SMARTDIAB: A Communication and Information Technology Approach for the Intelligent Monitoring, Management and Follow-up of Type 1 Diabetes Patients

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***Abstract*—SMARTDIAB is a platform designed to support the monitoring, management, and treatment of patients with type 1 diabetes mellitus (T1DM), by combining state-of-the-art approaches in the fields of database (DB) technologies, communications, simulation algorithms, and data mining. SMARTDIAB consists mainly of two units: 1) the patient unit (PU); and 2) the patient management unit (PMU), which communicate with each other for data exchange. The PMU can be accessed by the PU through the internet using devices, such as PCs/laptops with direct internet access or mobile phones via a Wi-Fi/General Packet Radio Service access network. The PU consists of an insulin pump for subcutaneous insulin infusion to the patient and a continuous glucose measurement system. The aforementioned devices running a user-friendly application gather patient's related information and transmit it to the PMU. The PMU consists of a diabetes data management system (DDMS), a decision support system (DSS) that provides risk assessment for long-term diabetes complications, and an insulin infusion advisory system (IIAS), which reside on a Web server. The DDMS can be accessed from both medical personnel and patients, with appropriate security access rights and front-end interfaces. The DDMS, apart from being used for data storage/retrieval, provides also advanced tools for the intelligent processing of the patient's data, supporting the physician in decision making, regarding the patient's treatment. The IIAS is used to close the loop between the insulin pump and the continuous glucose monitoring system, by providing the pump with the appropriate insulin infusion rate in order to keep the patient's glucose levels within predefined limits. The pilot version of the SMARTDIAB has already been implemented, while the platform's evaluation in clinical environment is being in progress.**

***Index Terms*—Closed-loop glucose control, diabetes management, home care, information and communication technologies, telemedicine.**

I. Introduction

TYPE 1 diabetes mellitus (T1DM), previously known as insulin dependent diabetes mellitus, is a chronic metabolic disease characterized by absence of insulin secretion due to destruction of pancreatic beta-cells. Inadequate T1DM treatment leads to short-term (hypoglycaemia and hyperglycaemia) and long-term (e.g., neuropathies, nephropathy, retinopathy, heart disease, and stroke) complications, whereas intensive glycaemic control has been shown to reduce the risk to develop such complications [1]. In T1DM, intensive glycaemic control is achieved by means of: 1) insulin therapy either through administration of multiple daily injections (MDI), known also as intensive conventional therapy, or through continuous subcutaneous insulin infusion (CSII) via insulin-pumps; and 2) regular self-monitoring of glucose levels by using either conventional finger-stick glucose meters (three to four times daily), or continuous glucose monitors (CGMs) that provide high frequency (e.g., every 5 min) measurements of glucose levels.

In order to improve the monitoring and glycaemic control of patients with diabetes mellitus both academic and diabetes technology industry research is focused on the design and development of personal sensors for CGM [2], [3], multisensor devices

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for physical activity monitoring [4], novel instruments for delivery of insulin [5], [6], advanced models of the glucose–insulin metabolic system for better understanding of the involved mechanisms [7], [8], computational algorithms for insulin treatment optimization [9], data mining and visualization tools for better management of diabetes data [10], and intelligent decision support systems (DSS) to be used for patients health status assessment and prediction of diabetes-related complications [11].

Additionally, several research efforts have been reported toward the design and development of a closed-loop artificial pancreas (AP). The AP includes three components: a sensor for automatic CGM, an automatic insulin delivery system, and a computational algorithm, which provides automatic estimation of optimum insulin infusion rate, closing the loop between the glucose sensor and the insulin delivery system, for the [12]. Despite the fact that the availability of accurate sensor and insulin delivery system is essential for an AP, they do not ensure the achievement of optimal glycaemic control under all conditions. The development of an algorithm able to control glucose levels through the provision of individualized estimations of the appropriate insulin infusion rate under various conditions and without human interventions is a challenge for control engineers. To this end, various classic and modern closed-loop control algorithms have been developed and evaluated both in *in silico* and *in vivo* trials [13]–[17]. The majority of these algorithms are based on the subcutaneous CGM and subcutaneous insulin delivery (sc–sc) route. It is expected that the development and deployment of a reliable, accurate, safe, and seamless device that mimic the biological pancreas requiring minimal human interventions will permit the home management and may be a potential cure for patients with T1DM.

Furthermore, advances in Information and Communication Technology have accelerated the design and implementation of telemedicine platforms [18], [19] for various diagnosis and treatment applications. Several telemedicine platforms have been proposed for diabetes monitoring and management [20]. Systems using Internet and Public Switched Telephone Network (PSTN), allows a diabetes patient to send glucose measurements to a hospital, where a physician with a set of tools for data visualization, analysis, and decision support can analyze them and advise the patient on appropriate treatment adjustment [21]–[23]. A communication platform based on embedded technology and use of Internet, mobile, and PSTN infrastructure for diabetes patients has also been presented in [24]. In the IDEATel project [25], Web-based computing and telecommunication networks have been established in both urban and rural economically disadvantaged areas within New York State. The project has involved 1500 diabetes patients. Another EU funded research project, entitled multiaccess services for managing diabetes mellitus ($\mathrm{M^2DM}$) [26], has proposed a high-performance Web and a computer telephony integration server that can be accessed using different communication links, such as standard telephone lines, mobile phones, and Internet. Users (physicians and all types of diabetes patients) can access information using customized applications, general applications and terminals. Core of the platform is the multiaccess organizer, which is responsible for the coordination of a series of software agents. Additionally, within the frame of the advanced insulin infusion using a control loop (ADICOL) project, a system consisting of a minimally invasive sc glucose sensor, a handheld PocketPC computer, and an insulin pump (D-Tron, Disetronic, Burgdorf, Switzerland) has been designed and developed. The system continuously measures and controls the glucose concentration in individuals with T1DM [27]. More recently, the ldquointelligent control assistant for diabetes, INCArdquo system (INCA) has been presented [28]. The INCA is a smart personal digital assistant that provides subjects with T1DM closed-loop control strategies based on the Guardian RT sensor (Medtronic), the D-Tron insulin pump (Disetronic Medical Systems), and a mobile general packet radio service (GPRS) based telemedicine communication system.

This paper refers to the design and development of a pilot platform named SMARTDIAB, which is based on the combined use of information and communication technologies for the intelligent monitoring, management, and followup of individuals with T1DM [29], [30]. The platform integrates mobile infrastructure, Internet technology, novel, and commercially available continuous glucose measurement devices and insulin pumps, advanced modeling techniques, control methods, and tools for the intelligent processing of diabetes patients information. The platform allows 1) intensive monitoring of glucose levels; 2) diabetes treatment optimization; 3) continuous medical care; and 4) improvement of quality of life of individuals with T1DM.

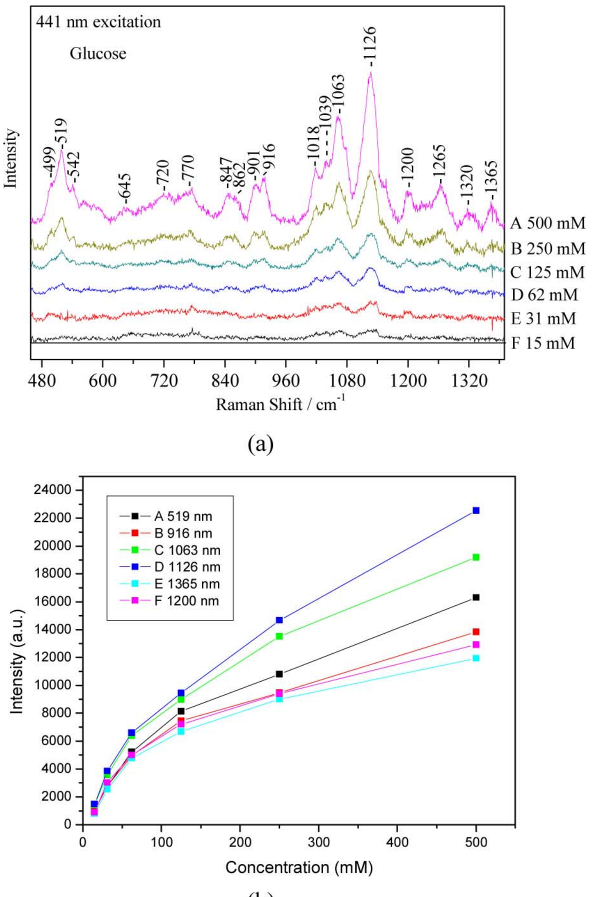
The rest of the paper is organized as follows. Section II presents the SMARTDIAB advancements in glucose measurement and closed-loop control technologies, while Section III describes the specifications and overall architecture of the SMARTDIAB platform. In Sections IV and V, design and implementation issues of the basic platform's units, the patient unit (PU) and the patient management unit (PMU), are presented. Section VI is dedicated to functional issues emphasizing on security aspects and service usage scenarios. The strategy toward SMARTDIAB evaluation is described in Section VII, while future research directions and conclusions are presented in Section VIII.

II. SMARTDIAB ADVANCEMENTS IN GLUCOSE MEASUREMENT AND CLOSED-LOOP CONTROL

Within the SMARTDIAB framework, a novel technology toward noninvasive glucose measurement has been investigated and a personalized strategy for closed-loop glucose control has been developed.

A. *Development of a Raman-Based Glucose Monitoring Device*

The novel glucose monitoring device is a low power (2–3 mW) Raman system based on a low wavelength (441 nm) excitation source. Under this resonance, Raman condition, information from glucose, and hemoglobin is acquired. Hemoglobin, the main source of fluorescence background signal in the blood Raman spectra, can be monitored, concurrently with the glucose spectrum, thus providing a clear spectral window through which the concentration of glucose in the clinically relevant region can be monitored.



(a)

(b)

Fig. 1. (a) Raman spectrum of glucose of various concentrations. (b) Calibration curve of glucose showing the intensity variation of peaks in glucose Raman spectra for different concentrations.

Fig. 1(a) illustrates the peaks of glucose in Raman spectroscopy. In particular, the marker bands of glucose at 1126 and 1063 cm^{-1} are very strong. In the calibration curve [see Fig. 1(b)], the response of glucose versus concentration can be monitored by following the most significant peaks of 519, 916, 1063, 1126, 1200, and 1365 cm^{-1}. It is clear that the efficiency of the Raman process is much better at low concentrations, with a linear relationship existing between the concentration of glucose and the spectral intensity. As the concentration of glucose increases, this linearity is lost. This is probably due to either quenching effects, and/or the inefficient Raman process due to low laser power used. At the same time, the spectrum of 40 μM hemoglobin has relatively weak peaks with the one at 1374 cm^{-1} being the only significant one. Even at low glucose concentrations of 15 mM, there is still the ability to observe clearly and separately glucose by following the strongest peak at 1126 cm^{-1} and hemoglobin at peak 1374 cm^{-1} (see Fig. 2). Such an outcome is very promising for future approaches of demanding clinical ranges of 2–5 mM.

B. Development of a Closed-Loop Glucose Control Strategy

In order to close the loop between the glucose monitoring device and the insulin pump, a control strategy has been developed, which takes into account patient's most recent glucose measurement, previous insulin infusion rate, and information related to carbohydrate contained in the meal, and provides real-time calculation of the appropriate insulin infusion rate. The developed control strategy is based on the use of 1) a personalized model for the simulation of glucose–insulin metabolism; and 2) a nonlinear model predictive controller (NMPC).

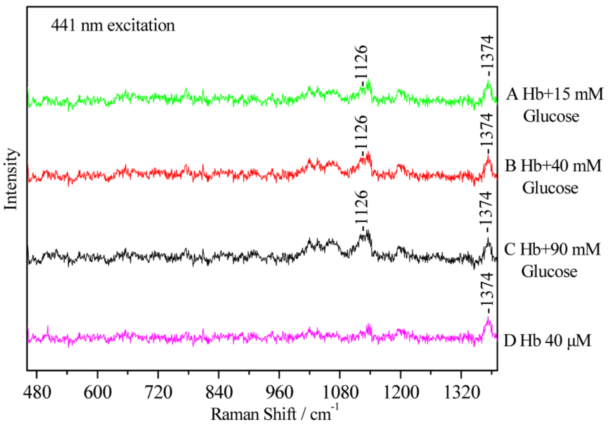


Fig. 2. Raman spectrum of glucose of various concentrations in the presence of hemoglobin.

1) Personalized Glucose–Insulin Metabolism Model: The model is based on the combined use of a compartmental model (CM), and a real-time artificial neural network (RT-ANN) [31], [32]. More specifically, information regarding meal intake is fed to the CM, which simulates the glucose absorption into the blood from the gut [33], [34]. CM's output along with the sc insulin intake and previous sc glucose measurement are applied to the RT-ANN, which models the patient's glucose kinetics and predicts subsequent glucose levels. The RT-ANN is a recurrent ANN (RANN) trained with the real-time recurrent learning algorithm (RTRL) [35], [36]. Through training with a specific T1DM individual's data, the proposed model can provide the NMPC with personalized glucose predictions [31], [32].

2) Nonlinear Model Predictive Controller: The NMPC [37] uses the aforementioned personalized glucose–insulin metabolism model along with an optimizer. The optimizer computes, at each sample time, future control movements based on the minimization of an appropriate cost function following a control law [38]. The cost function encompasses the differences between the model predictions and the desired performance over a predetermined time horizon. The objective of the control law is to drive future model outputs close to a target glucose level. It has to be noted that constraints on estimated insulin infusion rates are applied, in order to account for the insulin infusion pumps limitations and several patient-dependent characteristics (glucose tolerance, insulin sensitivity, etc.).

III. SMARTDIAB CONCEPT AND ARCHITECTURE

As presented in Fig. 3, the SMARTDIAB platform consists of two units: 1) the PU; and 2) the PMU. In the PU, patient's related information, e.g., glucose levels, insulin intake, diet, and physical activity is acquired and transmitted, through

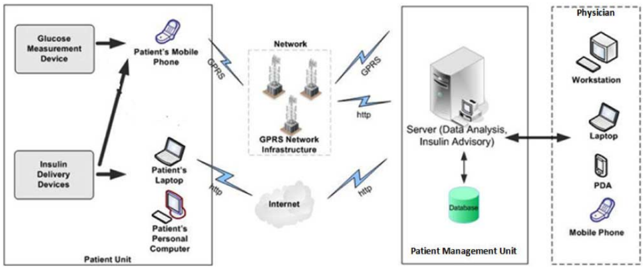


Fig. 3. General architecture of SMARTDIAB.

telecommunication networks, using cellular phones or PC/laptops to the PMU. The PMU can be accessed from both medical personnel and patients, with appropriate security access rights. In the PMU, advanced tools for the intelligent processing of the patient's data are provided to the physician, who is able to monitor the health evolution of the subject patient and make recommendation about his/her treatment. Furthermore, advanced computational tools permit the estimation of optimum insulin infusion rate in case the individual is under insulin pump treatment. Moreover, the T1DM individual can have a clear picture of his/her health status and how his/her habits influence the glucose profile. The major specifications of the PU are summarized in the following: 1) accurate, portable, lightweight devices for glucose measurement and insulin delivery; 2) visualization abilities; 3) wired and wireless communication capabilities; and 4) user-friendly interfaces. The specifications of the PMU comprise: 1) connectivity to the Internet and GPRS; 2) user-friendly interfaces; 3) ability to retrieve and manage patient information and data; and 4) advanced tools for data analysis, processing, modeling, decision support, and visualization.

IV. PATIENT UNIT

The PU consists of the following systems: insulin pump, continuous glucose sensor, and mobile phone. Data related with glucose levels (from CGMs or finger-stick measurement) and insulin delivery (injected dose or insulin infusion parameters), along with information regarding patient's lifestyle are acquired either manually or automatically in the PU and sent to the PMU.

A. *Insulin Pump*

An insulin pump that can be remotely programmed via the Internet has been developed within the SMARTDIAB frame. The insulin pump is a 3 mL dc motor syringe pump, which connects serially to IP-Connect, a mobile global system for mobile communications (GSM)/GPRS gateway, supporting transmission control protocol (TCP)/IP connectivity with the MicrelCare, (www.micrelcare.net) Web-based server, using proprietary digital communication protocol. IP-Connect is not a medical device in IEC6060. Peer availability, data privacy, and integrity during the transmission process are guaranteed through the use of several algorithmic techniques. Peer availability is achieved by periodic connection polling message streams. Data privacy and data integrity are ensured by using packet enciphering with the Triple Data Encryption Standard (3DES) encryption algorithm and data hashing by means of the secure hashing(SH-1) algorithm, respectively. Furthermore, transmission integrity is strengthened using layer acknowledgments and cyclic redundancy checks (CRC) algorithms on top of TCP packet control.

The insulin pump exchanges data with the PMU, through the Web-based connection of the MicrelCare server and the server that supports the PMU. The pump receives the estimated insulin infusion rate by the PMU in International Units/day every 5 min and sends back all pump events such as alarms, warnings and actual rate in the form of acknowledgments. The pump has an internal standard open loop programming that is activated automatically in case of data loss or connection failure, while it warns the user that open-loop infusion mechanism has been turned on, so that he/she takes over pump control.

B. *CGM Devices*

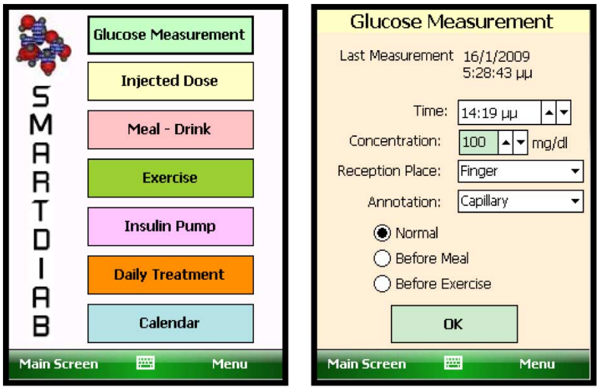
A flexible design was adopted for the PU able to support both the novel noninvasive CGM system based on Raman spectroscopy and commercially available glucose monitoring systems. The Raman-based device supports wired and wireless transmission of the glucose measurements to the central DB of the PMU, through the mobile phone or a laptop/PC. Glucose measurement data from commercial glucose monitoring devices can be downloaded to the mobile phone or a laptop/PC and then transmitted to the central DB of the PMU.

C. *Mobile Phone Application*

The mobile phone application (MPA) provides an easy way to an individual with T1DM to transmit his/her data to the PMU. MPA runs on mobile phones with Windows Mobile, .net 2.0 Compact Framework and MS SQL Server 2005 Mobile Edition installed. The three-tier architecture is followed [39]. Data are initially stored in a local DB on the mobile phone, and then, transmitted to the central DB of PMU via GPRS/3G or Wi-Fi. During the data transmission, a connection to a Web application is established, so that the local DB is synchronized with the remote DB. Extensible markup language (XML) messages, using the Simple Object Access Protocol (SOAP), are transmitted during the data exchange. The main menu of MPA is shown in Fig. 4(a). Selecting the appropriate button, data related to glucose measurements, injected/infused insulin, food/drink consumption, exercise, and calendar notes are stored. An example of the data entry dialog is shown in Fig. 4(b). The stored data is always accompanied by a timestamp. More options are available via the menu list. For instance, in case of discomfort, the patient may send an alert to the system, selecting the appropriate menu item. Then, provided that the mobile phone is equipped with a global positioning system (GPS) receiver, a geoinformation tag is attached to the transmitted data and the PMU receives the alert along with the position of the patient. This piece of information is crucial in cases of a possible diabetic coma.

V. PATIENT MANAGEMENT UNIT

The PMU is the core of the platform. The patient's data is transmitted either through Internet or the mobile telephony



Last Measurement 16/1/2009 5:28:43 μμ
Time: 14:19 μμ
Concentration: 100 mg/dl
Reception Place: Finger
Annotation: Capillary
● Normal
○ Before Meal
○ Before Exercise

(a) (b)

Fig. 4. Examples of MPA interfaces. (a) Main screen. (b) Glucose measurement panel.

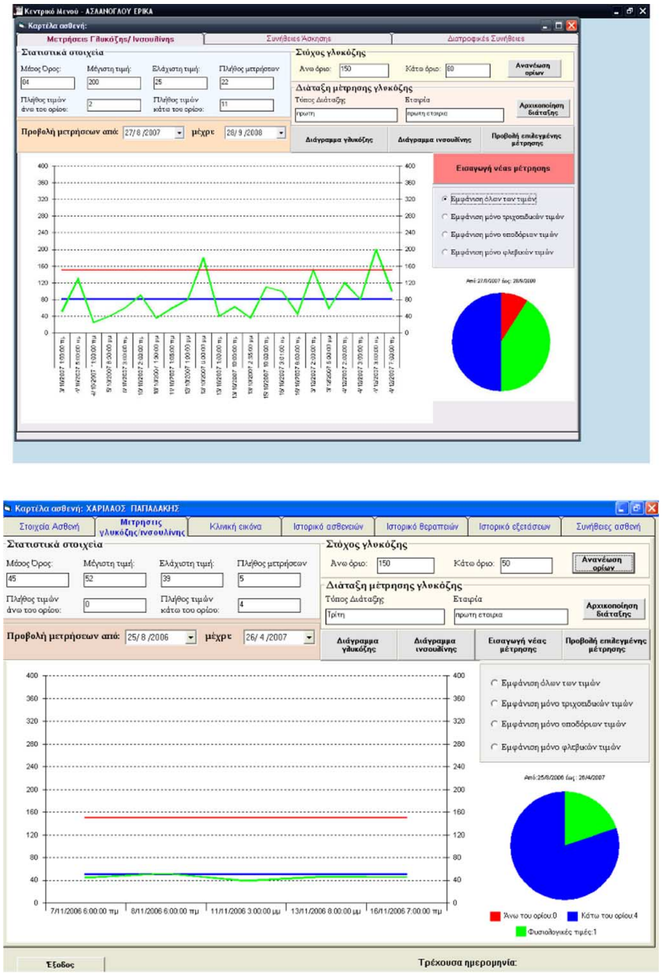
network to the medical center and/or home-care provider and/or diabetological institute. The data received at the Web server are available to both the physician via the medical center local area network (LAN), either wired or wireless, and the patient, via the Internet, through PC and laptops. The PMU consists of the following systems: the diabetes data management system (DDMS), a DSS that provides risk assessment for long-term diabetes complications, and the insulin infusion Advisory system (IIAS).

A. *Diabetes Data Management System*

The DDMS, installed in a Web server, permits individuals with T1DM to access remotely their status, and physicians to evaluate a patient's clinical state through appropriate front-end applications. The DDMS consists of a central DB and a series of data analysis tools.

The central DB is designed on the basis of the Health Level 7 (HL7) Standard enabling communication with the hospital information system, where the PMU will be deployed. In the DB, information related to patient's data, records regarding laboratory examination results, metaanalysis results, and comments about the patient health state are stored. The DB is ICD10 compliant concerning the knowledge entity of the diabetes disease.

As mentioned earlier, the PMU supports front-end applications, which provide a series of Web tools that permit to both individuals and physicians to manage remotely the diabetes-related data. The patient has the ability to keep diary of glucose values, therapeutic treatment, diet and exercise habits, clinical and laboratory examination results, other events, and at the same time to send/receive emails and comments to/from the physician. Furthermore, a set of statistical tools permit the progress evaluation of her/his health status over different time periods, while visualization tools support informative data presentation (e.g., pie charts, line charts, etc.). The physician through appropriate front-end applications has the ability to view and visualize patient's data, create, edit, and update the followed treatment, send/receive emails and comments to/from the patient. The DDMS's functionalities are provided through two major sets of front-end interfaces for the various Web applications,



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Ελάχιστη τιμή: 25
Πλήθος μετρήσεων 22
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Πλήθος τιμών κάτω του ορίου: 11
Άνω όριο: 150
Κάτω όριο: 60
Τύπος Διάταξης: πρωτη
Εταιρία: πρωτη εταιρια
Προβολή μετρήσεων από: 27/8 /2007 μέχρι 28/9 /2008
● Εμφάνιση όλων των τιμών
○ Εμφάνιση μόνο τριχοειδικών τιμών
○ Εμφάνιση μόνο υποδόριων τιμών
○ Εμφάνιση μόνο φλεβικών τιμών

Μέσος Όρος: 45
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Κάτω όριο: 50
Τύπος Διάταξης: Τρίτη
Εταιρία: πρωτη εταιρια
Προβολή μετρήσεων από: 25/ 8 /2006 μέχρι 26/ 4 /2007
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○ Εμφάνιση μόνο τριχοειδικών τιμών
○ Εμφάνιση μόνο υποδόριων τιμών
○ Εμφάνιση μόνο φλεβικών τιμών
Από:25/8/2006 έως: 26/4/2007
🟥 Άνω του ορίου:0
🟦 Κάτω του ορίου:4
🟩 Φυσιολογικές τιμές:1

Fig. 5. Examples of DDMS's interfaces (upper panel) for the diabetes patients, and (lower panel) for the physician.

one set for the diabetes patient, and another for the physician (see Fig. 5).

B. *DSS for Long-Term Diabetes Complications*

The DSS supports the prognosis of long-term diabetes complications [long-term diabetes complications DSS –(LTDC-DSS)]. The LTDC-DSS is able to predict probabilities for a T1DM patient to raise major complications of diabetes. The system is based on Cross Industry Standard for Data Mining (CRISP-DM) and on methodologies for business intelligence and data warehousing projects, proposed by the Kimball Group [40]. In the pilot version of the SMARTDIAB platform, the following long-term complications have been considered: retinopathy, nephropathy, neuropathy, coronary heart disease –(CHD), and hypertension. For each long-term complication, a separate data mining structure has been designed based on a three-layered feedforward ANN. Each ANN has been trained by the backpropagation algorithm, is fed with different inputs (data related to body mass index (BMI), data from the electronic medical record (EMR), lab results, development of long-term T1DM complications, and treatments) related to the complication under study, and provides as output the probability of an individual to raise a specific complication within a five year time frame from her/his T1DM treatment start.

C. Insulin Infusion Advisory System

The IIAS links the CGM device with the insulin pump, and estimates in real-time the appropriate insulin infusion rate in order to maintain glucose levels within normal range. The methodologies that have been used toward the development of the IIAS are described in Section II-B. The IIAS receives from the central DB, glucose records, insulin infusion rates, and information related to the carbohydrates intake and sends back to the central DB, the estimated insulin infusion rate. For patient safety reasons, whenever measured glucose concentration is lower than a predefined limit, the recommended by the IIAS insulin infusion rate is forced to be equal to zero, in order to prevent serious hypoglycemic episodes.

VI. FUNCTIONAL ISSUES

A. Patient Management

Two service usage scenarios are described in the following, in order to clarify how the different components are integrated into the SMARTDIAB platform and to illustrate the different ways the various systems interact to each other, taking also into account the time parameter.

1) Treatment based on Patient's Profile: Fig. 6(a) shows the process of the treatment of a T1DM patient and how the physician can be supported by SMARTDIAB in order to decide the necessary treatment alterations. More specifically, the T1DM patient uses the system's front-end interface to enter particular information concerning:

- personal data, such as height, weight, etc.;
- his/her personal logbook, consisting of important data, such as daily glucose level measurement, insulin intake, meal intake, and time of the action;
- medical record, such as medical exams, illness, etc.;
- lifestyle and daily habits, such as exercise, etc.

All the aforementioned information is stored in the central DB and is online available to the physician. Based on this information, the physician can use the platform to recommend alterations in patient's treatment, such as changes in the predefined glucose or insulin limits that can be tolerated by the patient, changes in insulin bolus dosage, in the nutrition program, or the exercise or even the pharmaceutical treatment, if considered necessary. These changes are stored in the central DB and are available online on patient's front-end application.

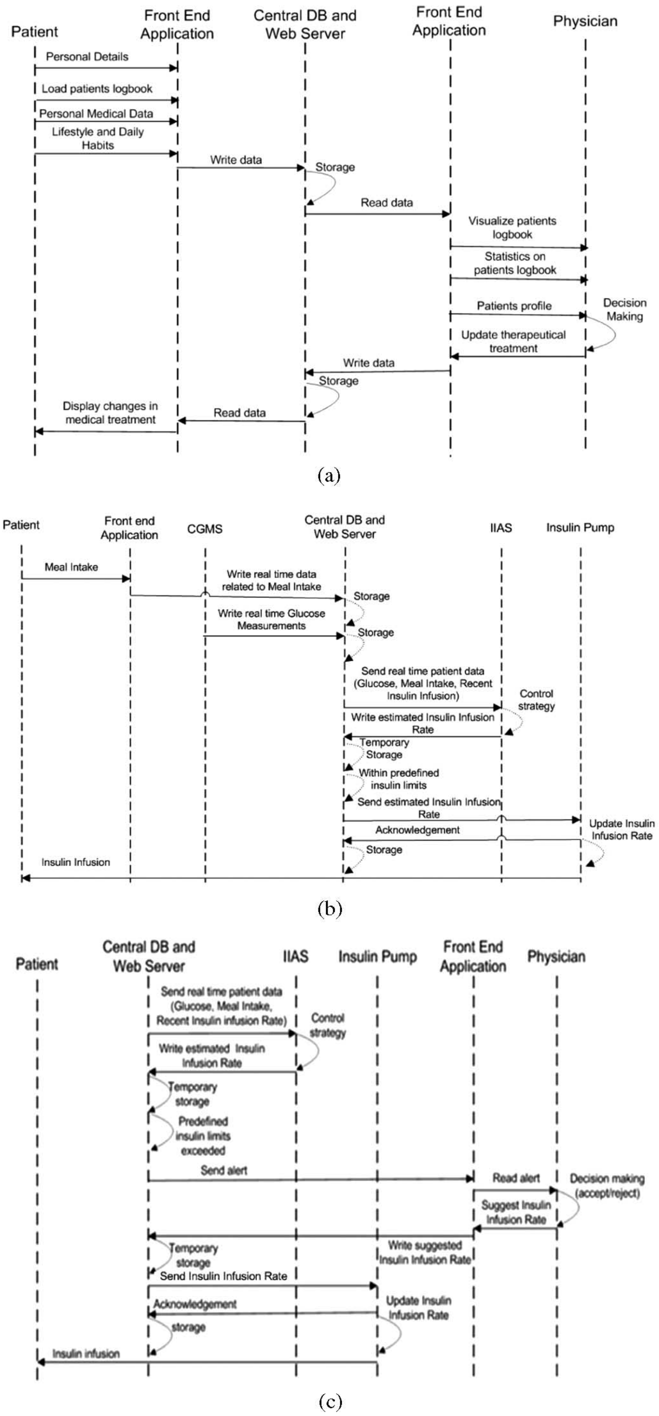

Fig. 6. Interaction diagrams. (a) For treatment update by the physician based on patient's profile. (b) Treatment update based on the closed-loop interaction between the T1DM patient's glucose monitoring device and the insulin pump. (c) For generation of alerts and physician's interference.

2) Closed-Loop Glucose Control: Fig. 6(b) shows the process of the treatment, based on the closed-loop interaction between the T1DM patient's glucose monitoring device and the insulin pump. Unless specific alerts are launched, based on the results of validation controls, for example, glucose and insulin are within accepted predefined limits, the closed-loop functions eternally. The T1DM patient enters meal intake in the corresponding front-end application, running either on laptop/PC or mobile phone, while glucose level measurements are automatically transmitted and stored in the central DB. The aforementioned data, along with stored recent insulin infusion rates provide input to the IIAS. The latter estimates and sends to the central DB, the recommended insulin infusion rate, which is temporarily stored. A validation control runs in the central DB, where the estimated insulin infusion rate is checked against a predefined range, resulting in two possible cases.

- Given that the estimated insulin infusion rate is within the approved predefined range, the central DB is responsible for transmitting the information to the insulin pump. The insulin pump sends an acknowledgment back to the central DB, in order to confirm the rate value and updates the rate at which insulin is infused to the patient. The related interaction diagram is shown in Fig. 6(b).
- When the estimated insulin infusion rate is exceeding the predefined limit, an appropriate alert is triggered and sent to the physician's front-end, who on his turn either finally accepts the IIAS suggestion or recommends a new insulin infusion rate. The physician's decision is transmitted back to the central DB, is temporarily stored and sent to the insulin pump, in order for the appropriate insulin rate to be infused to the patient. The corresponding interaction diagram is shown in Fig. 6(c).

B. Security Framework

The used security framework is based on a component design approach [41], [42], which is comprised of the following four main components.

1) Platform Component: Role-based access control (RBAC) was used to grant permissions to certain functionalities of the system for the three main categories of the users. RBAC was implemented using the object-oriented paradigm by authenticating the user to a role object in the DB. Thereafter, the role object loaded is passed as a parameter to the tasks that compose the overall functionality of the system and permission to invoke the task is granted to the initiating user according to her role. Furthermore, several different GUI views have been implemented and the final front-end is constructed after role assignment achieving an extra layer of transparency for the separate roles. Three basic role groups were defined in the system.

- The *patient role* that allows the patient to remotely access information concerning his/her current treatment status as well as any information stored in the DDMS.
- The *healthcare professional role* that gives access to the patient information in the DDMS. Each healthcare professional is tightly coupled with certain patients and can only view and alter their clinical information. An auditing mechanism ensures recording of every change made. This poses a strong security mechanism for intentional or nonintentional malalteration of information. Furthermore, the healthcare professional is provided with a smart interface to interact with the IIAS. He has the ability to enable reporting for all or part of the decision made by the system.
- The *administrator role* that allows knowledge administrators to import new knowledge entities in the system. New medications and diseases can be imported to the system for future use by healthcare professionals. Furthermore, new users and their roles can be defined.

User authentication is achieved at a DB scope through the usual username–password scheme. Hashing algorithms are implemented for secure transmission of user data. User-oriented data views provide further security by restricting access to specific medical data only to relevant users. On hardware level, a high level of redundancy is achieved using technologies, such as redundant array of inexpensive disk (RAID) with hard disk (HD) mirror imaging. Online transaction processing (OLTP) and online analytical processing (OLAP) algorithms that are implemented in the proposed system reside on different server machines to avoid interference between usual transactions on the patient object and decision support algorithms [43].

2) Network Component: This research resulted in the implementation of a system with increased extranet traffic consisting of critical data. IPSec on the network layer, secure socket layer (SSL) on the transport layer are used to ensure secured communication between the remote servers. SSL over GPRS ensures secure transmission from the mobile phone. Hypertext Transfer Protocol Secure (HTTPS) is the protocol relied on to deliver secure transmission via the DDMS component. The central DB is protected using a router with specific access lists as well as an application layer firewall–intrusion detection system (IDS) that continuously monitors network traffic [44].

3) Physical Component–Securing Access: The physical security component's main role is to prevent unauthorized users to physically contact the SMARTDIAB's devices. Furthermore, this subcomponent has to deal with the possibility of a natural disaster or possible lack of energy resources. Critical systems of the proposed project will operate in controlled environments, safe from intrusion [45].

4) Policy Component–Designing Guidelines: Establishing security policies, guidelines, and procedures is a critical step toward securing an infrastructure and its information [43], [44]. Policies set the overall tone and define how security is perceived. In the current information and communication technologies (ICT) platform, appropriate security policies have been designed and applied in such a way that they will protect confidential, proprietary, and sensitive information from unauthorized disclosure, modification, theft, or destruction.

VII. PILOT EVALUATION

In order to evaluate the SMARTDIAB's usability, a preliminary study is in progress in the MITERA General Maternity and Children's Hospital, Athens. The study is performed by the platform's developers, in cooperation with physicians and patients with T1DM and aims at analyzing the user's behavior and feelings when using the system. The evaluation of system usability is based on subjective questionnaires designed for patients and doctors, which acquire information related to efficiency, convenience, reliability, user acceptance, etc. [46]. The initial feedback from the end-users shows that the system is user friendly and allows the efficient management of diabetes data.

Furthermore, technical evaluation of the SMARTDIAB pilot version is carried out. In the following, aspects of the technical evaluation of SMARTDIAB's modules, emphasizing on the MPA, DDMS, and the IIAS, are presented.

A. Evaluation of MPA and DDMS

The technical evaluation of the MPA and DDMS has been focused on the examination of the provided service quality on wireless operation environment. To this end, the Wireshark

TABLE I
AVERAGE MEASURED VALUES OF DATA TT AND PRP OVER GPRS

	Morning			Noon			Evening		
Scenario	PS	TT	PRP	PS	TT	PRP	PS	TT	PRP
Twice / day	2.7	9.98	<5%	1.9	9.58	<5%	2.1	12.49	<5%
Once / day	4.9	16.80	<5%	4.9	16.42	<5%	4.9	17.06	<5%
Once / week	34	88.60	<5%	34	77.89	<5%	34	93.33	<5%

Values represent PS in KB and TT in seconds.

TABLE II
AVERAGE MEASURED VALUES OF DATA TT AND PRP OVER Wi-Fi

	Morning			Noon			Evening		
Scenario	PS	TT	PRP	PS	TT	PRP	PS	TT	PRP
Twice / day	1.5	8.79	<5%	2.2	18.00	<5%	1.2	6.67	<5%
Once / day	4.3	11.37	<5%	4.3	15.46	<5%	4.3	8.80	<5%
Once / week	30	36.38	<5%	30	42.15	<5%	30	39.02	<5%

Values represent PS in KB and TT in seconds.

network analyzer software has been used, in order to evaluate the transmission of the data stored in the mobile phone to the PMU's DB using either the GPRS or the Wi-Fi network. The used mobile phone was a HTC Touch Diamond 3G mobile phone with Windows Mobile 6.1. The evaluation has been performed in terms of average transmission time (TT), and average packet retransmission probability (PRP) throughout different periods of the day. The following schemes of data entry from an individual with T1DM have been considered.

1) *Data stored in the morning:* Blood glucose measurement, food intake, and blood pressure measurement.
2) *Data stored in the noon:* Blood glucose measurement and food intake (two meals).
3) *Data stored in the evening:* Blood glucose measurement, food intake (two meals), and exercise data.

Three different scenarios of data transmission between the mobile phone and the PMU Web server have been tested. The user sends her/his measurement to the Web server 1) twice per day; 2) once per day; and 3) once per week. It has to be noted that in scenario 1), one or two different schemes can coexist (e.g., {1 or 1+3}, {2 or 1+2}, and {2 or 2+3}), depending on the time of the day the user transmits the data. The results for different data packet sizes are summarized in Tables I and II for transmissions over GPRS and Wi-Fi network, respectively.

The simulation results indicate that the accurate and acceptable transmission of diabetes data from a 3G mobile phone to a Web server over the GPRS or the Wi-Fi network is feasible. Furthermore, the transmission over Wi-Fi is generally faster than the transmission over GPRS, especially in the evening hours.

B. Evaluation of the IIAS

A two-stage evaluation procedure has been followed: 1) evaluation of the personalized glucose–insulin metabolism model; and 2) evaluation of the IIAS ability for closed-loop glucose control. It has to be noted that although the preliminary results have shown that the novel spectroscopic technique can provide a real solution to the online noninvasive monitoring of blood glucose levels, the Raman system could not be used in the pilot evaluation of the SMARTDIAB platform. Thus, within the framework of the IIAS evaluation, the CGMS provided by Medtronic along with the Medtronic-Minimed Guardian RT (http://www.medtronic.com/) that provides real-time glucose readings every 5 min, have been used. The whole system consists of a tiny glucose-sensing device named "sensor," combined with a pager-sized device called a "monitor" attached to a belt or the waistline. The sensor is inserted subcutaneously into the abdomen, measures the levels of glucose in the interstitial fluid and sends the information to the monitor by means of wired (Medtronic's MiniMed device) or wireless (Medtronic-Minimed Guardian RT system) communication.

1) Evaluation of the Personalized Glucose–Insulin Metabolism Model: Data from 12 T1DM patients have been used for the development and retrospective evaluation of the personalized glucose–insulin metabolism model [47], [48]. The patients were monitored for a ten day period. For this period, all patients with T1DM have recorded information regarding the time and the amount of carbohydrates ingested and the insulin boluses administered for the meals or for correction purposes. For each patient, data corresponding to the 60% of the monitored days has been used for training purposes (model development), while the remaining 40% for testing (model evaluation).

In order to evaluate the performance of the developed models in terms of matching the predicted glucose profiles with the original ones, the RMSE, and the correlation coefficient (CC) between the values estimated by the models and the glucose levels measured by CGM have been calculated for a 30 min prediction horizon with estimation sample time equal to 5 min for the testing sets. The mean RMSE and the corresponding standard deviation (SD) were equal to 16.18 ± 4.02, while the mean CC and SD were equal to 0.94 ± 0.02. The aforementioned values show that the model can predict accurately the glucose profile and that the predicted profile follows the original one. Furthermore, in order to investigate the clinical accuracy of the proposed model, the continuous glucose error grid analysis (CG-EGA) has been performed [49]. The results show that the percentage of clinically accurate predictions is 87.83% at hypoglycemia (78.00% accurate + 9.83% benign), 99.99% at euglycemia (90.92% accurate + 9.07% benign), and 99.94% at hyperglycemia (89.50% accurate + 10.44% benign), indicating that the predictions are accurate in both physiological and critical ranges. The results from all patients show that the proposed hybrid model is able to predict the glucose profile based on the intelligent analysis of past data. It is important to note that the proposed model can be personalized to a specific patient, through appropriate real-time training with his/her own data. Thus, the model proved to be able to produce personalized accurate–both in terms of mathematical and clinical accuracy–glucose predictions for a 30 min horizon, and provide early recognition of hypoglycemic and hyperglycemic events.

2) Evaluation of the IIAS Ability for Closed-Loop Glucose Control: The novel IIAS has been evaluated using one-day data produced from the *in silico* patient taking into account regular meal profiles, corresponding to breakfast at 8:00 (50 g CHO),

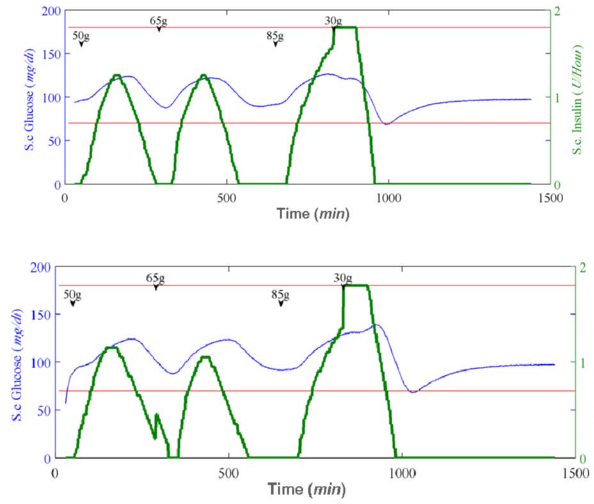

Fig. 7. Glucose (blue line), sc insulin infusion rate (green line), and amount and time of carbohydrates intake (black arrows) (upper panel) for noise with SD equal to 1% of current glucose, $t_{\mathrm{sc}} = 5$ min and $t_m = 0$ min, and (lower panel) for noise with SD equal to 1% of current glucose, $t_{\mathrm{sc}} = 10$ min and $t_m = 20$ min. The red lines show the normal glucose range.

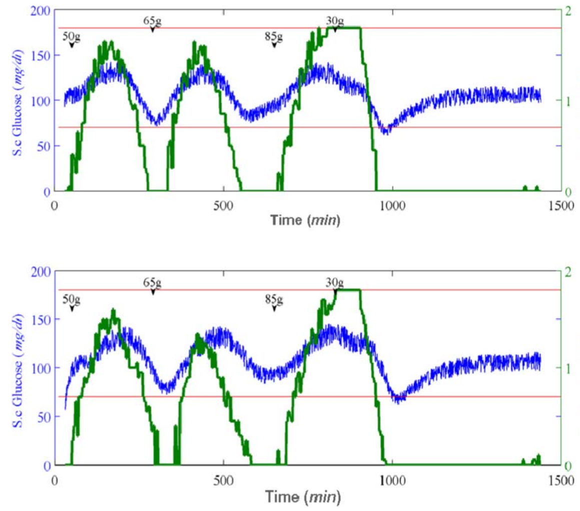

Fig. 8. Glucose (blue line), sc insulin infusion rate (green line), and amount and time of carbohydrates intake (black arrows) upper panel) for noise with SD equal to 20% of current glucose, $t_{\mathrm{sc}} = 5$ min and $t_m = 0$ min, and (lower panel) for noise with SD equal to 20% of current glucose, $t_{\mathrm{sc}} = 10$ min and $t_m = 20$ min. The red lines show the normal glucose range.

lunch at 12:00 (65 g CHO), dinner at 18:00 (85 g CHO), and a snack at 21:00 (30 g CHO) [37]. The resulted simulated sc glucose data was perturbed by additive white noise and time delays. Particularly, additive white noise with zero mean value and SD equal to either 1% or 20% of the current glucose value, was used to corrupt the sc glucose data. Furthermore, delays between blood glucose and sc glucose (t_{sc}), and due to the tubing in an *ex vivo* monitoring system (t_m) were considered and simulations for the following two sets of delay values: $t_{\mathrm{sc}} =$ 5 min and $t_m = 0$ min; $t_{\mathrm{sc}} = 10$ min and $t_m = 20$ min, were carried out. Whenever the glucose concentration was lower than 90 mg/dl, the insulin infusion rate was set to zero. In the NMPC operation of the IIAS, a constraint of 1.8 U/h was imposed to the maximum insulin infusion rate.

The results from the four simulation studies corresponding to combinations of the aforementioned white noise and time delay values, are presented in Figs. 7 and 8. All simulations have been performed with meal information (time and CHO are provided in Figs. 7 and 8). It is remarkable that the IIAS is able to respond even in the case of a large meal disturbance (e.g., ingestion of 85 g CHO at time 18:00) and regulate properly the insulin infusion rate, in order to keep glucose into physiological range and reduce glucose oscillations. From both figures, it is shown that the proposed IIAS is resilient to large noise levels in the glucose measurements, and it is able to handle time delays and disturbances due to real meal intakes. It is worth mentioning that the proposed IIAS is able to keep glucose levels close to euglycemia. The *in silico* results demonstrate that the IIAS is able to perform well in a wide range of conditions, including various noise levels, time delay, and different size of meals taken at any time of the day. Furthermore, the use of a real-time self-adaptive ANN permits the system personalization and the efficient deal of a changing environment.

The *in vivo* evaluation of the IIAS is in progress. The clinical trials are being conducted as a single-center investigation in the specialized juvenile diabetes center at the MITERA General Maternity and Children's Hospital using specific clinical protocol.

VIII. SUMMARY

In this paper, the SMARTDIAB platform has been presented, representing a unified approach for the intelligent monitoring, management, and followup of T1DM patients. The platform integrates mobile infrastructure, wireless personal area networks (WPAN), and Internet technology along with commercially available and novel glucose measurement devices, insulin delivery systems, advanced modeling and control techniques, and tools for the intelligent processing of the available diabetes patients information. The platform permits the continuous monitoring and the continuous provision of healthcare to T1DM patients using telemedicine, through GPRS network infrastructure, and the Internet. User-friendly Web and mobile phone interfaces along with advanced data processing functionalities allow for the optimization of diabetes mellitus treatment through computational tools for real-time personalized estimation of insulin infusion rate. Additionally, a central DB, containing patients related data (e.g., demographic data), clinical and laboratory exams, along with appropriate tools for data storage, management, mining and visualization allow healthcare professionals to assess the health status of their patients and update/modify the applied treatment. Furthermore, an intelligent DSS allows risk assessment for long-term diabetes mellitus complications.

The next step toward a complete evaluation study includes a validation procedure in various hospitals investigating the level of satisfaction of users requirements along with the corresponding cost-effectiveness study. Furthermore, although initial results have indicated that the proposed platform is accepted by the users, further investigation is needed in terms of both hardware and software modules, integrated in the SMARTDIAB platform. Emphasis will be given to the novel CGM device and the optimization of the proposed IIAS for closing the loop between the glucose-monitoring device and the insulin pump.

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K. Varotsis, biography and photograph not available at the time of publication.

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