Transactions of the Institute of Measurement and Control 26, 3 (2004) pp. 1−16

Intelligent alarms integrated in a multi-agent architecture for diabetes management

M. Elena Hernando, Gema García,
Enrique J. Gómez and Francisco del Pozo

Grupo de Bioingeniería y Telemedicina, E.T.S. Ingenieros de Telecomunicación.
Universidad Politécnica de Madrid, Ciudad Universitaria s.n., E-28040 Madrid, Spain

This paper describes the development of an intelligent agent that interprets blood glucose monitoring data received by a telemedicine-based diabetes management service. The agent generates automatic alarms when some deviations in the patient status are detected. The agent combines different methods to produce data summaries and automatic alarms based on statistics, rule-based techniques and model-based techniques. The rule-based analysis allows the detection of severe abnormalities using different time scales depending on the quality of the received information. The model-based analysis uses a physiological qualitative model implemented with a causal probabilistic network that detects deviations in the 'insulin effectiveness' along days. The KM (Knowledge Management) agent was tested with data from 11 patients with diabetes that used a telemedicine service during 1 year. The KM agent detected anomalous situations in the 100% of the cases where a therapy modification was decided by the healthcare professional; the agent detected abnormal data in 37% of transmissions, being able to decrease professionals' workload due to telemedicine. The advantages of an automatic response integrated in a telemedicine service are that it focuses doctors' and patients' attention on abnormal data and gives instantaneous feedback to patients reinforcing the education and the motivation aspects of the therapy.

Key words: causal probabilistic network; diabetes; intelligent alarms; telemedicine.

Address for correspondence: M. E. Hernando, Grupo de Bioingeniería y Telemedicina, ETSI Telecomunicación, Ciudad Universitaria s.n., E - 28040 Madrid, Spain. E-mail: elena@gbt.tfo.upm.es

 10.1191/0142331204tm119oa

Introduction

Diabetes mellitus is a chronic disease that affects more than 5% of the Western population and is responsible for up to 8% of national healthcare expenditure (Waldhäusl, 2001). Diabetes is characterized by an increased concentration of blood glucose due to an abnormal metabolism of carbohydrates related with the secretion of the insulin hormone. The metabolic disturbances generate severe, acute and long-term complications that are responsible for premature death and disability (de Leiva *et al.*, 1995).

The process of diabetes care is complex and requires patients taking an active role in the management of their illness. In Type 1 diabetes, the pancreas is unable to produce insulin and a treatment based on exogenous insulin administrations is required. The goal of the insulin therapy is to achieve normoglycaemia avoiding both the hypoglycaemia episodes that can cause coma and death, and the hyperglycaemia states that cause long-term complications such as neuropathy, nephropathy, retinopathy and cardiovascular diseases. The DCCT study (DCCT, 1993) demonstrated that the intensive insulin therapy (IIT), composed of the administration of insulin distributed into multiple daily injections, can reduce and delay the long-term complications. In IIT, the insulin blood concentration is similar to the profiles in normal subjects and lower blood glucose concentrations are achieved. The main inconvenience of the IIT is that it increases the incidence of hypoglycaemic episodes (DCCT, 1997) when the insulin doses are not properly adjusted to the diet, physical exercise or other events such as illness. Currently, IIT is recommended for type 1 diabetes, requiring patients to have a strong education in the management of their illness, and able to react in a proper manner under any situation that can appear during his/her daily life.

Nowadays, telemedicine is radically changing healthcare models, particularly in the way healthcare is currently delivered. Earlier experiences of telemedicine in diabetes management aimed at improving communication and co-operation between patients and doctors, but in many cases were limited to the transmission of computerized blood glucose profiles by telephone modem-based home glucose monitoring equipment (Billiard *et al.*, 1991). In some of these experiences, patients received advice over the telephone on insulin adjustments and food intake after transferring results to the clinical centre (Ahring *et al.*, 1992). Recently, telemedicine is being applied in wider-scale healthcare experiences as a main tool for the home care and diabetes education in patients (Wojcicki *et al.*, 2001; Bellazzi *et al.*, 2002b; Gómez *et al.*, 2002; Starren *et al.*, 2002).

Telemedicine is an effective way to support patients' decisions, providing them with a 'supervised autonomy' carried out remotely from the hospital (Gómez *et al.*, 2002), but telemedicine increases the amount of information the physicians have to process and it also demands a higher interaction with patients. For this reason, telemedicine increases physicians' workload and it is crucial to complement the new services with automatic data-processing tools able to focus the doctors' attention on abnormal data optimizing the time needed for data interpretation.

The analysis of blood glucose using different approaches is extensively reported in the literature: Kahn *et al.* (1991) analysed the correlation between insulin modifications and their effects in the blood glucose profiles; time series analysis are used to extract the blood glucose modal day (Deutsch *et al.*, 1994). Other works reported the use of expert systems for therapeutic advice delivery to patients at home (Levy *et al.*, 1989; Albisser *et al.*, 1996); rule-based reasoning was applied combined with mathematical models for the extraction of a BGL modal day (Lehmann *et al.*, 1994) and also for the identification of problems and the generation of a set of alternative suggestions dealing with insulin therapy, diet or physical exercise (Montani *et al.*, 1999).

This paper describes the development and integration of an intelligent agent that combines different methods to interpret blood glucose monitoring data received by the M2DM telemedicine service.

The M2DM telemedicine service

The aim of the M2DM telemedicine service is to provide new telemedicine services for diabetes care emphasizing the provision to physicians and patients of personal health services 24 h a day using a multi-access concept considering a full range of nonexpensive and widely accepted information technologies. The M2DM project (M2DM, 1999) was partially funded by the European Commission within the Information Society Technology Program. The M2DM Consortium is composed by five universities, four hospitals and two industrial partners from five European countries.

The M2DM makes possible the universal access to the information through the use of basic technologies with a wide penetration in the society (e.g., conventional telephone) combined with intermediate technologies supported by computers or mobile phone terminals (e.g. web, WebTV, SMS) and also combined with more advanced and innovative technologies (e.g., Palmtops; PDAs, WAP and GPRS) the use of which is limited to a smaller group of users due to their availability, costs or the required users' skills. The M2DM project builds a new environment of co-operation between patients and doctors in which, depending on their skills, preferences or the scenario of use, users can access the information through a set of integrated services with additional features for telecare and visit management, such as text and voice mailing; management of the electronic patient record; automatic generation of reports; intelligent alarms; tele-education and intelligent knowledge management (Bellazzi *et al.*, 2003).

The multi-access services are implemented with a multi-agent architecture (Hernando *et al.*, 2002) where several agents are coordinated by a middleware module called Organizer (Figure 1). Some of the 'M2DM agents' are in charge of communications with the different user terminals integrated within the M2DM Centre (named Communication Server agents) and other agents are in charge of data analysis and data processing (named Application Server agents). The number of agents present in a M2DM Centre is not limited *a priori* and it only depends on the kind of terminals that will be used at each site.

From January 2002, the M2DM system is installed and running, providing telemedicine services to the four hospitals from the three countries involved in the clinical trial. The study is performed as a randomized controlled trial, where

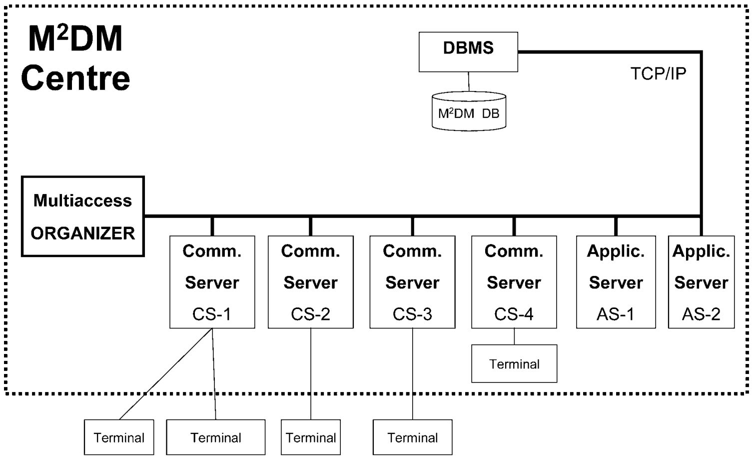

Figure 1 The multi-access server architecture composed by the common database and its management system (DBMS), the multi-access Organizer, the agents (CS: Communication Server; AS: Application Server) and the user terminals

80/80 patients (active vs controls) are involved (Bellazzi *et al.*, 2003). All the patients, both the experimental-group and the control-group patients, are followed by regular routine visits in the outpatient section of the evaluation centre using the standard visit schedule, when possible every 3 months (0, 3, 6, 9 and 12 months).

Automatic data-processing methods

One of the goals of the M2DM project is to supply the right knowledge to the right people in the right moment. For this reason, the M2DM service provides users with Knowledge Management (KM) tools (Bellazzi *et al.*, 2002a) that can be classified into three types according to the way they are activated: 1) activated on users' demand, including graphical data representation, mathematical simulation of blood concentrations for different insulin therapies, co-operative tools (García-Olaya *et al.*, 2002), etc.; 2) triggered by data reception, including automatic data processing for alarm generation; 3) triggered by the system, including dynamic preprogrammed notification of events according to the preferences of the own users, both patients and physicians.

This paper describes a KM agent triggered by data reception that generates automatic summaries and alarms when some deviations in the patient state are detected. The data analysis process has to extract as much information as possible under any situation of data completeness. For this reason, the KM agent combines different methods to analyse blood glucose monitoring data and insulin data, such as statistics, rule-based and model-based techniques, adapting its results to the data availability.

Statistic-based analysis

The statistic-based analysis is used both for the generation of a summary whenever new data is received at the telemedicine server and for extracting the basic information used in the rule-based and model-based analysis.

This analysis is based on the calculation of basic mathematical operation and first-order statistics on the blood glucose monitoring data. The blood glucose readings are classified as pre- or postprandial measurements associated to any of the four main daily intervals (associated with breakfast, lunch, dinner and night). The average and standard deviation is calculated both for all the measurements in the interval and also for each daily interval. Each blood glucose value is also compared with the pre- and postprandial targets defined for the specific patient. The result is the calculation of the absolute number of hypoglycaemias and hyperglycaemias within the interval and the percentages.

The analysis described above is done in two different time-scale levels: the first level includes the blood glucose measurements received in a single data transmission and the second level includes the past data aggregated with the new data. The results are presented to users as a text message whenever they send data to the telemedicine centre.

The outcome of this type of analysis is very robust if the number of readings included at each interval is high, but it can lead to erroneous conclusions under a situation of missing data. In order to help users in their interpretation process, the analysis outcomes are always presented together with the absolute number of days in the analysis period, the total number of readings and the number of readings associated to each pre- and postprandial interval.

Rule-based analysis

The rule-based analysis is used for the detection of severe abnormalities in patient control. Severity is defined as a combination of abnormal readings and its frequency in the analysis period. The definition of severe alarms can be considered patient independent, so hypoglycaemia and hyperglycaemia states are defined uniquely for the whole diabetic population. Hypoglycaemia is defined as any blood glucose reading under 70 mg/dl and hyperglycaemia is defined as any blood glucose reading above 200 mg/dl.

The definitions of the severe problems detected by the KM agent are the following:

- *Hypoglycaemia status*: the presence of hypoglycaemia values. The alarm is triggered if more than X hypoglycaemias per week are found.
- *Hyperglycaemia status*: the presence of hyperglycaemia values. The alarm is riggered if more than Y% of the readings are hyperglycaemias.
- *Oscillating status*: the simultaneous presence of hypo- and hyperglycaemia values. The alarm is triggered if more than Z hypos per week are found and more than V% of the readings are hyperglycaemias.
- *Hyper-insulination*: the administration of insulin decided by the patient is very high. The alarm is triggered if the reported insulin doses are W% higher or more than the dose prescribed by the diabetologist.

All the numerical values included in the definition of the rules (X, Y, Z, V, W) can be configured with different values for each clinical site. The patient state analysis is checked simultaneously using three different periods depending on the received information:

1) The period that covers the data received in the current communication process. This analysis is discarded when the number of days is small.
2) Pre-fixed periods: up to 2 weeks/1 month periods. This analysis includes past data stored in the database. These analyses are discarded when there exists a therapy update within the period.
3) The therapy related period: includes all the data sent after the last therapy update.

Figure 2 shows the glucose profile of a patient that triggered an alarm indicating a severe status of hyperglycaemia. The rule-based analysis was performed setting the rule values to $X = 7$, $Y = 65$, $Z = 4$, $V = 65$, $W = 100$. The data plot shows the presence of a majority of high blood glucose readings together with normal values and three hypoglycaemia readings.

When the KM agent detects any severe problem it generates two different text messages to notify the alarm to the patient and to the responsible physician. Users receive the notification by web, e-mail or SMS, according to their own preferences.

This type of analysis detects the general patient's state but it is sensible to the amount of missing data and also sensible to its distribution. For this reason, the KM agent performs a deeper analysis based on a physiological model able to detect abnormalities that appear in a specific daily interval (breakfast, lunch, dinner and night) with fewer data requirements.

Model-based analysis

The model-based analysis is used for detecting the deviations in the 'insulin effectiveness' over days according to a physiological model for diabetic patients represented with a causal probabilistic network (CPN) (Pearl, 1988), which is one of the approaches widely used within the artificial inteligence community to manage uncertainty. This causal model can manage uncertainty and data incom-

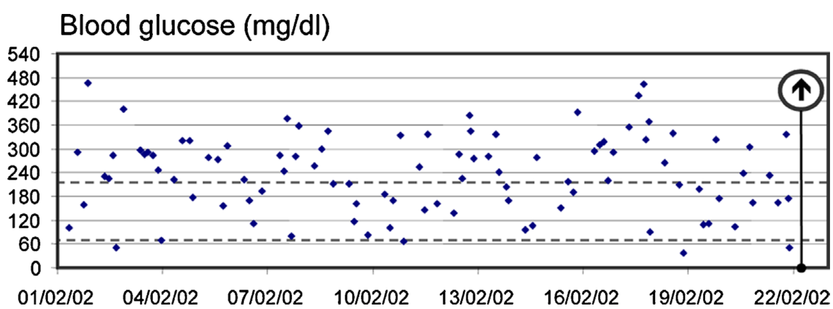

Figure 2 Real case of a patient with abnormalities in the metabolic control; rule-based analysis results for a 3-week period

pleteness, which are two of the main characteristics in the ambulatory monitoring of patients. In addition, the choice of CPNs facilitates the model reutilization mainly because it supports both diagnostic and predictive reasoning. The KM agent uses the CPN for the interpretation of data but it was previously used for simulation in an educational tool for diabetic patients (Hernando *et al.*, 2001).

The qualitative model: The model represents the day divided into four time intervals ('breakfast', 'lunch', 'dinner' and 'night' intervals). Figure 3 shows the representation of one of the four intervals using a CPN. The 'Insulin EFFECT' node can be defined as 'the metabolic effect of the plasma insulin on the blood glucose levels during the interval *X*'. This concept embraces both the insulin 'quantity' and its 'effect'; this means that it includes all the factors that can affect insulin effects, such as changes in the insulin sensitivity, in the exogenous administration, subcutaneous absorption, etc. The 'Insulin EFFECT' node represents the effectiveness of the insulin in the interval and, in combination with the carbohydrate (CH) intakes within the time interval (timing and amount), influences the blood glucose concentration and the presence/absence of ketonuria. The complete 24h CPN model concatenates four intervals and contains four 'Insulin EFFECT' nodes, which represent 'the metabolic patient's state' for a single day.

The inputs into the metabolic model are divided into two categories: self-monitoring patient data, which can be considered the 'symptoms' of the metabolic state, such as blood glucose and ketonury measurements (child nodes in the

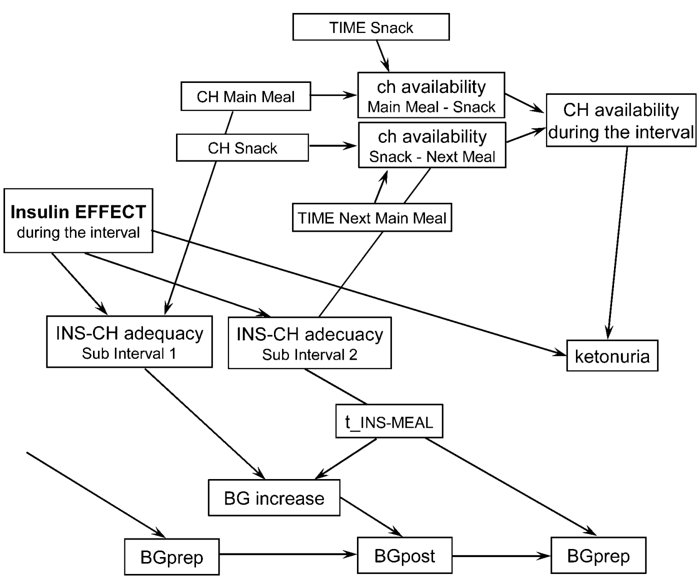

Figure 3 The CPN model for a daily interval. INS, insulin; CH, carbohydrates; BGprep, preprandial blood glucose measurement; BGpost, postprandial blood glucose measurement; t_INS-MEAL, time span between the insulin administration and the meal

network); and the 'causes' affecting these measurements, such as insulin, meals, meal time and time span between insulin injections and their associated meals (parent nodes in the network).

The physiological parameters of this model are qualitative; this means that no quantitative values in insulin units, in minutes or in grams are managed. In the CPN, each parameter is represented as a node with several qualitative states: blood glucose (low, normal, high, very high); carbohydrate intake (excessive, adequate, insufficient); time of a meal (early, adequate, late); ketonuria (negative, positive). The reason for using qualitative values is that, for example, one specific absolute delay of a meal in minutes can have different effects from one patient to the other, and even on the same patient at different stages of her illness. Doctors are not concerned with meal delays provided the patient's state is not affected negatively. The relations between the model parameters were obtained from experts and are expressed in qualitative terms, e.g., 'If a main intake is delayed, then it is possible that it will produce ketonuria and a low blood glucose measurement'.

The CPN model was evaluated as the core of Diabnet (Hernando *et al.*, 1996), a decision support system for therapy planning that integrated the CPN model in a hybrid architecture where the qualitative results were later on converted into quantitative insulin dose modifications adapted to the patient characteristics. The Diabnet system was tested with monitoring data from diabetic patients demonstrating the suitability of the qualitative CPN model for data interpretation (Hernando *et al.*, 2000). The current version of the CPN model is implemented in Java integrating the libraries developed in the Elvira project (Elvira Consortium, 2002).

Detection of the insulin effectiveness: The KM agent uses blood glucose readings as input and, when available, additional knowledge about patients habits (i.e., diet modifications) and the therapy compliance. This information has been registered by patients and transmitted to the telemedicine server using any of the multi-access terminals provided by the project (web forms, glucometers, PDAs, conventional phones, etc.).

The KM agent feeds the CPN with the data stored for the specific patient along all the days included in the analysis period. Patient-specific ranges are considered to classify blood glucose readings. The network infers the insulin effectiveness associated to each of the four daily periods giving qualitative information about the lack or the excess of exogenous insulin. The KM agent generates new alarms when the network gets the values 'insufficient' or 'excessive' for the insulin effectiveness at any of the four daily periods, focusing physician attention on those points where the insulin therapy should be modified to improve patients' metabolic control. After receiving the alarm, the physician can display the graphical representation of data in the analysed period to decide the appropriate therapy adjustment.

Figure 4 shows the result of the model-based analysis for the same patient than in Figure 2 and for the same period. The figure displays the 'insulin needs' associated with each of the four daily intervals. Positive values correspond to a decreased 'insulin effectiveness' meaning that the administered insulin having an effect in the interval was insufficient. Negative values correspond to an excess

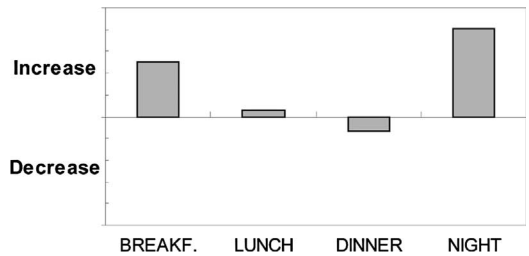

Figure 4 Model-based analysis results; insulin needs associated to the four daily intervals (breakfast, lunch, dinner and night)

of 'insulin effectiveness' and are related to the presence of low blood glucose and hypoglycaemia readings. Very positive or negative values indicate a problem in the patient's metabolic control and the need of a therapy adjustment at this point. The result of the model-based analysis shows abnormalities in the night and breakfast intervals.

Description of the KM agent

The KM agent has been integrated as a new agent in the multi-access architecture and is activated whenever new monitoring data is received at the central multi-access server from any patient. The KM agent is triggered whenever a new data reception event happens. The agent performs the automatic blood glucose and insulin data processing both for generating summaries for patients and for both generating alarms showing deviations in the patient state.

The KM agent co-operates with the existing communication agents to provide the analysis results to the recipient users. The communication of the KM agent with the Organizer follows the messages protocol defined in the multi-agent architecture for the co-ordination between the Organizer and the multi-access agents (Bellazzi *et al.*, 2003). Modifications in the previous communication protocol were not required. The integration in an specific clinical site requires the Organizer to be pre-programmed with a additional activity–event relationship that activates the KM agent whenever new monitoring data is received from a patient.

Figure 5 shows the complete process of co-ordination between the agents and the Organizer at the multi-access server: 1) the glucometer agent receives data from a patient, it stores them in the database and notifies the Organizer of a 'Data reception event' providing information about the author; 2) the Organizer consults the pre-programmed activity–event relationships in the database for this specific event and author; 3) the Organizer notifies the KM agent of the event, which performs the data analysis, detect the alarms and composes the messages for the users. Finally it sends the 'New message event' to the Organizer. 4) The Organizer again consults the pre-programmed activity–event relationships for this new event looking for the notification way preferred by each recipient (web, conven-

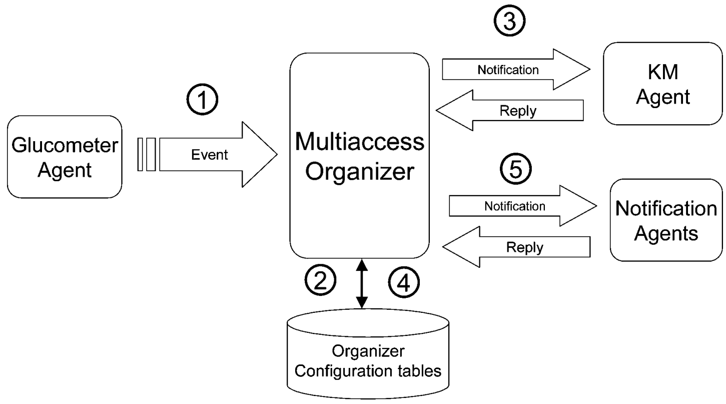

Figure 5 Interoperability between the KM agents and the Organizer

tional e-mail or SMS); and 5) the Organizer activates the correspondent/s notification agent/s that will deliver the message/s.

Figure 6 shows in more detail the actions performed by the KM agent using the UML notation. Data summaries and alarms are recorded in the database together with the information to identify the patient, the date of the analysis, the analysis period and other relevant information for alarm interpretation. This information is also available in other scenarios, such as the graphical visualization of monitoring data.

The KM agent generates a single test message that summarizes the results of the three data analysis methods and is structured as follows:

- Header: includes the general identification of the telemedicine service.
- Subheader: clearly distinguishes this type of messages from others generated by humans. It informs about the nature of the message – 'automatic message generated by the system' – and the reason – 'Reception of patient's monitoring data'/'Alarm in patient's monitoring data'.
- Body: the message body has three different sections:
  - Information about the blood glucose data received: date and time of the analysis and data summary (no. of measurements; global statistics; no. of hypoglycaemia values; no. of hyperglycaemia values; statistics along daily periods; etc.);
  - Information about the triggered alarms.
  - Information about the patient's whole monitoring data available at the hospital: this includes a blood glucose summary similar to the previous one for the whole period and information about other monitored variables, such as intakes, insulin daily adjustments, illness, etc.).
- Footer: includes the contact information of the personnel at the hospital (only for patients).

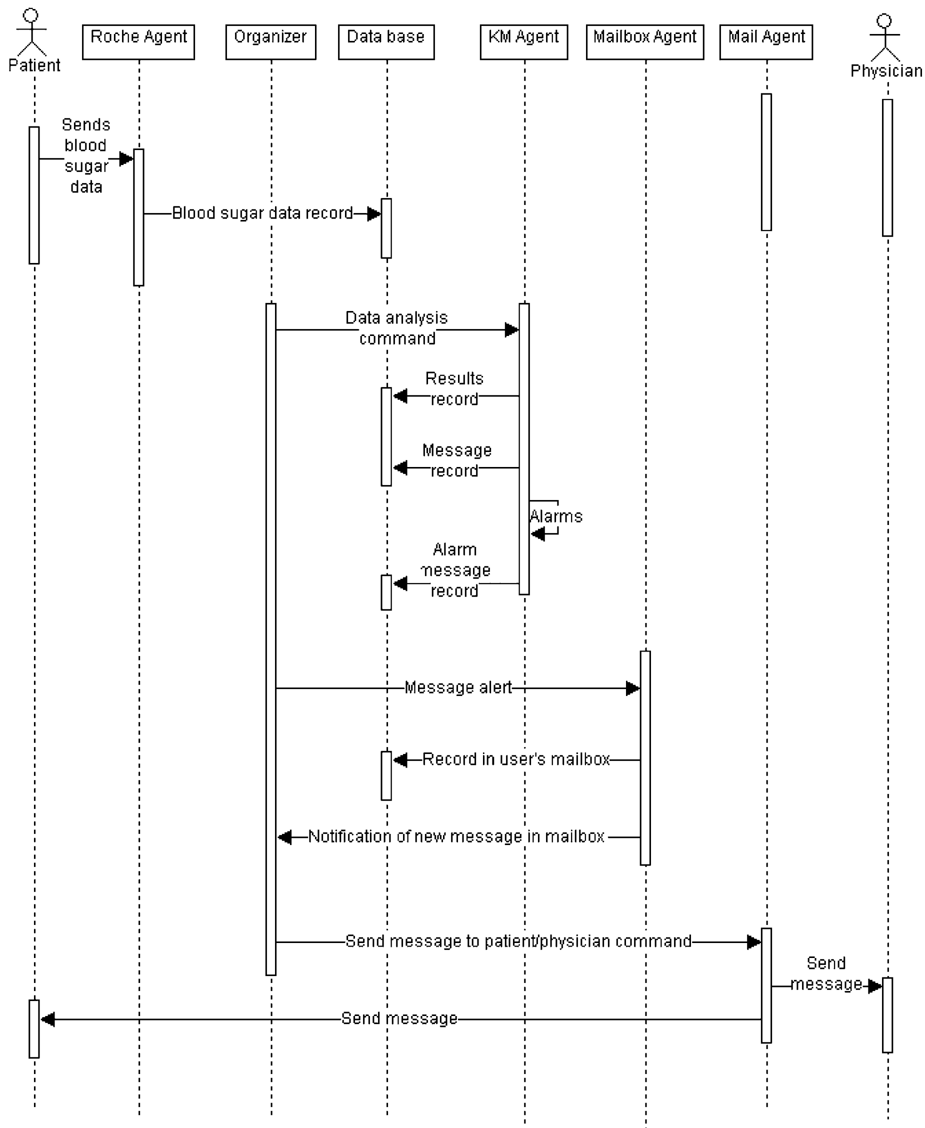

Figure 6 The KM agent functionality

Evaluation methodology 333

We tested the reliability of the KM agent previously to use it as a tool in clinical 334
practice. Evaluation is performed in two aspects: 1) comparison between the 335
abnormalities detected by the agent and therapy modifications prescribed by the 336
physician during the 1-year trial, and 2) simulating agent activation and data 337
analysis for all the times when patients sent data to the multi-access server, and 338

analysing the warning messages that would have been generated if the tool had been working in the service.

Data used to test the KM agent comes from 11 insulin-dependent patients that concluded the 1-year M2DM trial at the Hospital de Sant Pau i la Santa Creu, in Barcelona, Spain. Each patient used the M2DM services for 1 year and was provided with a glucometer and a Roche Acculink™ modem for data transmission, as well as Internet access to the web platform, where monitoring data could be registered manually. The data sent were registered in the central server and available to the physician immediately. When the physician opens a web session, the telemedicine service shows the last patients' data transfers and the physician goes to the patient electronic logbook to assess the patients' metabolic state and, if required, to prescribe a therapy modification.

Results

During the 1-year clinical evaluation of the telemedicine service, the physician used the telemedicine service to analyse patients' data whenever a new transmissions was done: patients performed 735 monitoring data transfers; the physician assessed 100% of them using the web application and decided 17 changes in the insulin therapy.

Blood glucose measures were frequently stored in the system (7997 total blood glucose readings) but the incidence of missing data is high because most of the daily blood glucose profiles were not complete. Figure 7 shows the distribution

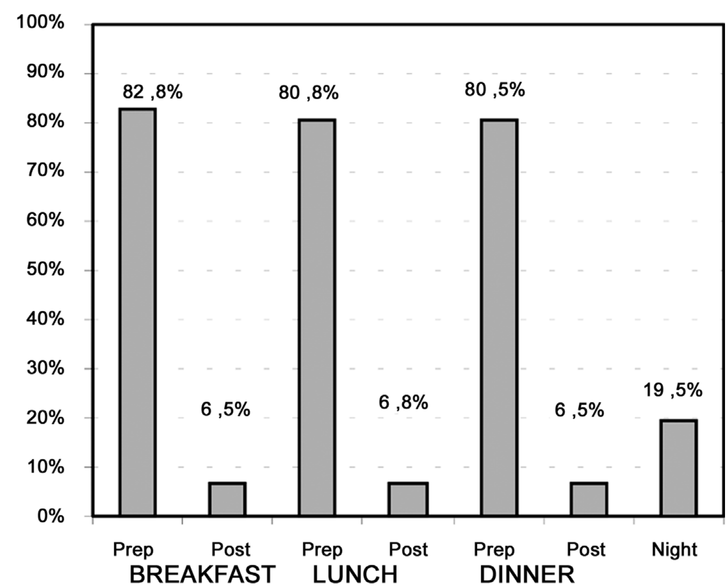

Figure 7 Percentage of available blood glucose measurements associated to preprandial and postprandial meal-time intervals

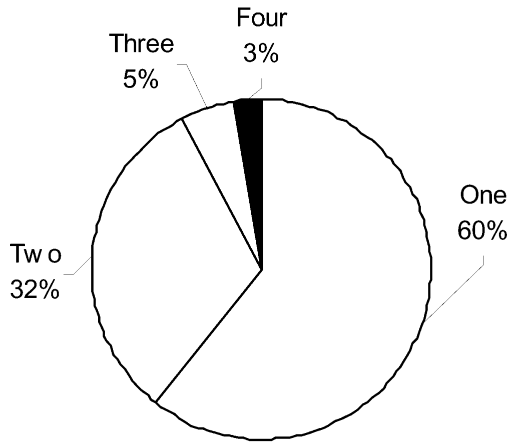

Figure 8 Distribution of the number of anomalous meal-time intervals detected by the KM agent ($n = 735$ data transfers)

of blood glucose readings registered at the server. The percentage of each kind of measure is referred to the maximum number of days with monitoring data from patients. A lower quantity of postprandial with respect to preprandial measures in daily profiles sent is shown.

Every physician's decision about therapy changes has been assessed with the KM agent, activating the data analysis process for each of the therapy change dates. The results obtained show that the KM agent triggered a warning in 100% of the cases where a therapy change was decided by the physician and in 94% of them the detected abnormalities were located in the same meal-time intervals where the physician modification was acting.

During the 1 year clinical study, patients performed 735 monitoring data transfers. In average, a patient receives from the KM agent 5.6 messages per month containing a summary of his/her metabolic state. The KM agent generated a warning in the 37% of data transmissions. Each warning contains an analysis showing deviations in the insulin needs for the four meal-time daily intervals. Figure 8 shows the percentage of meal-time intervals with abnormal results after the data analysis triggered by each data transfer performed by a patient. The results show that on most occasions, abnormal metabolic control (92% of cases) is restricted to one or two meal-intake intervals.

Discussion

The results of the statistic and the rule-based analysis can be presented to users in a very intuitive way because users are used to manage averages, percentages and rules. Both analyses are very reliable if the number of readings included at each interval is high, but they can deal to erroneous conclusions under situations of missing data. The rule-based analysis is very suitable for the detection of severe abnormalities in patient control but it does not provide information about the severity grade, which could help physicians in the therapy adjustment process.

The model-based analysis allows a deeper interpretation of data, providing information about the presence of a metabolic abnormality and also about the severity grade associated to the four time intervals (breakfast, lunch, dinner and night), focusing patient's and doctor's attention on the points where the therapy should be adjusted. On the other hand, the presentation to users of the model-based analysis results is more complex and less intuitive. The current work in the model-based analysis is centred in the evaluation of the most appropriate graphical representation both for patients and for doctors, in combination with the monitoring data. The current work in the rule-based analysis is the definition of additional rules for the detection of nonsevere abnormalities.

Conclusions

This paper presents a KM agent that combines different methods to analyse blood glucose monitoring data and insulin data, such as statistics, rule-based and model-based techniques. The combination of different methods to analyse blood glucose monitoring data and insulin data makes possible to extract relevant information about patient metabolic state under different situations of data completeness, usually present when implementing telemedicine services for chronic patients. The implantation of telemedicine services in clinical practice allows physicians the access to a large quantity of monitoring data not available before.

During the 1-year clinical evaluation of the telemedicine service, we found a high number of missing measurements. When comparing between the abnormalities detected by the KM agent and the therapy modifications prescribed by the physician, the results show that the KM agent detected an anomalous situation in the 100% of the cases where a therapy modification was decided by the health-care professional. The evaluation of results for each meal-time interval shows that anomalous situations are frequently present just at one or two meal-intake intervals, which focus physicians' and patients' attention on the points where a clinical intervention is required to improve the health state of patients with diabetes.

When simulating the agent activation for automatic alarm generation, the results show that the developed agent detected abnormal data in 37% of transmissions, so it can decrease professionals' workload due to telemedicine, as it could avoid physicians' intervention in 63% of cases.

The KM agent described in this paper has been successfully integrated in the M2DM multi-access server. Users can be aware of the data analysis results and warnings in two scenarios provided by the multi-access service: 1) notification scenarios – users are notified with text messages through web, e-mail or mobile SMS if they activate these features in their personal 'user's notification preferences'; 2) monitoring data review scenario – alarms are displayed in a graphical visualization of monitoring data. The processed information allows patients to compare their present metabolic state with the past, reinforces their knowledge about the effect of the therapeutic strategies and motivates them to continue registering information.

The advantages of integrating automatic response tools in a telemedicine service are clear because they provide two features that are very relevant in patients' care: 1) they give instantaneous feedback to patients, promoting patient interaction with the telecare organization and reinforcing their motivation to use the telemedicine system and 2) they focus doctors' and patients' attention on abnormal data preventing future risky situations. For this reason, the architecture of a telemedicine service should be designed to allow the integration of knowledge management tools in a seamless manner and without interfering with the existing functionalities. The presented work also shows the suitability of the M2DM architecture for the coordination of heterogeneous agents developed for different purposes such as multi-access communications and knowledge management ones.

Acknowledgments

This work has been partially funded by the European Commission Project M2DM (IST-1999-10315) and by the Spanish Research Council (Middlecare: TIC2002-02129; Red de Telemedicina (FIS G03/117). The authors wish to acknowledge the valuable work of all researchers of the Grupo de Bioingeniería y Telemedicina of UPM, specially to Angel García, Pedro Alvarez, F. Javier Perdices and Verónica Torralba for their contribution to the telemedicine service development. We specially acknowledge Dr Mercedes Rigla and Prof. Dr A. de Leiva from the Endocrinology and Nutrition Department at the Sant Pau Hospital in Barcelona, Spain, and Eulalia Brugués from Diabem, Spain, for their valuable contribution to this research work.

References

Ahring, K., Ahring, J.P., Joyce, C. and **Farid, N.R.** 1992: Telephone modem access improves diabetes control in those with insulin-requiring diabetes. *Diabetes Care* 15, 971–75.

Albisser, A.M., Harris, R.I., Sakkal, S., Parson, I.D. and **Chao, S.C.E.** 1996: Diabetes intervention in the information age. *Medical Information* 21, 297–317.

Bellazzi, R., Larizza, C., Magni, P., Montani, S., Carson, E., Roudsari, A., Hernando, M.E. and **Garcia, A.** 2002a: Deliverable 17: Methods for intelligence and KM–final report. EC M2DM project IST-1999-10315. Brussels.

Bellazzi, R., Larizza, C., Montani, S., Riva, A., Stefanelli, M., d'Annunzio, G., Lorini, R., Gómez, E.J., Hernando, E., Brugués, E., Cermeno, J., Corcoy, R., de Leiva, A., Cobelli, C., Nucci, G., del Prato, S., Maran, A., Kilkki, E. and **Tuominen, J.** 2002b: A telemedicine support for diabetes management: the TIDDM project. *Computational Methods & Programs in Biomedicine* 69, 147–62.

Bellazzi, R., Arcelloni , M., Bensa, G., Blankenfeld, H., Brugués, E., Carson, E., Cobelli, C., Cramp, D., d'Annunzio, G., De Cata, P., de Leiva, A., Deutsch, T., Fratino, P., Gazzaruso, C., García, A., Gergely, T., Gómez, E., Harvey, F., Ferrari, P., Hernando, E., Boulos, M.K., Larizza, C., Ludekke, H., Maran, A., Nucci, G., Pennati, C., Ramat, S., Roudsari, A., Rigla, M. and **Stefanelli, M.** 2003: Design, methods and evaluation directions of a multi-access service for the management of diabetes mellitus patients. *Diabetes Technology and Therapy* 5, 621–29.

Billiard, A., Rohmer, V., Roques, M.A., Joseph, M.G., Suraniti, S., Giraud, P., Limal, J.M, Fressinaud, P. and **Marre, M.**. 1991: Telematic transmission of computerised blood glucose profiles for IDDM patients. *Diabetes Care* 14, 130–34.

DCCT (Diabetes Control and Complications Trial) Research Group. 1993: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus, *New England Journal Medicine* 329, 977–86.

DCCT Research Group. 1997: Hypoglycemia in the Diabetes Control and Complications Trial. *Diabetes* 46, 271–86.

de Leiva, A., Lefèbvre, P. and **Nerup, J.** 1995: European dimension of diabetes research. *Diabetologia* 39, 5–11.

Deutsch, T., Lehmann, E.D., Carson, E.R., Roudsari, A.V., Hopkins, K.D. and **Sönksen, P**. 1994: Time series analysis and control of blood glucose levels in diabetic patients. *Computational Methods & Programs in Biomedicine* 41, 167–82.

Elvira Consortium. 2002: Elvira: An environment for creating and using probabilistic graphical models. In *Proceedings of the First European Workshop on Probabilistic Graphical Models* (PGM'02), Cuenca, Spain, 1–11.

García-Olaya, A., Gómez, E.J., Hernando, M.E., Perdices, F.J. and **del Pozo, F.** 2002: A middleware CSCW architecture for diabetes shared care. *EMBEC'02 (2nd European Medical & Biological Engineering Conference)*, 4–8 December, Vienna, 1376–77.

Gómez, E.J., Hernando, M.E., García, A., del Pozo, F., Cermeño, J., Corcoy, R., Brugués, E. and **de Leiva, A.** 2002: Telemedicine as a tool for intensive management of diabetes: the DIABTel experience. *Computational Methods & Programs in Biomedicine* 69, 163–77.

Hernando, M.E., Gómez, E.J., Del Pozo, F. and **Corcoy, R.** 1996: DIABNET: A qualitative model-based advisory system for therapy planning in gestational diabetes. *Medical Informatics* 21, 359–374.

Hernando, M.E., Gómez, E.J., Corcoy, R. and **del Pozo, F.** 2000: Evaluation of DIABNET, a decision support system for therapy planning in gestational diabetes. *Computational Methods & Programs in Biomedicine* 62, 235–48.

Hernando, M.E., Gomez, E.J. and **del Pozo, F.** 2001. Educational tool for diabetic patients based on causal probabilistic networks. *Lecture Notes in Artificial Intelligence* 2101, 203–207.

Hernando, M.E., García, A., Perdices, F.J., Torralba, V., Gómez, E. J., Bellazzi, R., Larizza, C., Arcelloni, M., Ortiz, F. and **Lázaro, C.** 2002: Deliverable 19: Multiaccess Telemedicine Services–demonstrator. EC M2DM project IST-1999–10315. Brussels.

Kahn, M.G., Abrams, C.A., Orland, M.J., Beard, J.C, Cousin, S.B., Miller, J.P. and **Santiago, J.V**. 1991: Intelligent computer-based interpretation and graphical presentation of self-monitored blood glucose and insulin data. *Diabetes Nutrition & Metabolism* 4, 99–107.

Lehmann, E.D., Deutsch, T., Carson, E.R. and **Sönksen, P.H.** 1994: Combining rule-based reasoning and mathematical modeling in diabetes care. *Artificial Intelligence in Medicine* 6, 137–60.

Levy, M., Ferrand P. and **Chirat, V**. 1989: SESAM-DIABETE, an expert system for insulin-requiring diabetic patient education. *Computers and Biomedical Research* 22, 442–53.

M2DM: multi-access services for the management of diabetes mellitus. EC Project. IST-1999–10315. http://aim.unipv.it/projects/M2DM

Montani, S., Bellocai, R., Larizza, C., Riva, A., d'Annuncio, G., Fiocchi, S., Lorini, R. and Stefanelli, M. 1999: Protocol-based reasoning in diabetic patient management. *International Journal of Medical Informatics* 53, 61–77.

Pearl, J. 1988: *Probabilistic reasoning in intelligent systems: networks of plausible inference*. San Mateo, California: Morgan Kaufmann.

Starren, J., Hripcsak, G., Sengupta, S., Abbruscato, C.R., Knudson, P.E., Weinstock R.S. and **Shea, S.** 2002: Columbia University's Informatics for Diabetes Education and Telemedicine (IDEATel) Project: Technical Implementation. *Journal of the American Medical Informatics Association* 9, 25–36.

Waldhäusl, W.K. 2001: Finally we have arrived in a new millennium. *Diabetologia* 44, 1–2.

Wojcicki, J., Ladyzynski, P., Krzymien, J., Jozwicka, E., Blachowicz, J., Janczewska, E., Czajkowski, K. and **Karnafel, W.** 2001: What can we really expect from telemedicine in intensive diabetes treatment: results from 3-year study on type 1 pregnant women. *Diabetes Technology Therapeutics* 3, 581.9.