Application of Artificial Intelligence for Virtually Assisted Prognosis of Diabetes: A NODDS Project

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ABSTRACT
We present a successful application of Artificial Intelligence (AI) methodologies in the context of a network oriented virtual care service for diabetic patients management, developed within the public-funded NODDS project. Several AI methods have been exploited to implement the NODDS functionality. Temporal Abstractions and other Intelligent Data Analysis techniques are used to analyse the patient's monitoring data; the Case Based Reasoning (CBR) methodology is applied to perform the Knowledge Management task. The NODDS service is being tested through a small on field trial; the first results, though preliminary, seem to substantiate the hypothesis that the use of an AI-based risk evaluation system could present an advantage in the management of type 1 diabetic patients, leading to a more tight control of the patients' metabolic situation, in a cost-effective way.

Keywords
Decision-support system; Diabetes mellitus; Insulin therapy.

1. INTRODUCTION
Diabetes Mellitus is a major chronic disease, affecting up to 3% of the population in the industrialised countries. In particular, Insulin Dependent Diabetes Mellitus patients need exogenous insulin injections to regulate blood glucose metabolism, in order to prevent ketoacidosis and coma, and to reduce the risk of later life invalidating complications. Long term complications may affect the central or peripheral nervous system and give rise to nephropathy, neuropathy, or cause blindness. These complications are costly to the health system and contribute to loss of productivity. Therefore, there is a continuous need for effective monitoring of the patient. In many cases, this requires follow up treatment by a number of medical professionals. The increase in therapy planning complexity and in costs is the obvious drawback [1]. Hence, efficient communication between these professionals is of paramount importance for effective patient management and control.

Diabetic patients management is a complex task as it normally consist of visiting patients every 2/4 months; during these visits the data coming from home monitoring are analysed, in order to assess the metabolic control achieved by the patients. Laboratory results and historical and/or anamnestic data are verified as well, to finally revise the patient's therapeutic protocol.This has spur the advocacy of the use of current advances of information technologies and decision-support systems may improve cost-effectiveness of insulin therapy, by reducing the number of periodical control visits, while increasing the patient/physician communication rate. The wireless communication technologies and the applicability of the World Wide Web, can make medical information becomes available and is processed in a distributed way over a wide-spread network [2]. This promises to make healthcare an automated virtual care environment for those who have suffered with chronic diseases such as diabetes and require high frequency patient-physician contact. Such an environment can provide intelligent and personalized monitoring services to patients, best-practice decision support to physicians, and cost control.

Several tools and advisory systems for therapeutic plan assessment are now available, both on a day-by-day and on a visit-by-visit basis [3], and for some of them the capability of providing proper decisions has been shown experimentally [4]. The exponential growth in the availability and in the use of telecommunication services pushes towards the integration of such tools in a networking environment, in order to provide long-distance assistance to patient, as well as long-distance monitoring capability to the physician [5]. The use of appropriate Artificial Intelligence (AI) techniques, such as knowledge based systems, Intelligent Data Analysis and Case Based Reasoning, may enhance the design of the overall service: it should be possible to allow the users exploiting an intelligent desk for periodic therapy assessment and revision. For these reasons, we have worked for the development of a an AI integrated network based system, that, reinforced by previous experiences, not only able to offer a new integrated solution to the Diabetes management problem but also data mining applications involving the identification of risk factors associated with the onset of diabetes.

2. The NODDS Project
Driven by the motivation already discussed above, NODDS (Network Oriented Diabetes Database Management System) is a Public funded project, concerned with the design, implementation and applicability of an AI based healthcare service to assist diabetes patients, able to provide physicians over a network with a collection of AI techniques for improving management of patients according to the best current medical practice. The aim of the project was to:

1. to provide patients with an effective treatment leading to good glycemic control, and to achieve a careful balance between insulin therapy, diet and physical activity, thus delaying the onset and/or slowing the progression of chronic complications;
2. to provide patients at home or in other non-clinical environments with an appropriate level of continuous and intensive care through web monitoring and AI consultation services, taking into account the needs of remote or isolated

individuals that are unable to reach frequently the hospital institutions;

3. to allow for a cost-effective monitoring of a large number of patients, automatizing data collection and the management of a large set of therapeutic protocols;
4. to support a continuous education of patients of their current status of exposure to risk & regime changing methods through AI consultation services;
5. to provide estimations of the blood sugar level based on their regime.
6. to allow the patient to customise the insulin therapy within the bounds established by the physicians.

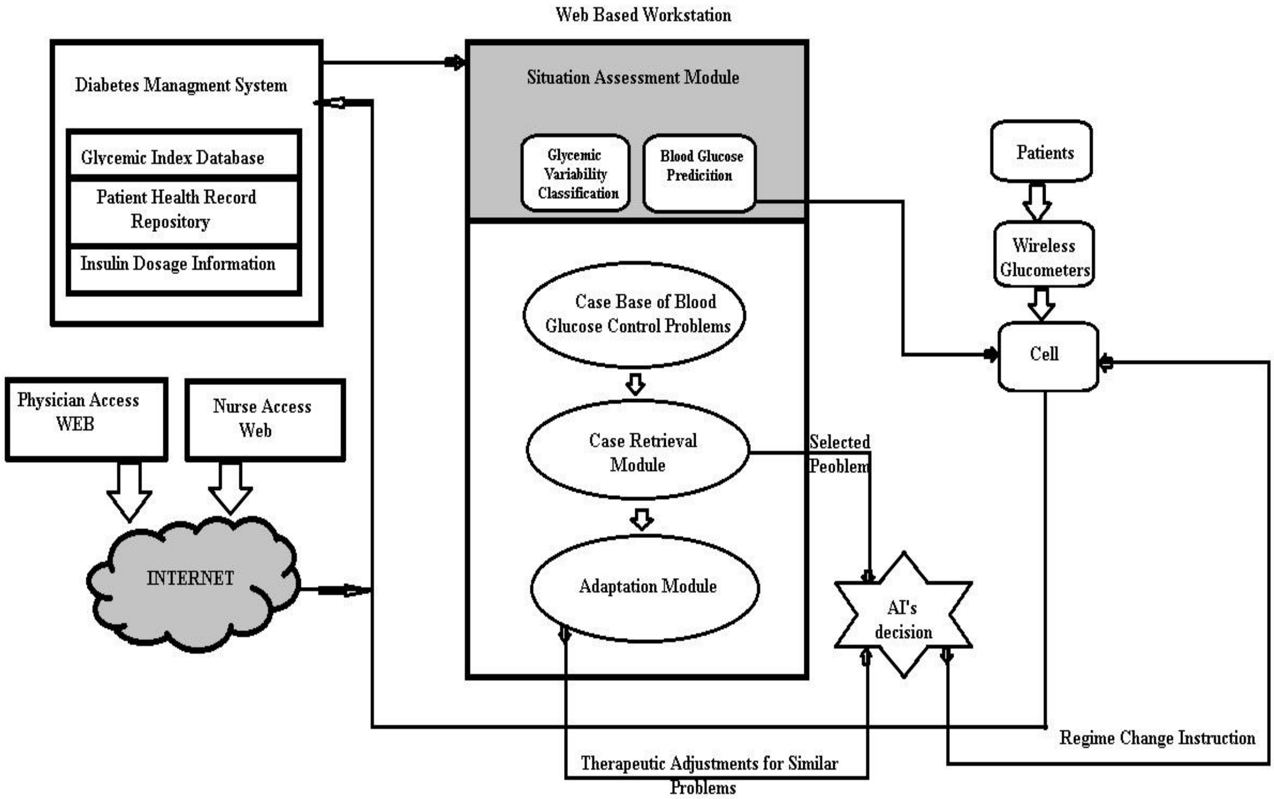

Fig:1. Overview of NODDS support system.

Patients collect metabolic data together with insulin and food intake information every day, through a wireless glucometer interconnected with diabetes managing app at their cell and that stores data in the Patients data base at web based Workstation (WBW). The WBW is a web-based workstation in which several distributed servers cooperate in a transparent way to make an AI managing diabetes mellitus through: consultation and analysis of the patients' data, communication with patients' home, revision of the therapeutic protocol and information repositories consultation. Whenever a probability for occurrence of the problem occurs, the AI sends an alarm and the regime change instructions to the patient through patient's app. NODDS is a one year project, which is at its final stages of completion. The NODDS services are being implemented and extensively tested at the CRIAD Laboratories in Junwani. Efforts are being made to make the system more users friendly & automatized.

3. Role of AI on NODDS decision

The NODDS System aims to

(1) Automatically detect problems in Blood Glucose (BG) control;
(2) Propose solutions to detected problems;
(3) Remember which solutions are effective or ineffective for individual patients.
(4) Calculate risk of complications for individual diabetic patients. The risk pattern of each diabetic patient is obtained using a Case-based Reasoning method.
(5) Updation of incorporated dynamics of glucose and insulin in a manner which reflects their clinical importance. This defines the relationships between changes in insulin dose and site and time of injection and glycaemic response. Hence, we can draft qualitative predictions of patient outcome of blood glucose profile.
(6) To provide regime change instructions when encounter a critical stage based on the prediction of glucose & insulin dynamics.

We selected case-based reasoning (CBR) as the initial approach because

(a) it provides support for tailored solutions based on similarity to known cases;
(b) diabetes management guidelines are general in nature, requiring personalization;
(c) a wide range of both physical and lifestyle factors influence Blood Glucose levels; and

(d) CBR has been successfully applied to managing other chronic medical conditions.

4. Situation Assessment

The first step in developing NODDS was to build a case base as a central knowledge repository. Although, initial BG data was available to have a baseline. This is because the life events coinciding with BG levels, used by AI to determine appropriate therapy, that were routinely recorded. To acquire contextualized cases for the system, we conducted a clinical research study involving 20 Type 1 Diabetes patients. Each patient participated for six weeks, manually entering daily BG, insulin, and life-event data into an experimental database through a web-based interface. AI reviewed the data, detecting BG control problems and recommending therapeutic adjustments. Patients implemented the recommended adjustments (or not), and AI reviewed subsequent data to evaluate the clinical outcomes, in an iterative cycle. Problems, solutions, and outcomes were structured into cases and stored in the case base. We were able to acquire more than 50 cases over the course of the clinical research study.

Internally, a case is represented as an object of a hierarchical Java class containing approximately 150 data fields. The case records an actual problem of nocturnal hypoglycemia. Hypoglycemia, or low BG, leads to weakness, confusion, dizziness, sweating, shaking, and, if not treated in time, seizures, coma, or death. Hyperglycemia, or high BG, contributes to long-term diabetic complications. Extremely high BG levels can cause diabetic ketoacidosis, a serious condition leading to severe illness or death. It is important to note that patients do not know when problems are impending and are frequently unaware of problems even once they occur. Typically in CBR [6] systems, reasoning begins with a known problem that can be readily described and elaborated. Solving a given problem entails finding and adapting the most similar, or most useful, case in the case base. In this domain, problems are not usually given, or known a priori, but must be detected in continuous patient data. Our approach was to model automated problem-detection routines on AI problem-detection strategies. We implemented rule-based routines to detect 14 common BG control problems identified by physicians.

Data retrieval is implemented as a two step procedure: a classification step, able to identify the class to which the current case could belong, and a proper retrieval step, meant to extract the "closest" cases. Classification relies on a Naive Bayes [7] strategy, a method that assumes conditional independence among the features given a certain class, but that is known to be robust in a variety of situations [8, 9] even in the presence of conditional dependencies.

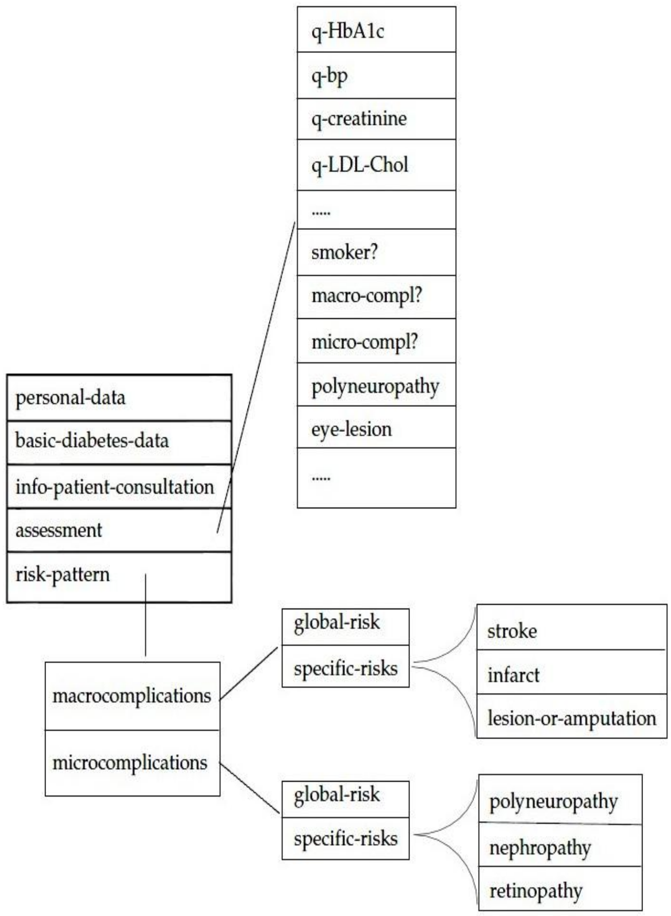

Fig 2. Taxonomy of classes of prototypical situations in pediatric NODDS patients.

For applying Naive Bayes, we calculate the probability that a case belongs to class c_i , given that the set of its features $f = \{f_1, f_2, \dots f_M\}$ is $\hat{f}$, through the following formula:

$$P(c_i|f = \hat{f}) \;\propto\; \prod_{j=1}^{M} p(c_i)p(f_j = \hat{f}_j|c_i)$$

The method classifies a case as belonging to the class that maximises $P(c_i|f = \hat{f})$. The conditional probabilities $p(f_j = \hat{f}_j|c_i)$ are obtained through the Bayesian update formula for discrete distributions [10, 11]; in particular, we use a re-parameterised version of the update formula known as *m-estimate* of probability [12], that modifies the prior knowledge with the information coming from the cases of the case memory as follows:

$$p(f_j = \hat{f}_j|c_i) = \frac{m\,\hat{p}_{ij} + \hat{N}_{ij}}{m + D_i}$$

Where $\hat{N}_{ij}$ is the number of cases in the case memory of class i whose feature $f_j$assumes the value $\hat{f}_j$, while D_i is the total number of cases in class i The medical knowledge is synthesised by the prior probability distribution $(\hat{p}_{ij})$, whose reliability is expressed by the implicit number of samples m. In other words, the larger is m, the larger is the confidence of the expert on the prior. Our initial case library was composed by 145 real cases from the histories of 29 pediatric patients. In our application, the prior probability value p_{ij} was derived from experts opinion through a technique described in [13, 14]. Retrieval may be performed just on the most probable class identified by the classification step, or on a subset of the most probable classes. In both situations the system relies on a Nearest-Neighbour (NN) technique and classical metrics, able to treat numeric and symbolic variables, and to cope with the problem of missing data, are applied to calculate distances [15]. When dealing with a large case base, our application implements a non exhaustive search procedure that exploits an anytime algorithm called Pivoting-Based Retrieval (PBR) [16], whose efficacy has been proved on a 10000 cases library.

5. Risk Evaluation

In this section we introduce the CBR method used by NODDS to solve the risk evaluation tasks. For each diabetic task the case base for the best precedent is searched and infers the risk according to that precedent. For a given collection of risk classes, a diabetic complication C, and a problem *p*, the task is to obtain the risk $R_i \epsilon R$ of *p* concerning C. For each complication C, this can be seen as a classification task where the goal is to identify the class in R to which *p* belongs. NODDS solves this classification task using following algorithm. Given a case base B containing diabetic patients classified into the collection of risk classes R for a diabetic complication C, and a problem *p* to be classified, that obtains the class $R_i \epsilon R$ to which *p* belongs. Intuitively, the algorithm follows a top-down strategy to build a description D containing the most relevant features of *p* such that all features in D are satisfied by a subset of cases in B. In general, cases in this subset belong to different solution classes in R. The Algorithm adds relevant features to D until the subset of cases satisfying D belong to one unique solution class R_i. It takes this class R_i as the solution for the current task, i.e. R_i is the risk of *p* concerning C. The algorithm is given as:

D: $=\emptyset$; R= $\{R_1 \ldots R_N\}$
<u>Function</u> Risk_evaluation(B, p, D)
S_D: = Discriminatory-set (D, B)
if $\forall e_i \in S_D \Rightarrow e_i \in R_i$ then return R_i
else $f_d :=$ Select-feature(p, B, R)
D':=Add-Feature(f_d, D)
Risk_evaluation(B, p, D')
end-if
end-function

The algorithm begins with the whole set of precedents B classified into the collection of risk classes R for a complication C, a problem *p* to be solved and the description D: $=\emptyset$; (i.e. D has no features). In the following we will explain this algorithm using an example.

Example 1. Let p be a patient with no macrocomplications (i.e. feature macro-compl? in Assessment has value false), high blood pressure and low albumin. In this example NODDS has to determine the risk $R_i \epsilon R$ for the macrocomplication C = stroke.

The set of cases $S_D \subseteq B$ that are subsumed by the description D is called discriminatory set.
Intuitively, a case c is subsumed by a description D when all the information contained in D is also contained in c, although c can contain more information. Initially D is an empty description, i.e. it is the most general description. Therefore D subsumes all the cases in B (i.e. S_D = B), and consequently D has to be specialized. The specialization of a description D is achieved by adding features to it. In particular, Risk_evaluation function adds a feature f with the value v that this feature has in the current problem p. After that, the new description D' = D + (f=v) has a smaller discriminatory set SD' formed by those cases subsumed by D'. Thus, specialization reduces the discriminatory set $S_D \subseteq S_D{'}$ at each step. The algorithm uses a heuristic measure based on the López de Mántaras distance [17] to determine the feature to be added. It specializes D by selecting one feature f from all the features used in p in the following way. Each feature fi in p induces a partition $P_i = \{S_{i1} \ldots S_{in}\}$ in the set S_D such that each $S_{ik} \subseteq P_i$ contains those patients in S_D having the same value v_k in the feature f_i. For instance, the presence or absence of macrocomplications will divide the set S_D (currently S_D = B) in two subsets: onecontaining those precedents having macrocomplications and the other one containing patients without macrocomplications. There is also a partition of S_D, called the correct partition P_c, that divides S_D according to the risk $(R_i \epsilon R)$ for the complication C. In the example, S_D is divided in subsets according to the values for the risk of stroke being unknown, low, moderate, high, and very-high.

For each partition P_i, Algorithm computes the López de Mántaras (RLM) distance [17] to the correct partition P_c. Intuitively, the RLM distance assesses how similar a partition is with respect to a referent partition (i.e. the correct partition), in the sense that the lesser the distance the more similar they are. The RLM distance was introduced as an alternative to the Quinlan's Gain [18] used in the ID3 inductive learning algorithm. The Quinlan's Gain is a selection measure that selects the object feature providing the highest information gain. RLM distance shows that normalizing the Quinlan's Gain in an appropriate way, we obtain a distance between partitions. Formally, given two partitions Pi and Pc of a set SD, the RLM distance between them is computed
as follows:

$$RLM(P_i, P_c) = 2 - \frac{I(P_i) - I(P_c)}{I(P_i \cap P_c)}$$

where, $I(P_i) = -\sum_{j=1}^{n} p_j \log_2 p_j$; $p_j = \frac{|S_D \cap S_{ij}|}{|S_D|}$

$$I(P_c) = -\sum_{k=1}^{m} p_k \log_2 p_k \,;\; p_k = \frac{|S_D \cap R_k|}{|S_D|}$$

$$I(P_i \cap P_c) = -\sum_{j=1}^{n} \sum_{k=1}^{m} p_{jk} \log_2 p_{jk}$$

$$p_{jk} = \frac{|S_D \cap R_k \cap S_{ij}|}{|S_D|}$$

where $I(P_i)$ measures the information contained in the partition P_i; *n* is the number of possible values
of the feature inducing P_i; *m* = Card(R); P_i is the probability of occurrence of class S_{ij} (R_j) i.e. the
proportion of examples in SD that belong to S_{ij} (R_j); $I(P_i \cap P_c)$is the mutual information of two partitions; and p_{jk} is the probability of occurrence of the intersection R_j Ç S_{ik},

i.e. the proportion of examples in SD that belong to R_j and to S_{ik}.

6. Conclusion

The encouraging results we obtained from the NODDS project verification phase at CRIAD Laboratories, though preliminary, seem to substantiate the hypothesis that the use of the diabetes therapy on a network oriented systems in association with decision support systems could present an advantage in the management of type 1 diabetic patients, leading to a more tight control of patient's metabolic situation, in a cost-effective way. As the system is currently used at the pediatric clinic, we will be able to collect additional data which, in our opinion, will probably enforce such conclusions.

We are tackling these challenges and forging ahead with plans to make intelligent diabetes management a reality for patients and physicians. We have a waiting list of patients who have volunteered to participate in clinical research studies. They are counting on us to translate the research into practical tools they can use. We envision a number of potential avenues of commercialization and use. In summary, diabetes management is more than a challenging domain for AI research. It is an opportunity for AI applications to impart a positive impact on the health and well-being of people with diabetes.

7. Acknowledgment

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