depends on

fitness, body mass index (BMI), age, etc. of a person. Its equation is given below, although it is easier to measure it by using Equation (11).

$$f_{AUCI} = \frac{325 f_{IBS} f_{CHO} \Delta t}{Vol} \tag{10}$$

Substituting Equations (10) into (9) yields the relationship between measured insulin response (AUC_I) and ingested food represented by ETS

$$\boxed{AUC_I = f_{AUCI} . ETS} \tag{11}$$

where AUC_I is the integrated insulin response, f_{AUCI} is a measurable function of the individual and ETS is a measurable function of the meal and is published for most foods[20] or can be calculated using Equation (8). In this study we verified the simple linear Equation (11), derived from first order principals, using measurements by Lee, Wolever and Bolognesi[10,11].

OBJECTS AND ADVANTAGES OF THE INVENTION

For people undergoing surgery it is imperative that the blood glucose levels of the patient be monitored and strictly controlled. Due to hyperglycaemia and insulin resistance being common in critically ill patients, even if they have no previous history of diabetes, insulin therapy is an integral part of effective medical care. It has been shown that intensive insulin therapy reduces morbidity, death from multiple-organ failure, bacteraemia, renal failure, red cell transfusions, polyneuropathy, mechanical ventilation, and surgical intensive care unit length of stay by 75%. Advantages thus include improved risk management for patients, and improved treatment efficiency, resulting in cost savings and quality of life for patients by reducing complications.

Said invention will aim to control the blood glucose level of the said patient by the administration of insulin and/or glucose. This will prevent said patient to enter into a hypoglycaemic or hyperglycaemic state. Said invention will also be able to control the enteral feeding rate to suit said patient's energy requirements.

It is important for the medical practitioner to know the exact blood glucose levels of patients, and what corrective action to take. Apart from reducing complications it is also necessary for creating appropriate meal plans, and prescribe insulin regimes for the patient. A secondary objective of this invention is thus to determine the Insulin and ETS Sensitivity of a diabetic patient, to facilitate ease of meal planning and insulin therapy. With the characterization test results known to the medical practitioner and patient, more accurate insulin administration will be possible. These sensitivity values are necessary for accurate blood glucose control.

SUMMARY

Said invention consists of a device able of controlling blood glucose level of a person especially those in intensive medical care following major operations. Said invention will frequently measure said person's blood glucose level and by using a control algorithm administer an appropriate amount of insulin and/or glucose. This will prevent hypoglycaemia or hyperglycaemia. Said device will also control the rate of enteral feeding to cater for the said persons energy requirements.

Said invention will also consist of a measuring means to measure ETS sensitivity and Insulin sensitivity. These values will be used in blood glucose control algorithm to configure the said system. Said invention can control feeding rate of enteral feeding substance or allow the patient to eat. In both cases the blood glucose level is controlled.

Said invention will be implemented as a medical treatment device satisfying safety requirements for medical instrumentation.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a possible hardware diagram for the bedside blood glucose monitor

Figure 2 shows the measured insulin response as a function of mass carbohydrates and glycaemic index (GI) of consumed food

Figure 3 shows the measured insulin response as a function of ETS consumed.

Figure 4 shows the short acting insulin required by type 1 diabetic and the normalized time integral insulin response for healthy patients vs. ETS ingested.

DETAILED DESCRIPTION

The characterisation method used by the invention is based on the ETS concept. ETS is a quantification method used to quantify the energy content of food. This simplifies blood glucose prediction and insulin dosage calculation. ETS can generally be used to relate different energy systems present in the human body to each other. In the discussion of this invention it will only be used in the diabetic context involving the different factors that may influence the blood glucose level.

The effect that ETS intake has on the increase of blood glucose concentration for the diabetic is approximated by a linear function.

$$Increase\ in\ blood\ sugar\ level = EC\ .\ ETS_{consumed} \qquad (12)$$

were EC is the ETS sensitivity.

The nutritional substance administered to the patient during the test should be carefully quantified in ETS. This can be done using ETS tables published in literature, databases available on the Internet or other products available. The patient's blood glucose level is measured every 30 minutes after the meal for the next 3 hours using a blood glucose monitor. The maximum value of these blood glucose level measurements will be used to calculate the rise in blood glucose level caused by the administration of nutritional substance. The level rise is the difference between the maximum level and the blood glucose level prior to the meal. ETS sensitivity (EC) can then be calculated.

$$EC = \frac{Increase\ in\ bloodsugar\ level}{ETS\ in\ nutritional\ substance} \qquad (13)$$

Said device will provide input means for entering values required in equation (13) for the ETS sensitivity calculation. The user can enter values for blood glucose level prior and after an elapsed time following the nutritional substance ingestion and also the amount of ETS in nutritional substance. The device may also provide a measuring means for measuring blood glucose levels therefore making external blood glucose measurement or the entering of blood glucose values not necessary.

The effect that insulin has on the decrease of blood glucose concentration for the diabetic can also be approximated by a linear function.

$$Decrease\ in\ blood\ sugar\ level = IC\ .\ I_{units\ injected} \tag{14}$$

The sensitivity of insulin value IC can be calculated by performing the second part of the test procedure. The insulin sensitivity value (IC) gives a good indication of how resistant the patient is to insulin.

The minimum value where the blood glucose level stabilizes is used to calculate the decrease in blood glucose level. This is merely the difference between the stabilized blood glucose level before the insulin administration and the stabilized blood glucose level after the insulin administration. The insulin sensitivity can then be calculated.

$$IC = \frac{Decrease\ in\ bloodsugar\ level\ resulting\ from\ insulin}{number\ of\ units\ insulin\ administered} \tag{15}$$

Said device will provide input means for entering values required in equation (15) for the Insulin sensitivity calculation. The user can enter values for blood glucose level prior and after an elapsed time following the insulin injection and also the amount of insulin units injected. The device may also provide a measuring means for measuring blood glucose levels therefore making external blood glucose measurement or entering of blood glucose values not necessary.

To calculate the corrective action needed to control the blood glucose level then becomes a simple task. The predicted blood sugar level can be calculated using equation 16.

$$BS_{predicted} = BS_{current} + EC.ETS_{consumed} - IC.I_{units\ injected} \tag{16}$$

If we want to control the blood sugar level in a safe range, we specify the $BS_{predicted}$ value as the desire blood glucose level $BS_{wanted,}$ and calculate the $I_{units\ needed.}$

$$BS_{wanted} = BS_{current} + EC.ETS_{consumed} - IC.I_{units\ needed} \tag{17}$$

Therefore the $I_{units\ needed}$ can be calculated by manipulating equation 17.

$$I_{units\ needed} = (BS_{current} - BS_{wanted} + EC.ETS_{consumed}) / IC. \quad (18)$$

If $I_{units\ needed}$ provides a positive value, then the value indicates the number of short acting insulin units to inject. If $I_{units\ needed}$ provides a negative value, this means that the blood glucose level will already be too low without injecting any insulin. This means that some food containing a certain amount of ETS should be eaten. To calculate the amount of ETS to be eaten to restore normal blood glucose levels equation 19 can be used.

$$ETS_{needed} = (BS_{wanted} - BS_{current}) / EC \quad (19)$$

It is important to calculate the ETS and insulin sensitivity values accurately using the device using the said device.

The calculation device will determine the Insulin sensitivity (IS) and the ETS sensitivity (ES) by using methods as described and will use output means to indicate said calculated results of said patient.

Equation (18) will be used for high-predicted blood glucose levels while Equation (19) will be used for low predicted blood glucose levels. Said invention will also take into account previous insulin administration and the resulting effect thereof on the blood glucose level.

Said device will provide input means for entering, capturing or measuring values relating to:

- ETS sensitivity,
- Insulin sensitivity,
- desired control blood glucose value,
- critical blood glucose ranges (warning levels),
- nutritional substance administration rate,
- other related parameters needed for functioning of the device.

Referring to Figure 1 the unit functions as follows: The unit is connected to a blood glucose monitor, which provides it with continuous or discrete blood glucose concentration measurements. These values can also be provided by hand, by using a separate blood glucose monitor. Using these values as guidelines and comparing it to

a user configurable set point, the unit then decides whether to administer insulin, glucose or no corrective action. The unit is also connected to an insulin and glucose dispenser, which could be implemented as an intravenous drip. The choice of corrective action is based on an insulin and glucose simulation model, with various integrated control system factors.

The device comprises of:

a. a means of selecting, entering or measuring blood glucose levels,

b. an output means for displaying information to the user,

c. an input means for obtaining information from the user,

d. a means of alerting the user or medical caretaker,

e. a means of calculating the blood glucose concentration from the blood samples,

f. a means of administering insulin to the patient,

g. a means of administering glucose to the patient,

h. a means of administering a nutritional substance to the patient,

i. a means for communicating with other computers or medical equipment to transfer data to and from the computer,

j. an input means for entering necessary parameter values and

k. a processing means for processing measured data and parameter values for use with blood glucose prediction algorithms.

CLAIMS

1. A BGL monitoring and adjusting device comprising:

- a calculating means for determining insulin sensitivity (IS) in a person including a processing means; a first set of parameters indicating blood glucose levels (BGL); a first input means for entering into the processing means two BGL values selected from the said first set of parameters respectively before and after the administration to the person of known insulin units (IU); wherein the IS of the said person is determined by the processing means by dividing the decrease between the two selected values with the administered IU; and output means for issuing the IS value;

- a measuring means for measuring the ETS sensitivity (ETSS) of the said person including a second set of parameters indicating blood glucose levels (BGL); and a second selecting means for selecting two BGL values on the said second set of parameters respectively before and after the intake of nutritional energy having known ETS values; wherein the ETS sensitivity of the said person is determined by dividing the increase between the two selected values concomitant with the ETS of the nutritional energy taken in;

- control means for regulating, in accordance with the IS and ETSS values obtained respectively from the calculating means and the measuring means, the rate of nutritional energy intake by the person and the insulin administered to the person, thus to maintain the BGL of the person between predetermined values.

2. A BGL monitoring and adjusting device comprising according to claim 1 with an input means for entering or capturing parameter values including

- Insulin Sensitivity,

- ETS Sensitivity,

- Nutritional Energy supply rate,
- Control blood glucose level,
- Blood glucose safety range,
- and other related blood glucose control parameters.

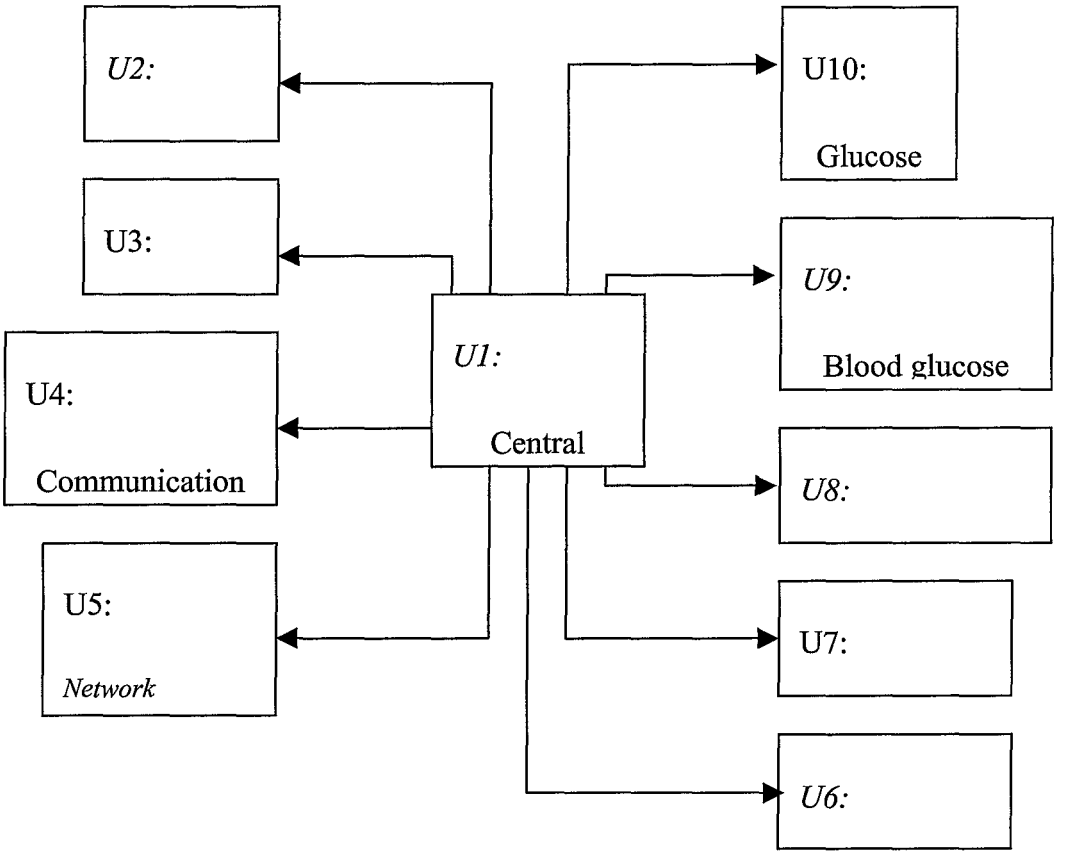

U2:
U3:
U4:
Communication
U5:
Network
U1:
Central
U10:
Glucose
U9:
Blood glucose
U8:
U7:
U6:

Figure 1

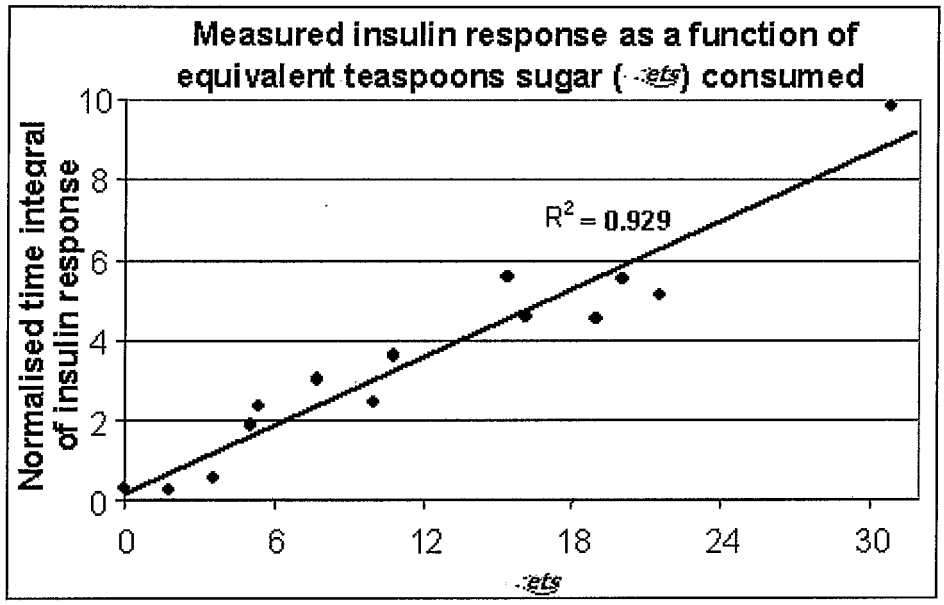


Figure 2

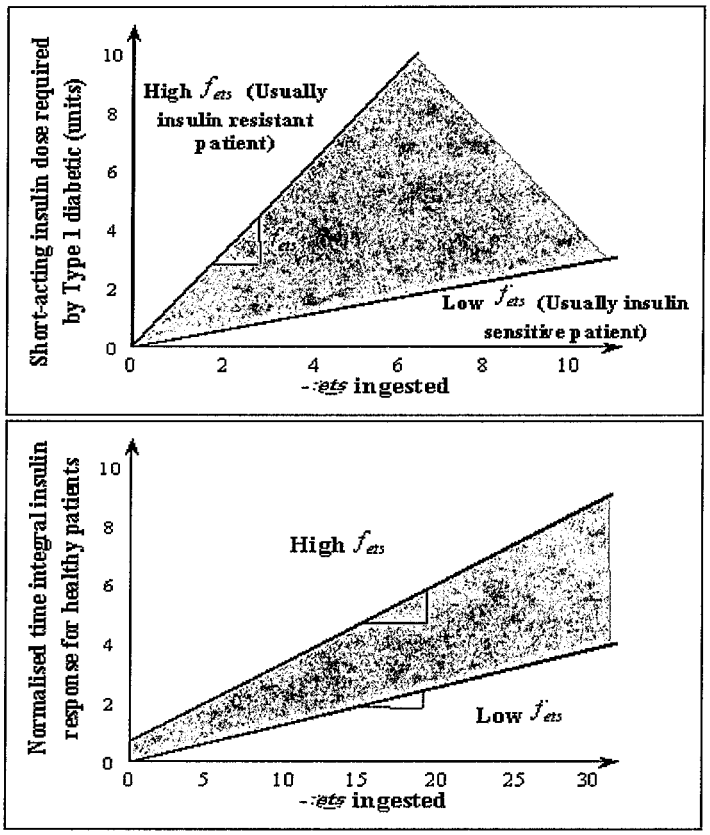
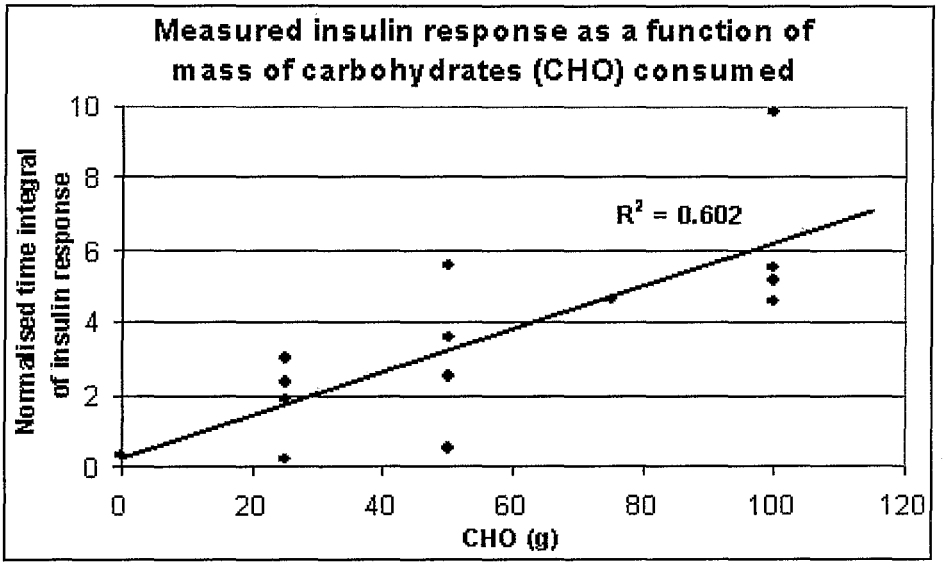


Figure 3


Measured insulin response as a function of mass of carbohydrates (CHO) consumed
Normalised time integral of insulin response
R² = 0.602
CHO (g)
0
2
4
6
8
10
0
20
40
60
80
100
120

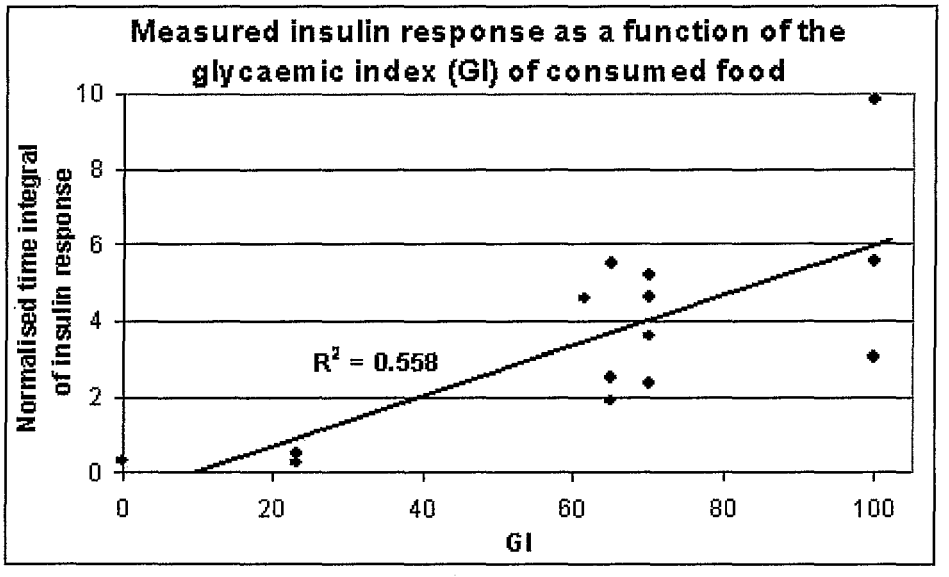

Measured insulin response as a function of the glycaemic index (GI) of consumed food
Normalised time integral of insulin response
R² = 0.558
GI
0
2
4
6
8
10
0
20
40
60
80
100

Figure 4

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***Table 1**: Pearson's R^2-values for correlations between normalised insulin response integrals ( ) and CHO, GI and values. The integrals were calculated from insulin response measurements by Wolever & Bolognesi0 and Lee & Wolever0.*

Test subject	Mass of carbohydrates (CHO)	Glycaemic ndex (GI)	Equivalent teaspoons sugar (ets)
1	0.345	0.451	0.734
2	0.380	0.395	0.803
3	0.408	0.506	0.805
4	0.456	0.521	0.882
5	0.430	0.398	0.710
6	0.226	0.718	0.631
7	0.628	0.237	0.745
8	0.624	0.355	0.877
9	0.792	0.378	0.874
10	0.603	0.558	0.929
11	0.718	0.377	0.915
12	0.834	0.228	0.848
13	0.745	0.186	0.736
14	0.622	0.403	0.826
15	0.614	0.226	0.784
Average R^2	**0.562**	**0.396**	**0.807**
% standard deviation / average R^2	**32**	**36**	**10**

APPENDIX C

LISTING OF J2ME CELLULAR PHONE PROGRAM

Listing 1: The listing of the J2ME application

```
import javax.microedition.midlet.MIDlet;
import javax.microedition.lcdui.Command;
import javax.microedition.lcdui.CommandListener;
import javax.microedition.lcdui.Display;
import javax.microedition.lcdui.Displayable;
import javax.microedition.lcdui.Form;
import javax.microedition.lcdui.List;
import javax.microedition.lcdui.TextField;
import java.lang.Character;

public class GlucMon extends MIDlet implements CommandListener{

private List lstMain,lstLvl1,lstBkd,lstBev,lstCer,lstDair,lstFru,lstRic,lstVeg,lstSna,lstMeat,lstExer;
private List lstBread,lstPastrie,lstCookies,lstMuffins,lstAlcohol,lstSodas,lstJuices,lstHotDrinks;
private List lstCereals,lstPorridge,lstCrackers,lstDairy,lstEgg,lstFresh,lstCanned,lstPasta,lstRice;
private List lstSpreads,lstVegBoiled,lstSoup,lstSweet,lstHealth,lstSavoury, lstWeight;
private Form frmMsr,frmCalc,frmRes,frmSet;
private Command cmdMsr,cmdExit,cmdBack,cmdCalc,cmdOK;
private Display display;
private TextField tfEat,tfExer,tfBS,tfEC,tfIC,tfBSset,tfEXC;
private String sBS;
private Integer iBS,iBSset,iEC,iIC,iEXC,iEts, iDos,iEat,iExer;
private char cTmp;

public GlucMon(){
    //Command setup
    cmdMsr = new Command("Select",Command.ITEM,0);
    cmdExit = new Command("Exit",Command.EXIT,0);
    cmdBack = new Command("Back",Command.BACK,0);
    cmdCalc = new Command("Calculate",Command.ITEM,0);
    cmdOK = new Command("OK",Command.OK,0);

    //Textfields setup
            tfEat = new TextField("Ate: ","3",2,TextField.NUMERIC);
            tfExer = new TextField("Exercised: ","1",2,TextField.NUMERIC);
            tfBS = new TextField("Bloodsugar: ","7",4,TextField.NUMERIC);
            tfEC = new TextField("EC :","1000",4,TextField.NUMERIC);
            tfIC = new TextField("IC :","1000",4,TextField.NUMERIC);
            tfBSset = new TextField("BS target :","5",1,TextField.NUMERIC);
```

```
            tfEXC = new TextField("EXC : ","1000",4,TextField.NUMERIC);

            //Main list setup
lstMain = new List("Menu",List.IMPLICIT);
lstMain.append("Measure blood glucose",null);
lstMain.append("Calculate dosage",null);
lstMain.append("Settings",null);
lstMain.append("Food values",null);
lstMain.append("Exercise values",null);
lstMain.addCommand(cmdExit);
lstMain.setCommandListener(this);

            //Measure form setup
frmMsr = new Form("Measurement");
frmMsr.append("Your blood glucose is 7.3 mmol/l");
frmMsr.addCommand(cmdOK);

//Calculate form setup
frmCalc = new Form("Calculations");
frmCalc.append(tfEat);
frmCalc.append(tfExer);
frmCalc.append(tfBS);
frmCalc.addCommand(cmdBack);
frmCalc.addCommand(cmdCalc);

//Result form setup
frmRes = new Form("Dosage");
frmRes.addCommand(cmdOK);

//Settings form
frmSet = new Form("Settings");
frmSet.append(tfEC);
frmSet.append(tfIC);
frmSet.append(tfBSset);
frmSet.append(tfEXC);
frmSet.addCommand(cmdOK);

//First level database list setup
lstLvl1 = new List("Main food groups",List.IMPLICIT);
lstLvl1.append("Baked",null);
lstLvl1.append("Beverages",null);
lstLvl1.append("Cereals & grains",null);
lstLvl1.append("Dairy & Egg",null);
lstLvl1.append("Fruit",null);
```

```
lstLvl1.append("Rice, Pasta, Spreads",null);
lstLvl1.append("Vegetables",null);
lstLvl1.append("Snacks",null);
lstLvl1.append("Meat & Fish",null);
lstLvl1.addCommand(cmdBack);

            //First level exercise list setup
lstExer = new List("Exercise values", List.IMPLICIT);
lstExer.append("Walking (3kmph)",null);
lstExer.append("Walking (6kmph)",null);
lstExer.append("Running (11kmph)",null);
lstExer.append("Tennis",null);
lstExer.append("Swimming",null);
lstExer.append("Cycling (21kmph)",null);
lstExer.append("Squash",null);
lstExer.addCommand(cmdBack);

//Weight list setup
            frmWeight = new List("Weight division",List.IMPLICIT);


//Second lvl database list setup
            lstBkd = new List("Baked",List.IMPLICIT);
            lstBkd.append("Bread",null);
            lstBkd.append("Pastries",null);
            lstBkd.append("Cookies/Rusks",null);
            lstBkd.append("Muffins/Pies",null);
            lstBkd.addCommand(cmdBack);

            lstBev = new List("Beverages",List.IMPLICIT);
            lstBev.append("Alcoholic",null);
            lstBev.append("Sodas",null);
            lstBev.append("Fruit juices",null);
            lstBev.append("Hot drinks",null);
            lstBev.addCommand(cmdBack);

            lstCer = new List("Cereals/Grains",List.IMPLICIT);
            lstCer.append("Cereals",null);
            lstCer.append("Porridge",null);
            lstCer.append("Crackers",null);
            lstCer.addCommand(cmdBack);

            lstDair = new List("Dairy/Egg",List.IMPLICIT);
            lstDair.append("Dairy",null);
```

```
lstDair.append("Egg",null);
lstDair.addCommand(cmdBack);

lstFru = new List("Fruit",List.IMPLICIT);
lstFru.append("Fresh",null);
lstFru.append("Canned",null);
lstFru.addCommand(cmdBack);

lstRic = new List("Rice/Pasta/Spreads",List.IMPLICIT);
lstRic.append("Pasta",null);
lstRic.append("Rice",null);
lstRic.append("Spreads",null);
lstRic.addCommand(cmdBack);

lstVeg = new List("Vegetables",List.IMPLICIT);
lstVeg.append("Boiled",null);
lstVeg.append("Soup",null);
lstVeg.addCommand(cmdBack);

lstSna = new List("Snacks",List.IMPLICIT);
lstSna.append("Sweet",null);
lstSna.append("Healthy",null);
lstSna.append("Savoury",null);
lstSna.addCommand(cmdBack);

lstMeat = new List("Meat/Fish",List.IMPLICIT);
lstMeat.append("All are 0",null);
lstMeat.addCommand(cmdBack);

//Third lvl lists
lstBread = new List("Bread",List.IMPLICIT);
lstBread.append("Roll 4",null);
lstBread.append("Slice white 3",null);
lstBread.append("Slice brown 2",null);
lstBread.addCommand(cmdBack);

lstPastrie = new List("Pastries",List.IMPLICIT);
lstPastrie.append("Dougnut glazed 6",null);
lstPastrie.append("Croissant 5",null);
lstPastrie.append("Pancake plain 1",null);
lstPastrie.addCommand(cmdBack);

lstCookies = new List("Cookies/Rusks",List.IMPLICIT);
lstCookies.append("Oatmeal 1",null);
```

```
lstCookies.append("Shortbread 2",null);
lstCookies.append("Rusk 6",null);
lstCookies.addCommand(cmdBack);

lstMuffins = new List("Muffins/Pies",List.IMPLICIT);
lstMuffins.append("Muffin 9",null);
lstMuffins.append("Meat pie 5",null);
lstMuffins.addCommand(cmdBack);

lstAlcohol = new List("Alcoholic",List.IMPLICIT);
lstAlcohol.append("Beer light 1",null);
lstAlcohol.append("Beer regular 2",null);
lstAlcohol.append("Wine 3",null);
lstAlcohol.addCommand(cmdBack);

lstSodas = new List("Sodas",List.IMPLICIT);
lstSodas.append("Diet 0",null);
lstSodas.append("Cola 8",null);
lstSodas.append("Regular 8",null);
lstSodas.addCommand(cmdBack);

lstJuices = new List("Fruit juices",List.IMPLICIT);
lstJuices.append("Orange 4",null);
lstJuices.append("Lemon 4",null);
lstJuices.append("Lime 4",null);
lstJuices.append("Grapefruit 4",null);
lstJuices.append("Tangerine 4",null);
lstJuices.append("Pineapple 5",null);
lstJuices.append("Apple 5",null);
lstJuices.append("Punch 6",null);
lstJuices.append("Grape 6",null);
lstJuices.addCommand(cmdBack);

lstHotDrinks = new List("Hot drinks",List.IMPLICIT);
lstHotDrinks.append("Coffee 0",null);
lstHotDrinks.append("Tea 0",null);
lstHotDrinks.append("Milk 1",null);
lstHotDrinks.append("One Sugar 1",null);
lstHotDrinks.addCommand(cmdBack);

lstCereals = new List("Cereals",List.IMPLICIT);
lstCereals.append("All-Bran 3",null);
lstCereals.append("Corn flakes 10",null);
lstCereals.append("Muesli 5",null);
```

```
lstCereals.append("Pronutro 3",null);
lstCereals.append("Raisinbran 5",null);
lstCereals.append("Rice Crispies 8",null);
lstCereals.append("Special K 6",null);
lstCereals.append("Tastee wheat 1",null);
lstCereals.append("Weet-Bix",null);
lstCereals.addCommand(cmdBack);

lstPorridge = new List("Porridge",List.IMPLICIT);
lstPorridge.append("Maize 4",null);
lstPorridge.append("Oatmeal 2",null);
lstPorridge.addCommand(cmdBack);

lstCrackers = new List("Crackers",List.IMPLICIT);
lstCrackers.append("Crackermeal 1",null);
lstCrackers.append("Provita 1",null);
lstCrackers.addCommand(cmdBack);

lstDairy = new List("Dairy",List.IMPLICIT);
lstDairy.append("Milk full cream 1",null);
lstDairy.append("Milk low fat 1",null);
lstDairy.append("Yoghurt fruit 4",null);
lstDairy.addCommand(cmdBack);

lstEgg = new List("Egg",List.IMPLICIT);
lstEgg.append("Egg 1",null);
lstEgg.addCommand(cmdBack);

lstFresh = new List("Fresh fruit",List.IMPLICIT);
lstFresh.append("Apple 2",null);
lstFresh.append("Banana 4",null);
lstFresh.addCommand(cmdBack);

lstCanned = new List("Canned fruit",List.IMPLICIT);
lstCanned.append("Fruit salad 6",null);
lstCanned.append("Pineapple 4",null);
lstCanned.addCommand(cmdBack);

lstPasta = new List("Pasta",List.IMPLICIT);
lstPasta.append("Pasta 3",null);
lstPasta.append("Macaroni & Cheese 3",null);
lstPasta.addCommand(cmdBack);

lstRice = new List("Rice",List.IMPLICIT);
```

```
                lstRice.append("Brown 4",null);
                lstRice.append("White 8",null);
                lstRice.addCommand(cmdBack);

                lstSpreads = new List("Spreads",List.IMPLICIT);
                lstSpreads.append("Jam/Marmalade 1",null);
                lstSpreads.append("Rest 0",null);
                lstSpreads.addCommand(cmdBack);

                lstVegBoiled = new List("Boiled Vegetables",List.IMPLICIT);
                lstVegBoiled.append("Beet 3",null);
                lstVegBoiled.append("Potato 1",null);
                lstVegBoiled.addCommand(cmdBack);

                lstSoup = new List("Soup",List.IMPLICIT);
                lstSoup.append("Meat 1",null);
                lstSoup.append("Vegetable 1",null);
                lstSoup.addCommand(cmdBack);

                lstSweet = new List("Sweet snacks",List.IMPLICIT);
                lstSweet.append("Chocolate bar 6",null);
                lstSweet.append("Nougat 7",null);
                lstSweet.addCommand(cmdBack);

                lstHealth = new List("Health bars",List.IMPLICIT);
                lstHealth.append("Granola 2",null);
                lstHealth.append("Granola choc 4",null);
                lstHealth.addCommand(cmdBack);

                lstSavoury = new List("Savoury",List.IMPLICIT);
                lstSavoury.append("Popped corn 2",null);
                lstSavoury.append("Potato chips 3",null);
                lstSavoury.addCommand(cmdBack);
}

//Do this on startup of application
public void startApp(){
    //Set up initial display
    display = Display.getDisplay(this);
    display.setCurrent(lstMain);

    //Initialise all needed variables
    iBS = new Integer(7);
    iBSset = new Integer(5);
```

```
        iEC = new Integer(1000);
        iIC = new Integer(1000);
        iEXC = new Integer(1000);
        iEts = new Integer(0);
        iDos = new Integer(0);
        iEat = new Integer(3);
        iExer = new Integer(1);
}

//Do this on application being paused
public void pauseApp(){
}

//Close application
public void destroyApp(boolean unconditional){
    lstMain=null;
}

//Handle commands
public void commandAction(Command c,Displayable d){
                if (c==cmdExit) {
     destroyApp(true);
     notifyDestroyed();
    }
   else if (c==cmdBack) {
                    if
(d==lstBkd||d==lstBev||d==lstCer||d==lstDair||d==lstFru||d==lstRic||d==lstVeg||d==lstSna||d==lstMeat){
                        lstLvl1.setCommandListener(this);
                        display.setCurrent(lstLvl1);
                    }
                    else if (d==lstBread||d==lstPastrie||d==lstCookies||d==lstMuffins){
                        lstBkd.setCommandListener(this);
                        display.setCurrent(lstBkd);
                    }
                    else if (d==lstAlcohol||d==lstSodas||d==lstJuices||d==lstHotDrinks){
                        lstBev.setCommandListener(this);
                        display.setCurrent(lstBev);
                    }
                    else if (d==lstCereals||d==lstPorridge||d==lstCrackers){
                        lstCer.setCommandListener(this);
                        display.setCurrent(lstCer);
                    }
                    else if (d==lstDairy||d==lstEgg){
                        lstDair.setCommandListener(this);
```

```
                display.setCurrent(lstDair);
            }
            else if (d==lstFresh||d==lstCanned){
                lstFru.setCommandListener(this);
                display.setCurrent(lstFru);
            }
            else if (d==lstPasta||d==lstRice||d==lstSpreads){
                lstRic.setCommandListener(this);
                display.setCurrent(lstRic);
            }
            else if (d==lstVegBoiled||d==lstSoup){
                lstVeg.setCommandListener(this);
                display.setCurrent(lstVeg);
            }
            else if (d==lstSweet||d==lstHealth|d==lstSavoury){
                lstSna.setCommandListener(this);
                display.setCurrent(lstSna);
            }
            else{
      lstMain.setCommandListener(this);
     display.setCurrent(lstMain);
          }
}
else if (d==frmCalc && c==cmdCalc) {
 if (tfBS.size()>0){
                //Init result variables
  iEts= new Integer(0);
                iDos= new Integer(0);

  //Convert tfBS to integer
  iBS=new Integer(Integer.parseInt(tfBS.getString()));
  iBSset = new Integer(Integer.parseInt(tfBSset.getString()));
  iEC = new Integer(Integer.parseInt(tfEC.getString()));
  iEat = new Integer(Integer.parseInt(tfEat.getString()));
  iEXC = new Integer(Integer.parseInt(tfEXC.getString()));
  iExer = new Integer(Integer.parseInt(tfExer.getString()));

  if (frmRes.size() > 0){
            frmRes.delete(0);
     }
  if (iIC.intValue()!=0){
        iDos = new Integer((iBS.intValue()*1000-iBSset.intValue()*1000+iEC.intValue()*iEat.intValue()
                -iExer.intValue()*iEXC.intValue())/iIC.intValue());
            iDos = iBS;
```

```
                    }
        if (iDos.intValue() < 0){
            iEts = new Integer((iEXC.intValue()*iExer.intValue()-
iBS.intValue()*1000+iBSset.intValue()*1000)/iEC.intValue());
            frmRes.append("Eat "+iEts.toString()+" ets");
        }
        else {
                        frmRes.append("Inject "+iDos.toString()+" units");
                    }
        frmRes.setCommandListener(this);
        display.setCurrent(frmRes);
      }
    }
    else if(c==List.SELECT_COMMAND){
                if (d==lstMain){
          if (lstMain.getSelectedIndex()==0){
           frmMsr.setCommandListener(this);
           display.setCurrent(frmMsr);
           tfBS.setString("7");
          }
          else if (lstMain.getSelectedIndex()==2){
           frmSet.setCommandListener(this);
           display.setCurrent(frmSet);
          }
          else if (lstMain.getSelectedIndex()==3){
                        lstLvl1.setCommandListener(this);
                        display.setCurrent(lstLvl1);
          }
          else if (lstMain.getSelectedIndex()==4){
                        lstExer.setCommandListener(this);
                        display.setCurrent(lstExer);
          }
          else {
              frmCalc.setCommandListener(this);
              display.setCurrent(frmCalc);
          }
                }
                else if (d==lstLvl1){
          switch(lstLvl1.getSelectedIndex()){
           case 0:
              lstBkd.setCommandListener(this);
              display.setCurrent(lstBkd);
              break;
           case 1:
```

```
            lstBev.setCommandListener(this);
            display.setCurrent(lstBev);
            break;
        case 2:
            lstCer.setCommandListener(this);
            display.setCurrent(lstCer);
            break;
        case 3:
            lstDair.setCommandListener(this);
            display.setCurrent(lstDair);
            break;
        case 4:
            lstFru.setCommandListener(this);
            display.setCurrent(lstFru);
            break;
        case 5:
            lstRic.setCommandListener(this);
            display.setCurrent(lstRic);
            break;
        case 6:
            lstVeg.setCommandListener(this);
            display.setCurrent(lstVeg);
            break;
        case 7:
            lstSna.setCommandListener(this);
            display.setCurrent(lstSna);
            break;
        case 8:
            lstMeat.setCommandListener(this);
            display.setCurrent(lstMeat);
            break;
        case 9:
            lstExer.setCommandListener(this);
            display.setCurrent(lstExer);
    }
            }
            else if (d==lstBkd){
                switch(lstBkd.getSelectedIndex()){
                  case 0:
                   lstBread.setCommandListener(this);
                   display.setCurrent(lstBread);
                   break;
                  case 1:
                     lstPastrie.setCommandListener(this);
```

```
                display.setCurrent(lstPastrie);
                break;
            case 2:
                lstCookies.setCommandListener(this);
                display.setCurrent(lstCookies);
                break;
            case 3:
                lstMuffins.setCommandListener(this);
                display.setCurrent(lstMuffins);
                break;
        }
    }
    else if (d==lstBev){
        switch(lstBev.getSelectedIndex()){
            case 0:
                lstAlcohol.setCommandListener(this);
                display.setCurrent(lstAlcohol);
             break;
            case 1:
                lstSodas.setCommandListener(this);
                display.setCurrent(lstSodas);
                break;
            case 2:
                lstJuices.setCommandListener(this);
                display.setCurrent(lstJuices);
                break;
            case 3:
                lstHotDrinks.setCommandListener(this);
                display.setCurrent(lstHotDrinks);
                break;
        }
    }
    else if (d==lstCer){
        switch(lstCer.getSelectedIndex()){
            case 0:
                lstCereals.setCommandListener(this);
                display.setCurrent(lstCereals);
             break;
            case 1:
                lstPorridge.setCommandListener(this);
                display.setCurrent(lstPorridge);
                break;
            case 2:
                lstCrackers.setCommandListener(this);
```

```
                display.setCurrent(lstCrackers);
            }
        }
        else if (d==lstDair){
            switch(lstDair.getSelectedIndex()){
             case 0:
                lstDairy.setCommandListener(this);
                display.setCurrent(lstDairy);
              break;
             case 1:
                lstEgg.setCommandListener(this);
                display.setCurrent(lstEgg);
                break;
            }
        }
        else if (d==lstFru){
            switch(lstFru.getSelectedIndex()){
             case 0:
                lstFresh.setCommandListener(this);
                display.setCurrent(lstFresh);
              break;
             case 1:
                lstCanned.setCommandListener(this);
                display.setCurrent(lstCanned);
                break;
            }
        }
        else if (d==lstRic){
            switch(lstRic.getSelectedIndex()){
             case 0:
                lstPasta.setCommandListener(this);
                display.setCurrent(lstPasta);
              break;
             case 1:
                lstRice.setCommandListener(this);
                display.setCurrent(lstRice);
                break;
             case 2:
                lstSpreads.setCommandListener(this);
                display.setCurrent(lstSpreads);
                break;
            }
        }
        else if (d==lstVeg){
```

```
                switch(lstVeg.getSelectedIndex()){
                 case 0:
                    lstVegBoiled.setCommandListener(this);
                    display.setCurrent(lstVegBoiled);
                  break;
                 case 1:
                    lstSoup.setCommandListener(this);
                    display.setCurrent(lstSoup);
                    break;
                }
            }
            else if (d==lstSna){
                switch(lstSna.getSelectedIndex()){
                 case 0:
                    lstSweet.setCommandListener(this);
                    display.setCurrent(lstSweet);
                  break;
                 case 1:
                    lstHealth.setCommandListener(this);
                    display.setCurrent(lstHealth);
                    break;
                 case 2:
                    lstSavoury.setCommandListener(this);
                    display.setCurrent(lstSavoury);
                    break;
                }
            }
            else if (d==lstMeat){
                switch(lstMeat.getSelectedIndex()){
                 case 0:
                  break;
                }
            }
            else if (d==lstExer){
                switch(lstExer.getSelectedIndex()){
                 case 0:
                  break;
                }
            }
}
else {
 lstMain.setCommandListener(this);
 display.setCurrent(lstMain);
}}}
```

APPENDIX D

EXAMPLE ETS VALUES

BAKED

BREAD

Bread roll - **5** ets
Slice white bread - **3** ets
Slice brown bread - **3** ets

PASTRIES

Dougnut glazed - **6** ets
Croissant - **5** ets
Plain pancake - **2** ets

COOKIES+RUSKS

Oatmeal cookie - **1** ets
Shortbread cookie - **2** ets
Rusk - **4** ets

MUFFINS+PIES

Typical muffin - **9** ets
Typical meat pie - **4** ets

BEVERAGES

ALCOHOLIC

Beer light, can - **1** ets
Beer regular, can - **2** ets
Wine, glass - **1** ets

SODAS (can)

Diet soda - **0** ets
Cola - **7** ets
Soda regular - **7** ets

FRUIT JUICES (glass)

Orange, Lemon, Lime - **4** ets
Grapefruit, Tangerine - **4** ets
Pineapple, apple - **5** ets
Fruit punch - **6** ets
Grape juice - **5** ets

HOT DRINKS

Coffee, Tea - **0** ets
Milk, cup - **1** ets
Sugar, teaspoon - **1** ets

CEREALS & GRAINS

CEREALS (cup)

All-Bran Flakes - **3** ets
Corn Flakes - **9** ets
Muesli - **5** ets
Pronutro - **7** ets
Raisinbran - **5** ets
Rice Crispies - **8** ets
Special K - **4** ets
Tastee Wheat - **2** ets
Weet-Bix biscuit - **3** ets

PORRIDGE (cup)

Maize meal, soft - **3** ets
Maize meal, stiff - **3** ets
Oatmeal / Oats - **2** ets

CRACKERS (biscuit)

Crackermeal - **1** ets
Provita - **1** ets
Melba toast - **3** ets

DAIRY+EGG

DAIRY

Chocholat milk, cup - **1** ets
Ice cream,2 scoops &cone- **4** ets
Ice cream per scoop - **2** ets

Milk shake,glass - **10** ets
Milo made with milk, cup - **4** ets
Milk, low fat, cup - **1** ets

Milk, full cream, cup - **1** ets
Yoghurt, full cream,cup - **1** ets
Yoghurt,fruit, cup - **4** ets

EGG

Large egg - **0** ets

FRUIT

FRESH FRUIT

Apple, med - **2** ets
Apricot, med - **1** ets
Avocado, med - **3** ets
Banana,med – **4** ets
Grapefruit, med – **2** ets
Grapes, cup – **3** ets
Lemon/Lime,med – **1** ets
Mango, med – **4** ets
Orange, med – **2** ets
Papaya, med – **2** ets
Pears, med – **2** ets
Watermelon, cup – **1** ets

CANNED FRUIT (cup)

Fruit salad in syrup – **6** ets
Peaches in syrup – **6** ets
Pears in syrup – **4** ets
Pineapple in syrup – **8** ets

RICE, PASTA, SPREADS

PASTA (cup)

Pasta - **3** ets
Macaroni & Cheese - **3** ets

RICE (cup)

Brown rice - **4** ets
White rice - **5** ets
Wild rice - **5** ets
Rice paella - **2** ets

SPREADS (teaspoon)

Bovril,Butro, Butter, Cashew butter, Cheese spreads, Chicken spreads, Fish Paste, Margarine,Marmite, Meat Paste, Pate, Peanut butter, Chicken spread, Ham and Cheese spread, Sandwich spread - **0** ets
Jams, Marmalades - **1** ets

VEGETABLES

BOILED VEGETABLES

Beet, tablespoon - **0** ets
Broccoli, tablespoon **0** ets
Cabbage, tablespoon - **0** ets
Carrots, tablespoon - **0** ets
Corn yellow, cup - **0** ets
Peas, green tablespoon - **0** ets
Potato, medium - **5** ets
Pumpkin, tablespoons - **0** ets
Sweet potato, medium - **4** ets
Spinach, tablespoons - **0** ets
Tomato, medium - **1** ets

SOUP (cup)

Meat soup - **1** ets
Vegetable & Meat soup - **3** ets
Vegetable soup - **1** ets

SNACKS

SWEET SNACKS

Bar-one 40g - **4** ets
Fudge plain piece - **3** ets
Jellybeans each - **1** ets
Kit Kat Wafer, 50g - **6** ets
Liquorice All Sorts each - **1** ets
Marshmallows, each - **1** ets
Chocholate bar small - **5** ets
Nougat bar, 60g - **7** ets
Super C each - **1** ets
Toffee each - **1** ets

HEALTH BAR

Granola bar, 20g - **2** ets
Granola bar choc, 20g - **4** ets

SAVOURY

Pop corn, air pop, 30g - **2** ets
Potato chips, 30g - **3** ets
Potato chips, light - **1** ets

MEAT & FISH

MEAT & FISH

All meat and fish - **0** ets

Exercise ets expenditure for 30 minutes of

Your Weigth	Walking (3 km/h)	Walking (6 km/h)	Running (11km/h)	Tennis	Swimming	Cycling (21 km/h)	Squash
40 kg	½ ets	1½ ets	3 ets	1½ ets	1 ets	2 ½ ets	2 ets
60 kg	1 ets	2 ets	4½ ets	2½ ets	1 ½ ets	3 ½ ets	3 ets
80 kg	1½ ets	3 ets	6½ ets	3 ets	2 ets	4 ½ ets	4 ets
100 kg	2 ets	3½ ets	8 ets	4 ets	2½ ets	6 ets	5 ets