Expert Systems with Applications 40 (2013) 7354–7366

Contents lists available at ScienceDirect

Expert Systems with Applications

journal homepage: www.elsevier.com/locate/eswa

Using causality modeling and Fuzzy Lattice Reasoning algorithm for predicting blood glucose

Simon Fong [a,*], Sabah Mohammed [b], Jinan Fiaidhi [b], Chee Keong Kwoh [c]

[a] Department of Computer and Information Science, University of Macau, Taipa, Macao
[b] Department of Computer Science, Lakehead University, Thunder Bay, Ontario P7B 5E1, Canada
[c] School of Computer Engineering, Nanyang Technological University, Singapore, Singapore

ARTICLE INFO

Keywords:
Insulin-dependent diabetes mellitus
Diabetes therapy
Medical decision-support
Fuzzy Lattice Reasoning
Predictive Apriori

ABSTRACT

Blood glucose measurement is an important feedback in the course of diabetes treatment and prognosis. However, predicting the blood glucose level is not an easy task in the course of insulin treatment. There are many factors influencing the results (internal, environmental and behavioral factors). Previous attempts for predicting high levels of blood glucose utilize data related to insulin production, insulin action, or both by using time series forecasting and using of non-linear classification model. In this paper, we propose a more generic approach for predicting blood glucose levels using Fuzzy Lattice Reasoning (FLR). FLR allows us to deal with reasoning using specialist's knowledge acquisition and generation of rules base to increase the accuracy of predicting blood glucose level. In addition to the improved accuracy by FLR, the resultant rules contain some min–max ranges of variables making them flexible for diagnosis at the precise timing of the intervention and alarm. The new model is tested in comparison to other classical machine learning methods by using real-life diabetes dataset from AAAI Spring Symposium on Interpreting Clinical Data; superior accuracy is found and the efficacy of the model is verified through computer experiments. As far as we know, this is the pioneer work modeling temporal diabetes datasets into descriptive rules using FLR.

1. Introduction

Diabetes mellitus is a prevalent metabolic disease affecting 347 million people worldwide, according to the fact sheet[1] released by World Health Organization in March 2013. In UK, 2.9 million people are suffering from diabetes mellitus in 2011 that constitutes to 4.45% of the population. By 2025, it is projected to have 5 million people in UK inflicted with diabetes.[2] For another instance, the prevalence rate of diabetes mellitus is more critical[3] as it rose to 13.7% of the Turks population in 2010. This global epidemic is a chronic and incurable metabolic disorder that is characterized by either deficiency of insulin secretion or reduced sensitivity of the body tissues to insulin. The former is called Type-I diabetes which is also known as insulin-dependent diabetes mellitus (IDDM) where the body fails to produce insulin possibly due to autoimmune destruction of pancreatic β-cells. Without this important hormone, the patients' body cells may starve to death because the glucose in the bloodstream just cannot be absorbed. The latter type is known as Type-II non-insulin-dependent diabetes mellitus and it is usually associated with body over-weight and lack of physical activity. Type-II non-IDDM probably will nevertheless lead to insulin treatment eventually. As a result, especially in Type-I IDDM, medical intervention of insulin replacement has become central in diabetics therapy.

The basis of the diabetic therapy is to replace the lack of insulin by regular exogenous insulin infusion with a right dosage each time, for keeping the patients alive. However, maintaining the blood glucose levels in check via exogenous insulin injection is a tricky and challenging task. Despite the fact that the reactions of human bodies to exogenous insulin vary, the concentration of blood glucose can potentially be influenced by many variables too (Ginsberg, 2009). These variables include but are not limited to BMI, mental conditions, hormonal secretion, physical well-being, diets and lifestyles. Their effects make a synthetic glucose regulation process in diabetic patients highly complex as the bodily reaction to insulin and other factors differs from one person to another. It is all about a matter of a right dosage and the right timing of insulin administration, for regulating the fluctuation of blood glucose concentration at a constant level. According to the standards of medical care in diabetes, by American Diabetes

* Corresponding author. Address: Faculty of Science and Technology, University of Macau, Av. Padre Tomás Pereira Taipa, Macau SAR. Fax: +853 2883 8314.
E-mail addresses: ccfong@umac.mo (S. Fong), sabah.mohammed@lakeheadu.ca (S. Mohammed), jinan.fiaidhi@lakeheadu.ca (J. Fiaidhi), asckkwoh@ntu.edu.sg (C.K. Kwoh).

[1] Fact based on WHO media center: http://www.who.int/mediacentre/factsheets/fs312/en/index.html.
[2] Fact based on WHO media center: http://www.who.int/mediacentre/factsheets/fs312/en/index.html.
[3] Source: Anatolia News Agency, 10/14/2010.

0957-4174/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.eswa.2013.07.035

Association (American Diabetes Association, 2007), hyperglycemia can occur when the blood glucose level stays chronic above 125 mg/dL over a prolonged period of time. The damages are on different parts of the body, such as stroke, heart attack, erectile dysfunction, blurred vision and skin infections, just to name a few. At the other end, hypoglycemia occurs when the content of glucose ever falls below 72 mg/dL. Even for a short period of time, hypoglycemia can develop into unpleasant sensations like dysphoria, dizziness, and sometimes life-threatening situations like coma, seizures, brain damage or even death.

Manually devised treatment plans have been made formulated for diabetes patients based on the regular decisions about the daily insulin inputs. The application of insulin should be given at regular intervals to the patients such that a recommended target range (American Diabetes Association, 2007) of 70–140 mg/dL blood glucose could be sustained in a patient's body. As aforementioned, multiple factors are to be considered in making such decision, which are filled with dynamicity, uncertainty, variability and sometimes risks. The decision process is far from trivial, because of the ambiguity of many variables. From the patients' perspective especially those who opt for independent home treatment with self-monitoring blood glucose test kit and insulin injections, it is desirable to have a personalized blood glucose predictor. The predictor could advise them on modulating the insulin therapy daily with respect to the timing, dosage and the anticipated near future blood glucose, given the information of food intake and other physical activities.

In the light of this motivation, a recent research attempt was made in developing a personalized blood glucose control device called DIAdvisor. The core of the decision making module of DIAdvisor and the like (Cescon, Dressler, Johansson, & Robertsson, 2009), is usually a collection of decision rules that represent different daily situations of a normal non-diabetic person of similar body weight and age to that of the patient. Thereby any hyper/hypoglycemic deviation could be detected and even foretold by the decision rules. However, these decision rules usually are being generalized from a population of non-diabetic individuals. The rules should be made adaptive in a sense that the advisory system can be personalized for any individual patient, so that the recommended therapeutic mode can be fine-tuned. The adaptive aspect is important because the insulin sensitivity for each patient differs, so do their physiological and psychological experiences that happen every day – food intake patterns, stress level, illness and exercise habits etc. Therefore this motivation forms the basis of this research work being reported here.

The rest of the paper is structured as follow. A history of mathematical modeling in the interaction of glucose–insulin, as well as recent advances in implementing these theoretical models into computerized programs is discussed in Section 2 Related research work. Our proposed approach in predicting the blood glucose level based on the generation of fuzzy rules by lattice computing is detailed in Section 3. Computer simulation over real diabetic patients' temporal data is carried out, and the results are reported in Section 4. The efficacy of the proposed model is discussed in Section 5, in comparison to other popular machine learning methods. Section 5 concludes the paper.

2. Related research

With respect to modeling the relations between insulin and blood glucose concentration, a pioneer work by Ackerman, Gatewood, Rosevear, and Molnar (1965) studied a simplified and linearized model of the human glucose regulatory system in 1965. The system is called Auckerman model that can predict a damped sine wave response to an oral glucose load. In the study they compared predictions based on the model with measurements of blood glucose and blood insulin concentrations during the oral glucose tolerance test. As an early piece of work, they attempted to develop a simple mathematical model of the glucose–insulin system which gave a reliable valuation of the glucose-tolerance curve for diagnostic. In 1970 Delia Corte, Romano, Voeghelin, and Serio (1970) followed Ackerman's model in which 317 oral glucose tolerance curves have been analyzed rigorously. Della Corta et al. validated Acherman's hypothesis on the glucose intestinal absorption. They debunked that the intestinal absorption rate of glucose was not statistically changed in diabetes mellitus, but decreased with age. By best-fitting curve method, they also analyzed that there is a noticeable disagreement with the medical diagnosis of 15% of the cases. They explained that half of the error is the inherent error of the method, and the other half is attributed to an erroneous medical diagnosis due to the uncertainty in the diagnosis of the numerous cases. Perhaps more sophisticated modeling approach is needed.

The momentum of studying the relations between insulin and glucose did not stop however. At the turn of millennium, the physiological relations were formally and mathematically modeled via differential equations as an intravenous glucose tolerance test by Gaetano and Arino (2000). This was known to be the modification of the minimal model which was developed earlier, to a dynamic model with the model outcome that always admits a globally asymptotically stable steady state. The interaction model was then further extended to discrete and continuous dynamical systems with consideration of the time delay effect by Li and Kuang (2001) in 2001. Subsequently the interaction model was extended further by the same research team (Mukhopadhyay, De Gaetano, & Arino, 2004) proving that the system is globally asymptotically stable. Bennett and Gourley (2004) improved the differential equations in the interaction model with time delay explicitly incorporated by the Lyapunov functional approach. The resulting interaction model consists of three differential delay equations that simulate the diminishing effects of insulin and the ultradian oscillations in pancreatic insulin secretion. The model is complete with proven theorems on global asymptotic stability. Wang, Li, and Kuang (2009) utilized Michaelis–Menten kinetics which is a well-known is response function in chemical reaction, for modeling insulin therapies for both types 1 and 2 diabetes mellitus more accurately. The insulin degradation rate assumes Michaelis–Menten kinetics which does not degrade to infinity when resource is overly available.

Given the mathematical cornerstone firmly laid for modeling the interaction between insulin and blood glucose as evident by a number of related theoretical publications in the literature, researchers started to eye on some computerized tools that implement the regulatory mechanisms for insulin administration. Application-wise, a good overview indicating other bibliography on software tools for the glucose–insulin regulatory system and diabetes is presented in Makroglou, Li, and Kuang (2006).

There is no shortage of prediction models in machine-learning research community that claimed to be able to do blood glucose prediction. One of the most significant works is by Maciejowski (2002) who formulated predictive diabetic control by using a group of linear and non-linear programming functions that take into consideration of variables and constraints. The other direction related to blood glucose prediction is time-series forecasting (Ståhl & Johansson, 2009), which take into account of the measurements of the past blood glucose cycles, in order to do some short-term blood glucose forecast. Another popular choice of algorithm in implementing a blood glucose predictor is artificial neural network (Akmal, Ismail, & Zainudin, 2011; Gogou, Maglaveras, Ambrosiadou, Goulis, & Pappas, 2001; Otto, Semotok, Andrysek, & Basir, 2000) which non-linearly maps daily regimens of food, insulin and exercise expenditure as inputs to a predicted output. Although

neural network predictors usually can achieve a relatively high accuracy (88.8% as in Akmal et al. (2011)), the model itself is a black-box where the logics in the process of decision making are mathematical inference. For example, numeric weights associated in each neuron and the non-linear activation function. Recently some researchers advocated applicability of decision trees in predicting diabetic prognosis such as batch-training model (Han, Rodriguez, & Beheshti, 2009) and real-time incremental training model (Zhang, Fong, Fiaidhi, & Mohammed, 2012). The resultant decision tree is in a form of predicate logics IF–THEN–ELSE rules which are descriptive enough for decision support when the rules are embedded in some predictor system, as well as for reference and studies by clinicians. However, one major drawback on decision tree is the rigidity in conditional-testing at each decision tree node. A precise value (sometimes called threshold) is computed at each node during the decision tree model induction, for testing against the attribute values of a new instance leading to a predicted target class. A typical decision rule will look like this,

'IF *Last_insulin_inj_time* $\leqslant$ 109.2mins AND *Last_insulin_dose*==2.5units AND *Carbohydrate_in_lunch* $\geqslant$ 87 grams AND ...
THEN *predicted_glucose_next_hour*==161.3 mg/dL.'

This should work fine as long as the daily routine of a patient is constant and his therapeutic measurements are always absolute. This assumption seldom holds true as our lifestyles may change over time, that means our diets as well as the injection frequency and timing may diverge.

Along the direction of adaptive rules whose conditional values can change over time in modeling the dynamic interaction between insulin and blood glucose, a tunable fuzzy logic controller (FLC) is proposed in 2010 (Richard et al., 2010) for physicians to tailor insulin dosing based on blood glucose goals for any particular patient. The time-series of blood glucose levels and the changing rates of blood glucose are continuously feeding in the FLC. The blood glucose data are then fuzzified into five categories: very high, high, normal, low and very low. The categorical data are then mapped into a decision table which consists of logical rules predefined according to the expert judgments of the physician. Depending on the discrete input values, an appropriate insulin dosing is recommended by referencing across these logics in the decision table. The design of FLC is simple, and claimed to enable setting the personalization factor for scaling the insulin dose for each individual patient. While the FLC is effective in providing useful reference information after the input measurements are fuzzified and monitored, the effectiveness of the whole approach replies on the manual calibration of the decision rules. The weighting factors in the decision rules are however subjectively tuned at will based on the physician's professional judgments.

In 2012, a similar work (Kalpana & Senthil Kuma, 2012) was proposed where the FLC was extended for incorporating more input variables than those of blood glucose, such as BMI, blood pressure, pregnancy record and age etc. The proposed model is limited to only fuzzifying the input variables to categorical data; thereafter the discrete data are used to train a classifier for stereotyping new instances to some patient group. In Kalpana and Senthil Kuma (2012), the classification is for categorizing patients into different youth groups after fuzzifying the input attributes. The application however is for studying the propensity of the disease instead of attempting to customize the insulin dosing for a particular patient. There are dozens of other researchers who studied the diabetes problem by using static patients' records instead of a temporal sequence of events for real-time diabetes therapy. Such references are listed in the literature survey in Kalpana and Senthil Kuma (2012).

As a concluding remark, most computerized tools designed for diabetes therapy like a black box mapping of an input space to an output. And the input data are usually static and are being generated either over a population or patient-specific but profiled over a long period of time. Therefore future prediction can be inferred from long historic patterns which assume to be more or less unchanged and stationary by conventional time-series forecasting methods. Here we want to investigate a comprehensible-rule generation system that predicts the future blood glucose level based on dynamic (hence realistic) scenario where a mix of insulin doses and blood glucose levels were being applied and being measured unevenly over the timespan.

3. Prediction of glucose level based on fuzzy logic: the FLR approach

In order to accommodate such "fuzziness" and allowance of variation of the patients' lifestyles which are of a realistic issue, a new methodology of descriptive and fuzzy rules generation is proposed in this paper. The enabling classifier in our proposed methodology is called Fuzzy Lattice Reasoning (FLR) classifier, coupled with Predictive Apriori for controlling the lattice dimension. More details will be given in the following sections. In the context of rule-based decision support for diabetes therapy, FLR has the advantages of generating rules that are fuzzy in nature, namely each testing condition comes with a range of minimum and maximum values; missing values and even missing testing conditions (if any) are allowed in the model induction process. In other words, rules with incomplete set of tests would be generated. A comprehensive collection of descriptive rules with different dimensions (hence different number of testing attributes) will be produced as output. Instead of insisting on value-for-value tests over all the necessary attributes as in normal decision tree model, FLR rules offer relaxed testing ranges; and they have rules of different number of dimensions (testing attributes) available. Hence decision support for patients who might change their monitoring episodes over time can be carried out by FLR rules. The archetypical contribution of this paper is the flexibility and availability of logical rules which are suitable for decision making over measurement inputs of irregular patterns.

3.1. Method background: defining fuzzy lattice and the generation of fuzzy rules

Lattice theory continues to excite researchers for its ability to model both uncertain information and disparate types of lattice-ordered data (Kaburlasos & Petridis, 1997). Fuzzy lattice is a mathematical concept for defining fuzzy partial-order relation (Khezeli & Nezamabadi-pour, 2012a). Moreover, Fuzzy Lattice Reasoning (FLR) classifier was introduced to induce descriptive, decision-making rules for a given data domain (Kaburlasos, Athanasiadis, & Mitkas, 2007). The original FLR model employs an inclusion measure function which is basically a linear positive valuation function (Liu, Xiong, & Fang, 2011). This paper describes an enhanced Fuzzy Lattice Reasoning (FLR) classifier based on three step method for generating the fuzzy rules see Fig. 1. The tri-step method consists of mainly three processes, (1) Data pre-processing for cleaning as well as transformation of transactional data to normalized training data; (2) Causality modeling, mainly it is for estimating the maximum cardinality or dimension of rules via measuring the quality of frequent patterns between the influencing factors and the effect; (3) Fuzzy rule generation process, FLR is adopted for producing descriptive fuzzy rules that have variable dimensions up to the maximum cardinality obtained from the previous process (Acharya & Modi, 2011). The results will be a set of fuzzy rules that have

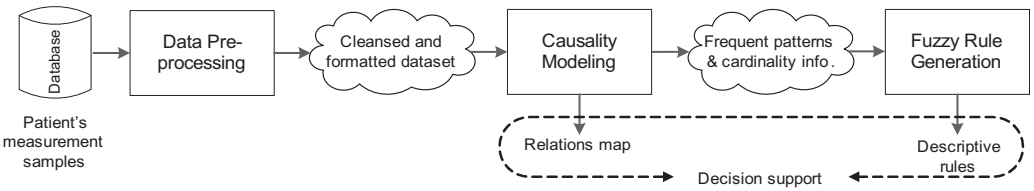

Fig. 1. Fuzzy rule generation methodology for flexible IDDM therapeutic decision support.

optional number of conditional tests for the use of further decision support. Each one of these rules is guaranteed to be frequent, by the process of causality modeling and the overall accuracy of the FLR model would be gauged as well.

3.1.1. Data pre-processing

The data used in this experiment are the diabetes dataset from AAAI Spring Symposium on Interpreting Clinical Data[4]. Though full details about this dataset are described in the next section, it is worth mentioning that this data represents a typical flow of measurement records that would find in any insulin therapy management. Our aim is to generalize the model that would work over typical IDDM transactional data.

The IDDM data are called transactional data because the data is a temporal series of events. Again, typically there are three groups of events in an insulin therapy, blood glucose measurement (both pre/post meals and ad hoc), insulin injections (of different types) and amount of physical exercises. The events are coded in the transactional data as shown in Table 1. The events are time-stamped. However, there is no rigid regularity on how often each of these events would happen. A rough cyclical pattern can be however observed that goes by spacing the insulin injections over a day; and the corresponding cycle of blood glucose fluctuation follows closely. These cycles loop over day after day, though without specific timing of every event. One can approximately observe an average of three or four injections are being applied. The timings as well as the extents of the observable events are thus fuzzy in nature, so should be the descriptive rules provided by the rule generation model – this forms the cornerstone of our research here.

In Fig. 2, a sample of these repetitive cycles of events is shown for illustrating this fuzzy concept. Most importantly the irregular pattern of events gives rise to computational challenges in generalizing an accurate machine learning model. The occurrences of the events are fuzzy in nature, such that there is neither fixed timing interval nor certainty in recurrence. For instance in Fig. 2, at close-up, the longitudinal events are paced irregularly, so are their amounts at each shot. Events of insulin injections and blood glucose measurements are more or less interleaved and repeated over time though in some uneven cycles; exercises and sometimes hypoglycemia happen occasionally. In the example presented in Fig. 2, two views are provided. The 4-months adaption of insulin injection shows a relatively long-term pattern over time (Fig. 2(a)); two exceptionally high doses of insulin over units of 100 were given; more importantly the insulin pattern is never periodically exact, although some cycles are seen repeating (Hinshaw et al., 2013). The overall insulin intake looks increasing over time from the initial month to the last month. Some events of hypoglycemia have occurred too, sporadically, as represented by red dots in the graph. A zoomed-in view of higher resolution is shown in Fig. 2(b), where the timing of the insulin injections is clearly seen. Though the insulin injections are repeating over time, the exact times of injections are seldom the same for any two injections. Sometimes, NPH and Regular types of injections are taken at the same time. Fig. 3 shows a change of habit in blood glucose measurements, the frequency has reduced across fifty days by dropping the pre-lunch and pre-supper measurements. The graphs demonstrate an important fact that the patterns of timing and doses of insulin injections are rather fuzzy.

Usually for training a classifier model, a normalized relational data format is needed that is characterized by fixed columns of attribute values plus a target value at the last column. This way, the input attribute values of new instance would be mapped to a target class. One possible conversion is counting on the number of insulin injections taken a day, together with their total daily amount, and relates them to the fluctuation of blood glucose measured over 24 h. Since ambiguity is a feature of the classifier encouraged here, the data are transformed without referencing to any fixed daily timeframe (e.g. 24 h). So the length of time between every type of insulin injected and the latest blood glucose measurement obtained forms a record of training instance. Additional attributes are added to the dataset for creating some meaningful interpretation of the events; for example, GTM – whether the current blood glucose level is greater than the mean. This target class can be possibly extended to indicating whether the current blood glucose level falls into zones beyond the acceptable range by some expert-defined standard. Alternatively the target class can be replaced by other significant events such as the occurrence of prolonged hyperglycemia (computed by successive high values of blood glucose), hypoglycemia and symptoms of critical illness, etc. (Dassau et al., 2010). The choice of target class depends on the objectives of the decision support tool. The data transformation is facilitated by a Java program which functions during the data pre-processing step as depicted in Fig. 1.

The transformed training instances are unordered so the reliance of the temporal sequence is relinquished. The temporal sequence is not necessary meant to be absolutely regular anyway, assuming that the patient is undertaking a loosely controlled lifestyle. The transformed dataset is patient-specific as it reflects the non-linear patterns of insulin adaptations corresponding to the subsequent blood glucose levels. The following Fig. 4 shows some sample transactional data and the transformed data respectively. For simplicity, the transformed data contains only the main factors where additional factors such as exercises, fasting information and physiological conditions can be optionally included in the training data.

3.1.2. Causality modeling

The prime objective of causality modeling in our proposed methodology is to determine the maximum cardinality allowed in the fuzzy lattice that is to be generated in the subsequent process. This is done via Predictive Apriori (PA) algorithm for two reasons. Firstly PA is specialized in computing quantitatively the 'predictability' hence the relationship between the factors and the resultant class. Secondly and more importantly, the input factors can be singular or in multiple as long as there exist some linear (direct) or non-linear (indirect) relationship between them and the target class. Given this feature, it is possible to find out the maximum number of possible factors that are related to the

[4] http://www.aaai.org/Press/Reports/Symposia/Spring/ss-94-01.php.

Table 1
A list of possible events with codes that can be found in a typical IDDM insulin therapy.

33 = Regular insulin dose
34 = NPH insulin dose
35 = UltraLente insulin dose
48 = Unspecified blood glucose measurement
57 = Unspecified blood glucose measurement
58 = Pre-breakfast blood glucose measurement
59 = Post-breakfast blood glucose measurement
60 = Pre-lunch blood glucose measurement
61 = Post-lunch blood glucose measurement
62 = Pre-supper blood glucose measurement
63 = Post-supper blood glucose measurement
64 = Pre-snack blood glucose measurement
65 = Hypoglycemic symptoms
66 = Typical meal ingestion
67 = More-than-usual meal ingestion
68 = Less-than-usual meal ingestion
69 = Typical exercise activity
70 = More-than-usual exercise activity
71 = Less-than-usual exercise activity
72 = Unspecified special event

target class while the predictability of the whole model is still strong. The maximum number of factors would be the same figure for the maximum dimension of fuzzy lattice (Khezeli & Nezamabadi-pour, 2012b).

The rationale for this approach is based on the classical concept of Apriori, which states that 'any subset of a frequent item set must also be frequent.' If let's*** say PA found a rule that has a frequent item set of size four, the subsets of this item set of sizes three, two and one would also be frequent meaning that they will also be significant on par with the mother frequent item set of size four. PA establish a frequent item set by searching over the dataset with an increasing threshold that tightens the criteria for the best n rules with a sufficiently high confidence value, called accuracy. Taken from the PA results that run from our experimental dataset, the following two rules show the associations of four factors respective to predicting the two target class values respectively. The two rules are qualified because their accuracy values are sufficiently high >90%. Consequently these two rules signify that the maximum cardinality for the fuzzy lattice should be four, assumed that the minimum required accuracy is 0.93738. Of course more factors can be subsumed and it raises the maximum cardinality for the fuzzy lattice, by compromising the minimum required accuracy with a lower value – it relaxes the criteria for passing more candidates in the frequent item set hence expanding its size. Readers who want more technical details of PA are referred to Scheffer (2001). It worth noting that the values associated with the four factors do not matter in this process as these specific values will be extended to fuzzy memberships.

$$\left\{\left\{\begin{matrix}\text{Time\_from\_last\_regular\_insulin}\\ =0.220139\end{matrix}\right\}\cup\left\{\begin{matrix}\text{Time\_from\_last\_NPH\_insulin}\\ =1.004167\end{matrix}\right\}\right.$$
$$\left.\cup\left\{\begin{matrix}\text{Last\_regular\_dose}\\ =7\end{matrix}\right\}\cup\left\{\begin{matrix}\text{Last\_NPH\_dose}\\ =13\end{matrix}\right\}\right.$$
$$\Rightarrow\left\{\begin{matrix}\text{GTM}\\ =\text{High}\end{matrix}\right\}\exists\,\mathit{Accuracy}(0.95924)$$

$$\left\{\left\{\begin{matrix}\text{Time\_from\_last\_regular\_insulin}\\ =0.581944\end{matrix}\right\}\cup\left\{\begin{matrix}\text{Time\_from\_last\_NPH\_insulin}\\ =0.998611\end{matrix}\right\}\right.$$
$$\left.\cup\left\{\begin{matrix}\text{Last\_regular\_dose}\\ =5\end{matrix}\right\}\cup\left\{\begin{matrix}\text{Last\_NPH\_dose}\\ =16\end{matrix}\right\}\right.$$
$$\Rightarrow\left\{\begin{matrix}\text{GTM}\\ =\text{Low}\end{matrix}\right\}\exists\,\mathit{Accuracy}(0.93738)$$

3.2. Fuzzy rule generation

The Fuzzy Lattice Reasoning Classifier (FLR) which was proposed by Athanasiadis (2007) in 2007 serves as the core of the fuzzy rule generation module. FLR is acclaimed by its ability to produce descriptive and yet fuzzy (thus flexible) rules by modeling a mathematical lattice as the main induction model. The model is induced by computing the disjunctions of interval conjunctions of the training data. At the same time, it increments the size of the diagonal (so called cardinality) of the rules proportional to a predefined maximum threshold called *rhoa*. While the total amount of rules may not be known in advance, the rules increase their number as *rhoa* value rises. Since different cardinalities of rules would be generated, rules from consisting of a single factor up to the maximum number of factors will be produced. This feature caters well for testing instances which may not necessary have a full set of factors required. The beauty of FLR is known for its flexibility in accommodating testing instances that may be perforated with missing values or even missing attributes (Zimmermann, Lopes, Polleres, & Straccia, 2012).

The reasoning environment for classification by FLR is founded over the notion of Fuzzy Lattices which is described as follow. A lattice $\mathcal{L}$ which is an algebraic expression based on a non-empty partial ordered set called poset, is defined as $\langle\mathcal{L};\wedge,V\rangle$. The two binary operations $\wedge$, V on $\mathcal{L}$ are associative, commutative and idempotent, satisfying the absorption law. For any two elements, $i,j\in\mathcal{L}$, $\wedge$ is called a 'meet' operation for $i\wedge j=inf\{i,j\}$ that have a greatest lower bound, or infimum (*inf*). And those that have a least upper bound the operation is called a 'join', supremum (*sup*), so $i\wedge j=sup\{i,j\}$. $\mathcal{L}$ is said to be complete as long as all its subsets subsume a greatest lower bound and a least upper bound. It can also be non-void when missing element and do not care element are considered to have existed in $\mathcal{L}$, which are symbolized by O and I respectively. For Cartesian product lattice, where $\mathcal{L}=\mathcal{L}_1\times\mathcal{L}_2\times\cdots\times\mathcal{L}$ that contains n constituent lattices, the two operations meet and join have the following effects: the meet operation is given by $\{i_1,\cdots,i_n\}\wedge\{j_1,\cdots,j_n\}=\{i_1\wedge j_1,\cdots,i_n\wedge j_n\}$, whereas the join operation is denoted as $\{i_1,\cdots,i_n\}\vee\{j_1,\cdots,j_n\}=\{i_1\vee j_1,\cdots,i_n\vee j_n\}$. With this ability, it is possible for diverse constituent lattices to combine into a product lattice, thereby disparate types of data like numeric data sets, fuzzy sets, and symbols etc. can potentially be separated or joined with ease in the context of lattices.

In FLR, general lattice is modified to be a fuzzy lattice of a pair $\langle\mathcal{L},\mathcal{F}\rangle$, where $\mathcal{F}$ is a membership function such that $\mathcal{F}:\mathcal{L}\times\mathcal{L}\to[0,1]$ and $\mathcal{F}(i,j)=1.i\Longleftrightarrow j$. With a full set of fuzzy lattices, a reasoning framework is established and it serves as the core of decision making for the insulin therapy management. All is required is to extract the fuzzy rules from the fuzzy lattice $\langle\mathcal{L},\mathcal{F}\rangle$ The rule antecedent is implemented by a fuzzy lattice element in a fuzzy lattice rule; then its consequence (target of inference) is derived from the fuzzy inclusion measure which works as a truth function. A fuzzy lattice rule is therefore denoted as a pair $\langle x,y\rangle$ where $y\in Y$ is a target class label, x is an element in $\langle\mathcal{L},\mathcal{F}\rangle$, thus the $x\to y$ is mapping the element x from $\mathcal{L}$ to a target y via *mathalF*. Given x and z are elements of $\mathcal{L}$, the degree of truth for governing $x\to y$ vs. that of $z\to y$ by the fuzzy membership function, *calF* , is considered to be:

$$T(z,x)=\mathcal{F}(z,x)=\frac{\upsilon(x)}{(\upsilon z\vee x)}\tag{1}$$

where υ is a valuation function that applies on lattice $\mathcal{L}$ with the a real positive function that satisfies the conditions:

$$\upsilon(i)+\upsilon(j)=\upsilon(i\wedge j)+\upsilon(i\vee j)\tag{2}$$

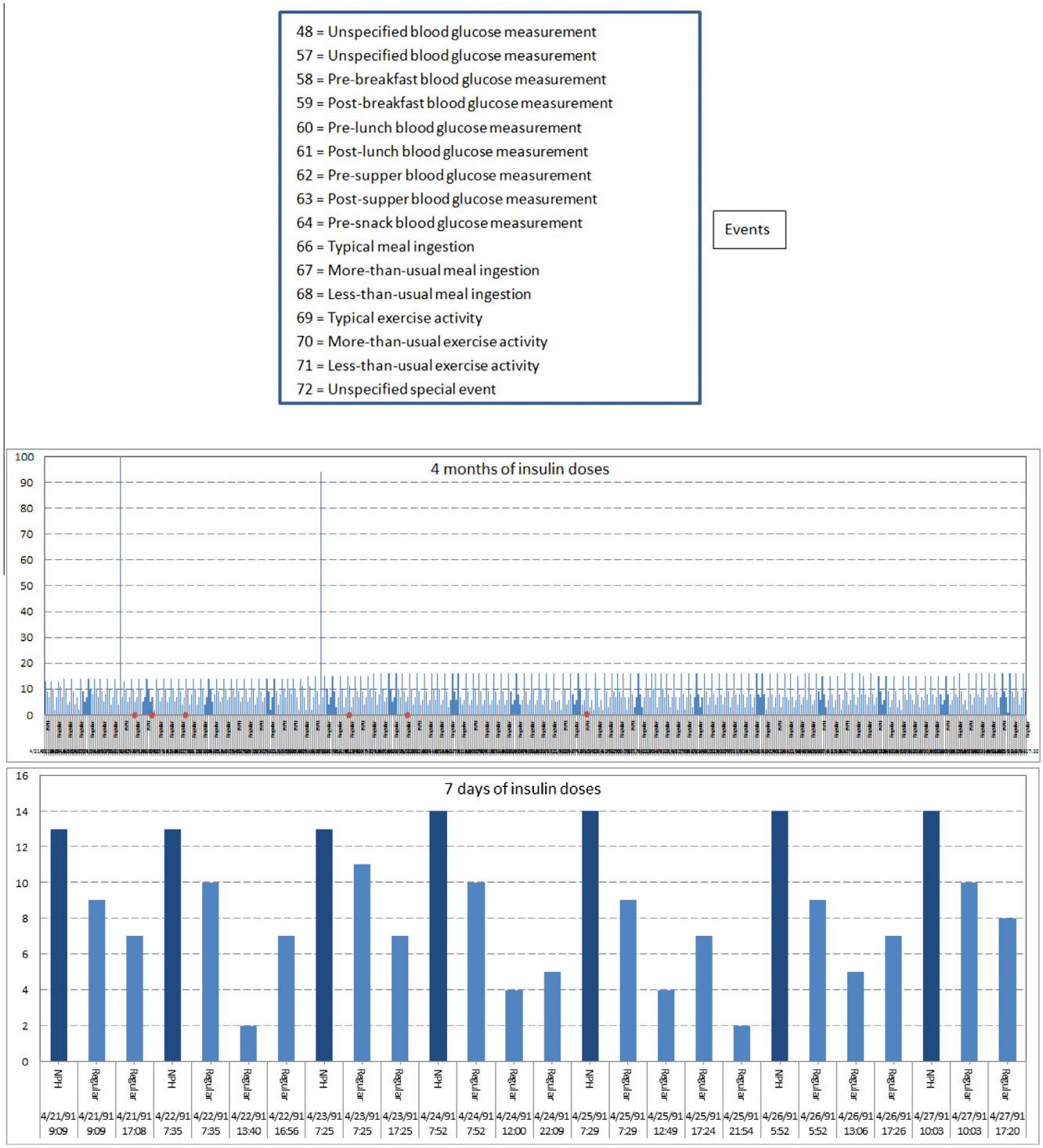

Fig. 2. Irregular patterns of IDDM events, data taken from a subset of AAAI Spring Symposium on Interpreting Clinical Data. Above (a): adaption of insulin for 4 months. Below (b): adaption of insulin injections for 7 days.

$$i < j \iff \upsilon(i) < \upsilon(j) \tag{3}$$

The fuzzy membership function here is taken by an inclusion measure on a complete $\mathcal{L}$ called ϑ, for the mapping $\vartheta : \mathcal{L} \times \mathcal{L} \to [0,1]$. The inclusion measure holds when the following conditions are satisfied where $i, j, k \in \mathcal{L}$:

$$\vartheta(i, O) = 0, \forall i \neq O \tag{4}$$

$$\vartheta(i, i) = 1 \tag{5}$$

$$i \leqslant j \Rightarrow \vartheta(k, i) \leqslant \vartheta(k, j) \tag{6}$$

$$i \wedge j < i \Rightarrow \vartheta(i, j) < 1 \tag{7}$$

Kaburlasos (2006) has devised an efficient representation for fuzzy lattices as $\langle \mathcal{L}, \ell^{+} \rangle$ and $\langle \mathcal{L}, \ell^{-} \rangle$, where $\upsilon(O) = 0$ and,

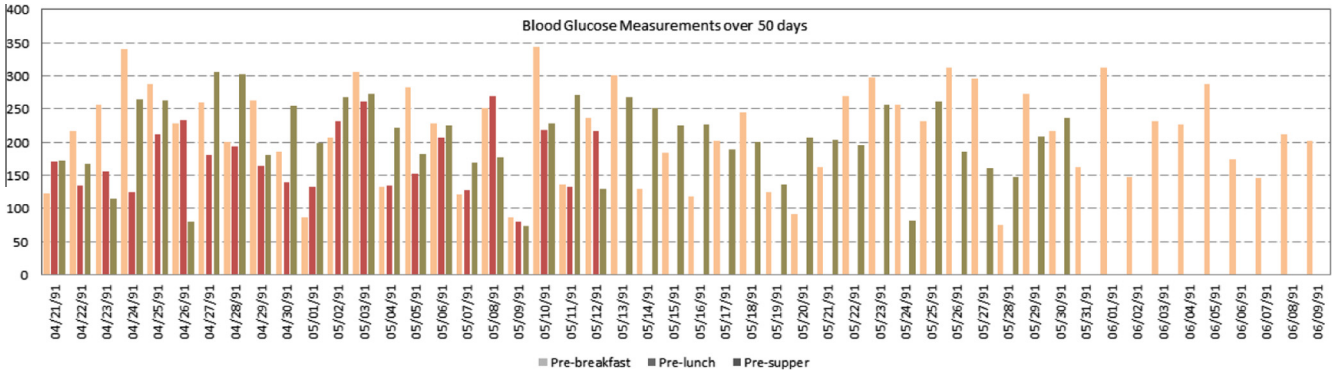

Fig. 3. Periodic patterns of blood glucose measurements, data taken from a subset of AAAI Spring Symposium on Interpreting Clinical Data.

Date/Time	Event	Value
4/21/91 9:09	Pre-breakfast_blood_glucose_measurement	100
4/21/91 9:09	Regular_insulin_dose	9
4/21/91 9:09	NPH_insulin_dose	13
4/21/91 17:08	Pre-supper_blood_glucose_measurement	119
4/21/91 17:08	Regular_insulin_dose	7
4/21/91 22:51	Unspecified_blood_glucose_measurement	123
4/22/91 7:35	Pre-breakfast_blood_glucose_measurement	216
4/22/91 7:35	Regular_insulin_dose	10
4/22/91 7:35	NPH_insulin_dose	13
4/22/91 13:40	Regular_insulin_dose	2
4/22/91 16:56	Pre-supper_blood_glucose_measurement	211
4/22/91 16:56	Regular_insulin_dose	7
4/23/91 7:25	Pre-breakfast_blood_glucose_measurement	257
4/23/91 7:25	Regular_insulin_dose	11
4/23/91 7:25	NPH_insulin_dose	13
4/23/91 17:25	Pre-supper_blood_glucose_measurement	129
4/23/91 17:25	Regular_insulin_dose	7
4/24/91 7:52	Pre-breakfast_blood_glucose_measurement	239
4/24/91 7:52	Regular_insulin_dose	10
4/24/91 7:52	NPH_insulin_dose	14
4/24/91 12:00	Regular_insulin_dose	4
4/24/91 17:10	Pre-supper_blood_glucose_measurement	129
4/24/91 22:09	Unspecified_blood_glucose_measurement	340
4/24/91 22:09	Regular_insulin_dose	5
4/25/91 7:29	Pre-breakfast_blood_glucose_measurement	67
4/25/91 7:29	Regular_insulin_dose	9

Time_from_last_NPH_insulin	Last_NPH_dose	Time_from_last_regular_insulin	Last_regular_dose	Type_of_bgm	Bgm_value	GTM	Hypo
0.332638889	13	0.332638889	9	supper	119	Low	N
0.934722222	13	0.602083333	7	breakfast	216	High	N
0.389583333	2	0.136111111	2	supper	211	High	N
0.993055556	13	0.603472222	7	breakfast	257	High	N
0.416666667	13	0.416666667	7	supper	129	Low	N
1.01875	13	0.602083333	7	breakfast	239	High	N
0.3875	14	0.215277778	4	supper	129	Low	N
0.984027778	14	0.388888889	5	breakfast	67	Low	N
0.413194444	14	0.190972222	4	supper	206	High	N
0.932638889	14	0.331944444	2	breakfast	77	Low	N
0.481944444	14	0.180555556	5	supper	228	High	N
1.174305556	14	0.692361111	7	breakfast	259	High	N
0.303472222	14	0.303472222	10	supper	256	High	N
0.94375	14	0.640277778	8	breakfast	109	Low	N
0.35	14	0.35	10	supper	96	Low	N
0.95625	14	0.60625	7	breakfast	128	Low	N
0.249305556	14	0.249305556	9	lunch	192	High	Y
0.382638889	14	0.133333333	5	supper	263	High	N
1.000694444	14	0.618055556	8	breakfast	179	High	N
0.21875	14	0.21875	10	lunch	88	High	N
0.416666667	14	0.197916667	4	supper	185	High	N
0.998611111	14	0.581944444	7	breakfast	86	Low	Y
0.191666667	14	0.191666667	10	lunch	60	High	Y
0.594444444	163	0.594444444	7	breakfast	147	Low	N
0.420833333	13	0.177083333	5	supper	207	High	Y
0.232638889	14	0.232638889	10	lunch	81	High	N

Fig. 4. Samples of periodic patterns of blood glucose measurements, data taken from a subset of AAAI Spring Symposium on Interpreting Clinical Data. Left (a): transactional data format; Right (b) relational data format after data transformation.

$$\ell^{+}(i,j) = \frac{\upsilon(j)}{(\upsilon i \vee j)} \tag{8}$$

$$\ell^{-}(i,j) = \frac{(\upsilon\, i \wedge j)}{\upsilon(i)} \tag{9}$$

They can be extended to define the lattice of closed intervals, L^c, with an isomorphic function $\varphi : \mathcal{L}' \to \mathcal{L}$, as follow:

$$\ell^{c+}([i,j],[k,l]) = \frac{\upsilon^{c([k,l])}}{\upsilon^{c}([i,j] \vee [k,l])} = \frac{\upsilon^{c([k,l])}}{\upsilon^{c}([i \wedge k, j \vee l])} = \frac{\upsilon(\varphi(k)) + \upsilon(l)}{\upsilon(\varphi(i \wedge k)) + \upsilon(j \vee l)} \tag{10}$$

$$\ell^{c-}([i,j],[k,l]) = \frac{\upsilon^{c}([i,j] \wedge [k,l])}{\upsilon^{c([i,j])}} = \frac{\upsilon^{c}([i \vee k, j \wedge l])}{\upsilon^{c([i,j])}} = \frac{\upsilon(\varphi(i \vee k)) + \upsilon(j \wedge l)}{\upsilon(\varphi(i)) + \upsilon(j)} \tag{11}$$

With the inclusion measure that serves as the fuzzy membership function properly defined, the FLR reasoning environment, $\mathbb{C}$, is about having commonly activation of a collection of fuzzy lattices rules.

$$\mathbb{C}_{\langle \mathcal{L},\mathcal{F}\rangle \to Y} \succcurlyeq \{x_1 \to y, x_2 \to y, \cdots x_m \to y\}, x_i \in \mathcal{L}, \mathcal{F}, y_j \in Y, i = 1..m, j = 1..c \tag{12}$$

And reasoning in FLR becomes a task of computing the degree of truth among the classifier rules in the format of fuzzy lattice rules. Inducing the fuzzy lattice rules is similar to finding a function $f : X \to Y$ that associates each object in the partially ordered training set $\{x_1, x_2, \cdots, x_n\} \in Obj$ with a target class $y \in Y$ where $Y = \{y_1, y_2, \cdots, y_c\}$ is a set of given classes. X, when assumed to be a complete lattice can contain any type of data structures, from numeric vectors to mixed data formats. A fuzzy membership $\mathcal{F} : X \times X \to [0,1]$can be calculated by certain positive valuation function as well as inclusion measure, via the Eqs. (8)–(11). The induction process for a fuzzy lattice rule classifier is done basically by joining the lattice rules that belong to the same class; the joining (expansion) of the lattice grows to lattice rules of greater length (with more conditional factors). Without losing the generality, the training algorithm for a fuzzy lattice rule classifier of size S, $\mathcal{C}_{\mathcal{L},\mathcal{F}\to Y} \succcurlyeq \{x_1 \to y_1, x_2 \to y_2, \cdots x_S \to y_S\}$ is presented below:

Step 1: Start with an empty lattice $\mathcal{C}_{\mathcal{L},\mathcal{F}\to y}$ with size $S = 0$. Initialize a user-defined threshold ϱ for regulating the lattice growth size, where $\varrho \in [0,1]$.

Step 2: Load in the next training instance $\langle z, y\rangle$, format it to a fuzzy lattice rule $z \to y$, and append it to the initially set rules in $\mathcal{C}_{\mathcal{L},\mathcal{F}\to\mathcal{Y}}$. Repeat until the end of the training instances.

Step 3: Calculate the fuzzy degree of inclusion $\mathcal{F}(z \leqslant x_S)$, $\forall s = 1 \ldots S$ hyper-dimension of the antecedent z to the antecedents of all the set rules in $\mathcal{C}_{\mathcal{L},\mathcal{F}\to Y}$.

Step 4: The set rules in compete with each other. Select a winner rule $x_K \to y_K$ given an optimization equation,

$$K = \arg^{MAXIUM}_{s\in\{1\ldots S\}} \mathcal{F}(z \leqslant x_s) \tag{13}$$

Step 5: An assimilation condition is determined by both $y = y_K$ and $diag(z \vee x_K) < \varrho$. If the condition of assimilation arises then replace the antecedent x_K of the winner rule $x_K \to y_K$ with the join-lattice rule $z \vee x_K \to y_K$. Go back to Step 2. Else if the condition of assimilation does not arise, then go back to Step 3.

The threshold criterion ϱ (*rhoa*) is user-defined, that influences effectively the total number of generated rules as well as the overall performance quality of the fuzzy lattice classifier. In the next Section, experiments with varying vales of ϱ are tested for finding an optimum between the lattice size and the desired minimum performance. Rules that are generated follow the general format as below. Groups of rules are pointing to each specific target class label, and each rule is computed with a support percentage, implying its accuracy in predicting the target class. Most importantly each of the testing attributes carries a fuzzy range with a min and max value.

$$\mathcal{L}^Y = \begin{bmatrix} \langle min_1|a_1|max_1 \cup min_2|a_2|max_2 \cup \cdots min_{m-1}|a_{m-1}|max_{m-1} \cup min_m|a_m|max_m \Rightarrow class = y_1|s\%\rangle \\ \langle min_1|a_1|max_1 \cup min_2|a_2|max_2 \cup \cdots min_{m-1}|a_{m-1}|max_{m-1} \cup min_m|a_m|max_m \Rightarrow class = y_2|s\%\rangle \\ \vdots \\ \langle min_1|a_1|max_1 \cup min_2|a_2|max_2 \cup \cdots min_{m-1}|a_{m-1}|max_{m-1} \cup min_m|a_m|max_m \Rightarrow class = y_{C-1}|s\%\rangle \\ \langle min_1|a_1|max_1 \cup min_2|a_2|max_2 \cup \cdots min_{m-1}|a_{m-1}|max_{m-1} \cup min_m|a_m|max_m \Rightarrow class = y_C|s\%\rangle \end{bmatrix} \tag{14}$$

4. Experiments

The proposed methodology is designed to crunch on a diabetic patient's event records, in the raw format of transactional data, and outputs a set of descriptive rules with fuzzy min–max for decision support. In order to verify the efficacy of the proposed methodology, samples of the diabetes datasets are tested in the computer simulation experiments. We would want to see how the fuzzy rules are to be acquired between the balance of accuracy and amount from the data, by controlling the lattice threshold variable called ϱ. The FLR algorithm is compared with other classical machine learning algorithms too, in the same environment of rule-generation from the perspective of model accuracy.

4.1. The testing dataset

The dataset is acquired from a contest at the 1994 Artificial Intelligence in Medicine Spring Symposium (AIM 94). The conference has a topic called 'Interpreting Clinical Data' by which a set of data about outpatient monitoring and management of IDDM, is kindly made available by Michael Kahn, MD, PhD, Washington University, for participants to use. Now the dataset is archived in the Machine Learning Data Repository[5] by University of California Irvine that can be downloaded for free.

The dataset contain records of 70 patients worth of physiology and pathophysiology of diabetes mellitus as well as its treatment, so called maintenance therapy. Since our proposed model is patient-specific, the dataset of only the first patient is used in our experiment. Two types of recording sources the diabetes patient records were chronicled, electronic logging device and paper logs. In the dataset that we adopted in the experiment, electronic source of logging device was used that offered more precise time-stamps than paper forms. In the dataset file which is in raw text format, each record consists of four fields per line. The four fields are: (1) date stamp, in mm/dd/yyyy format; (2) time stamp in minutes:seconds format; (3) code value that gives meaning to the event; and (4) the corresponding value of the code in the record. The fields of date- and time-stamps are merged in our data, converting to universal time values as serial numbers. E.g. concatenating 6/5/1991 with 13:45 gives a serial number of 33394 + 0.572917. The simplicity of the serial number makes training the FLR taking date/time as a singular numeric field convenient. The serial number can easily be reverted to date/time format when it comes to human interpretation. The meanings of the codes are given in Table 1. The dataset in our use has 7146 records spanning from 4/21/1991 to 9/23/1991. In daily average, the data contains approximately 1.923076 blood glucose measurements, 2.923076 regular insulin doses and 1.076923 neutral protamine Hagedorn (NPH) insulin doses which is intermediate-acting insulin for fast effect. There are 51 cases of hypoglycemic symptoms occurrences in the time frame. The descriptive statistics of the dataset is shown in Table 2. Regular Insulin: onset 15–45 min, time-of-peak 1–3 h, and effective-duration 4–6 h; NPH Insulin: Onset 1–3 h, time-of-peak 4–6 h, and effective-duration: 10–14 h.

As it can be seen from Table 2, this particular diabetic patient has higher than normal blood glucose (BG) concentration in all three timings of measurement. Though it is normal that BG concentration fluctuate even in people who have normal pancreatic hormonal function, this patient has some extremes of measurements considering a normal pre-meal BG ranges approximately 80–120 mg/dl. The applications of insulin over time help subside the extreme BG swings.

4.2. Simulation results

The computer simulation focuses mainly on the Fuzzy It was conducted in Weka[6] programming environment; Weka stands for Waikato Environment for Knowledge Analysis which is a popular suite of machine learning algorithms for solving data mining problems. All the algorithms are written in Java, developed at the University of Waikato, and open sourced under the GPL. The computer hardware platform on which the experiments are conducted consists of an Intel Core i5–2520 M 2.50 GHz Processor and 4 Gb installed memory. The technical task in pre-processing/transforming event data stream to transactional data records is enabled by a Java program.

Two sets of experiments are run by using the diabetics IDDM dataset as described in Section 3.1. One is to test out the optimal configuration of FLR for generating fuzzy rules with acceptable accuracy. The other one is to compare the performance of FLR with other popular machine learning algorithms. The performance results during the FLR model induction are tabulated in Table 3, by varying the lattice threshold parameter, $\varrho \in [0, 1]$, called *rhoa*. The same performance results are charted in Fig. 5 for qualitative interpretation.

Performance results include the accuracy of the model, Kappa statistics, and the normalized gain ratio in rule generation. All the values of the performance results are normalized to [0,1] where 0 is the minimum and 1 is the maximum. The accuracy is simply the percentage of the correctly classified rules over the total number of rules. It serves as the main performance of the model indicating how 'useful' it is pertaining to prediction. Individual

[5] http://archive.ics.uci.edu/ml/datasets/Diabetes.

[6] Source: Anatolia News Agency, 10/14/2010.

rules generated by the model are evaluated by the performance of accuracy as well. Each rule is assessed by how often (in%) they have correctly classified the instances. In Weka, the option for training/testing is set to 10-fold cross validation, which is a common way in statistics to validate how well the results of a data mining model will generalize to any independent dataset. It works by randomly partitioning the full dataset to two subsets, one being the training segment and the other one being the testing segment. The testing segment serves as unseen samples for assessing the performance of the induced model; of course the testing segment has already had the predefined class labels, so the software would be able to score the accuracy of the model that was trained by the training subset. This process is repeated ten rounds, again randomly on different positions of the full dataset, in order to obtain unbiased performance results. Each time the cross-validation is performed over different random partitions. The final performance scores are those averaged over the ten rounds.

Kappa statistics is generally used in data mining, statistical analysis and even assessment of medical diagnostic tests (Kaburlasos, 2006), as an indicator on how 'reliable' a trained model is. It basically reflects how consistent the evaluation results obtained from multiple inter-observers are and how well they are agreed upon. A full description of the Kappa statistics can be found in Viera and Garrett (2005). Generally a Kappa of 0 indicates agreement is equivalent to chance, where as a Kappa of 1 means perfect agreement. It loosely defines here as reliability by saying a model that has a high Kappa value is a consistent model that would expect about the same level of performance (in this case, accuracy) even when it is tested with datasets from other sources. The Kappa statistics is computed here from the 10-fold cross-validation with each fold of different combination of partitions (training and testing) as different inter-observers.

A gain-ratio performance indicator, the increase of accuracy over the number of rules generated, is adopted here especially for FLR. By increasing the lattice threshold, *rhoa*, the lattice size grows as well as the amount of rules. However, it is desirable to observe the gain ratio as the improvement of accuracy per rule generated. If we let α_r be the accuracy of a lattice model $\mathcal{L}_\varrho$ where and $\varrho = r$, $r \in [01,]$, the gain ratio ζ_r and the normalized gain ratio $\hat{\zeta}_r$ are then defined as:

$$\zeta_r = \frac{\alpha_r}{\#rules_r}, \text{and } \hat{\zeta}_r = \frac{|\zeta_r - \min(\zeta_i, : i = 0..1)|}{\max(\zeta_i, : i = 0..1) - \min(\zeta_j, : j = 0..1)} \quad (15)$$

The last performance criterion in relation to the quality of a FLR model is the amount of rules being generated. Although there is no thumb-rule regarding how many rules a model must generate, generally rules that are of good accuracy and high Kappa value are favored; equally important, the rules that are generated should be balanced across different target class labels. For example, if there are m different target classes, the ratio of the rules pointing to each class should be ideally equal to $1/m$. It may be acceptable if the ratio is slightly more or less of this value. Otherwise, rules are of imbalance among the classes and this may lead to biased (hence undesirable) accuracy of the prediction model. In our experiment, we define a performance criterion called *balance_index*, β_r for consideration of evaluating a lattice model $\mathcal{L}_\varrho$ where $\varrho = r$, $r \in [01,]$. β_r is denoted as follow when $m = 2$ as in our experiment:

$$\beta_r = 1 - \left| \frac{rules\#(class1) - rules\#(class2)}{total_{rules}\#} \right| \quad (16)$$

Therefore choosing an optimal model is multi-objective consideration of several factors: accuracy, Kappa value, number of rules generated and the balance index of the rules. All these factors, in the case of FLR, depend on the choice of *rhoa* parameter which governs the growth size of the lattice model.

In the second part of the experiment, without being exhaustive, several popular machine learning models are tested vis-à-vis with the FLR model. The five algorithms of choice are Artificial Neural Network (ANN), Bayesian Network (BayesNet), Logistic Regression (LR), Repeated Incremental Pruning to Produce Error Reduction (Ripper), and Support Vector Machine (SVM). ANN, LR and SVM belong to the group of black-box prediction models where rules are not generated explicitly from the models. BayesNet which is also known as Belief Network is incremental in nature; it is a probabilistic representation model, having a network of conditional dependencies exemplified over a directed acyclic graph. All these algorithms have been used extensively in similar diabetic symptoms prediction; some of which have been introduced in the previous section of this paper. For details of these algorithms, readers are referred to a comparative evaluation of these algorithms that has been reported in this paper (Fong & Cerone, 2012). For fairness of the comparison, all the selected algorithms have been fine-tuned in advance with the best-performing parameters, e.g. FLR with *rhoa* = 0.9. The experiment for the comparison is executed in the same computing environment, including both the hardware and software; the same diabetic IDDM dataset is used, and the same 10-fold cross-validation option is selected across each experiment trial for each algorithm. Since some models only predict without generating the rules, the evaluation assessment is focused only on the quality aspect of the model without considering about the rules. The comparative performance results of the algorithms are visualized in Fig. 6 with the performance values labeled in the bar chart.

5. Discussion

In consideration of a FLR model with reasonable performance, some recommended values for the *rhoa* parameters include 0.63, 0.85, 0.89 and 0.9. This reasoning is derived from the results presented in Fig. 5. These values represent both the local peak and perhaps global peaks of the performance curves. As the curve of the normalized gain ratio shows, the lattice grows with increasing number of rules and simultaneously enhancing the accuracy, from *rhoa* value 0 up to about 0.68 and the gain gets stagnant – stalls at a small value close to zero. This implies the lattice starts to become mature without further significant growth in terms of large increase in accuracy per additional rule, at *rhoa* = 0.68 and afterwards. So naturally one would select an optimal *rhoa* parameter value from 0.68 onwards; there are then three best performers at *rhoa* = 0.85, 0.89 and 0.9. Each of the three values produces equally best accuracy (90%) and highest Kappa value (0.94). However, considering the *balance_indices* among the three choices, it seems *rhoa* = 0.9 offers the evenest balance in the number of rules between the two target classes – 0.97 vs. 0.87 and 0.78.

However, when it comes to a calibration choice between generating many and few rules, there is no standard as it depends on the application and perhaps the user's preference. Sometimes, having fewer rules may be advantageous when the costs of tests are high. Nevertheless in our case here, the cardinality of the model remains the same, meaning the number of conditional factors to be examined is the same across the models $\mathcal{L}_\varrho \sim$ of four choices of *rhoa* values. Testing with many rules indicate a thorough testing which can refine the prediction result, therefore generally models with many rules such as our case here when *rhoa* = 0.9 (it yields 29 fuzzy rules in contrast to eight rules at *rhoa* = 0.63), highest accuracy and the most balanced distribution of rules among the classes can be achieved. Furthermore, the accuracy and the Kappa values in our FLR model are highly positively correlated; the Pearson value for the two performance figures is 0.999981127656942, which is almost a perfect score in their movements. This may be another benefit of FLR model.

Table 2
Statistics of blood glucose measurement and insulin doses in the testing dataset.

	Blood glucose measurement (mg/dl)			Insulin doses	
	Pre-breakfast	Pre-lunch	Pre-supper	NPH	Regular
Min.	55	54	43	13	1
Max.	335	306	343	163	11
Average	169.7185185	141.074074	161.2352941	16.89209	6.59375
Median	163	133.5	156.5	16	7

Table 3
Performance results of the FLR model with different values of rhoa.

Rhoa	Accuracy	Kappa	#Rules	#Rule_low	#Rule_high	Balance_index	Gain (acc/rule)	Normalized_gain
0	0.73	0.4481	2	1	1	1	0.3650	1.0000
0.1	0.73	0.4481	2	1	1	1	0.3650	1.0000
0.2	0.73	0.4481	2	1	1	1	0.3650	1.0000
0.3	0.73	0.4481	2	1	1	1	0.3650	1.0000
0.4	0.73	0.4481	2	1	1	1	0.3650	1.0000
0.5	0.73	0.4481	2	1	1	1	0.3650	1.0000
0.51	0.72	0.4281	2	1	1	1	0.3600	0.9859
0.52	0.73	0.4481	2	1	1	1	0.3650	1.0000
0.53	0.73	0.4481	3	1	2	0.666666667	0.2433	0.6580
0.54	0.73	0.4481	3	1	2	0.666666667	0.2433	0.6580
0.55	0.75	0.4898	4	2	2	1	0.1875	0.5010
0.56	0.78	0.5521	4	2	2	1	0.1950	0.5221
0.57	0.75	0.4906	4	2	2	1	0.1875	0.5010
0.58	0.79	0.5735	5	2	3	0.8	0.1580	0.4180
0.59	0.84	0.6764	5	2	3	0.8	0.1680	0.4462
0.6	0.87	0.7373	5	2	3	0.8	0.1740	0.4630
0.61	0.9	0.7987	6	2	4	0.666666667	0.1500	0.3956
0.62	0.91	0.8187	6	2	4	0.666666667	0.1517	0.4002
0.63	**0.93**	**0.8592**	**8**	**3**	**5**	**0.75**	**0.1163**	**0.3007**
0.64	0.92	0.8395	6	3	3	1	0.1533	0.4049
0.65	0.86	0.7173	8	4	4	1	0.1075	0.2761
0.66	0.85	0.6973	9	4	5	0.888888889	0.0944	0.2394
0.67	0.85	0.6973	7	3	4	0.857142857	0.1214	0.3152
0.68	0.87	0.7381	10	6	4	0.8	0.0870	0.2184
0.69	0.86	0.7173	10	3	7	0.6	0.0860	0.2156
0.7	0.86	0.7177	9	3	6	0.666666667	0.0956	0.2425
0.71	0.86	0.7177	11	4	7	0.727272727	0.0782	0.1937
0.72	0.89	0.7788	9	4	5	0.888888889	0.0989	0.2519
0.73	0.86	0.7177	10	5	5	1	0.0860	0.2156
0.74	0.91	0.8193	11	5	6	0.909090909	0.0827	0.2064
0.75	0.92	0.8395	13	6	7	0.923076923	0.0708	0.1728
0.76	0.92	0.839	11	6	5	0.909090909	0.0836	0.2090
0.77	0.91	0.8187	12	6	6	1	0.0758	0.1870
0.78	0.91	0.819	12	6	6	1	0.0758	0.1870
0.79	0.92	0.8397	12	6	6	1	0.0767	0.1894
0.8	0.93	0.8597	14	7	7	1	0.0664	0.1606
0.81	0.93	0.8599	16	7	9	0.875	0.0581	0.1373
0.82	0.95	0.8998	15	7	8	0.933333333	0.0633	0.1519
0.83	0.95	0.8999	15	7	8	0.933333333	0.0633	0.1519
0.84	0.94	0.8798	17	7	10	0.823529412	0.0553	0.1293
0.85	**0.97**	**0.94**	**18**	**7**	**11**	**0.777777778**	**0.0539**	**0.1254**
0.86	0.96	0.92	19	8	11	0.842105263	0.0505	0.1159
0.87	0.96	0.9199	22	10	12	0.909090909	0.0436	0.0965
0.88	0.95	0.8999	23	10	13	0.869565217	0.0413	0.0900
0.89	**0.97**	**0.94**	**27**	**12**	**15**	**0.888888889**	**0.0359**	**0.0749**
0.9	**0.97**	**0.94**	**29**	**14**	**15**	**0.965517241**	**0.0334**	**0.0679**
0.91	0.96	0.92	32	15	17	0.9375	0.0300	0.0582
0.92	0.95	0.8999	34	17	17	1	0.0279	0.0524
0.93	0.94	0.8798	38	19	19	1	0.0247	0.0434
0.94	0.9	0.7994	46	23	23	1	0.0196	0.0289
0.95	0.9	0.7994	51	25	26	0.980392157	0.0176	0.0235
0.96	0.94	0.8796	59	27	32	0.915254237	0.0159	0.0186
0.97	0.93	0.8597	68	32	36	0.941176471	0.0137	0.0123
0.98	0.93	0.8597	83	39	44	0.939759036	0.0112	0.0054
0.99	0.93	0.8597	96	45	51	0.9375	0.0097	0.0011
1	0.93	0.8597	100	48	52	0.96	0.0093	0.0000

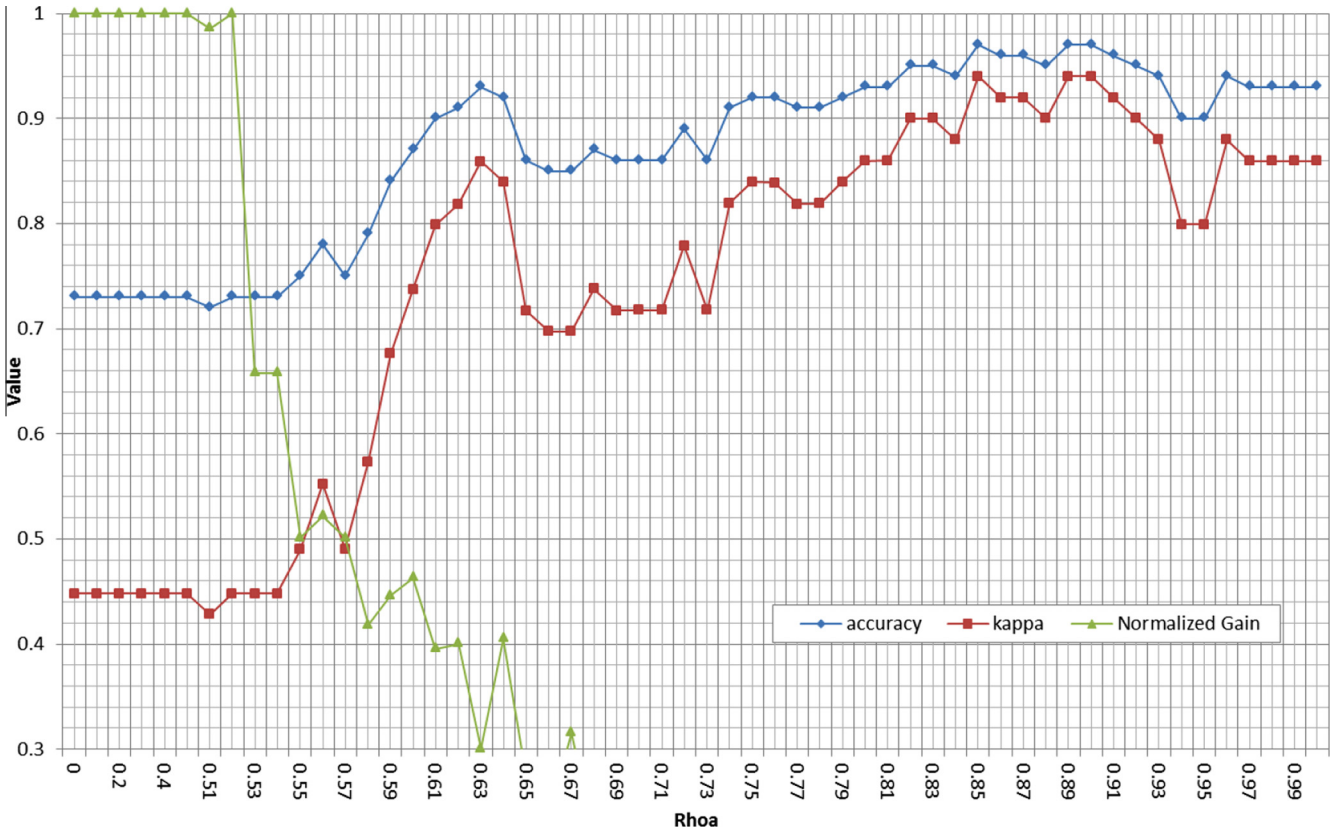

Fig. 5. Performance curves of the FLR model with different values of *rhoa*.

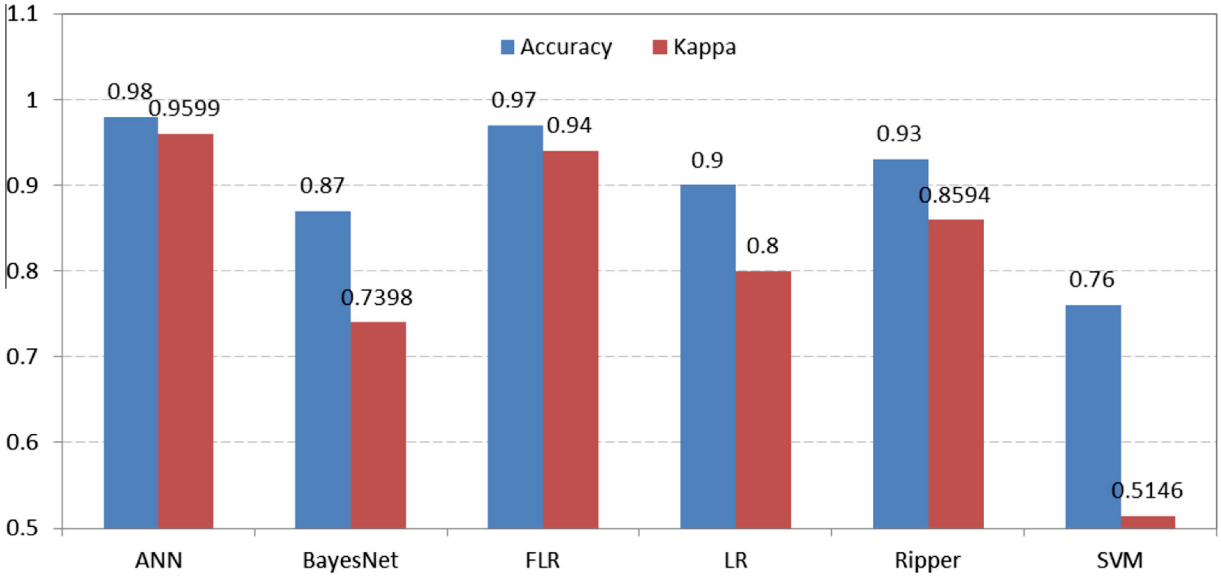

Fig. 6. Comparison of different machine learning algorithms for diabetic prediction.

Without being exhaustive we illustrate some of the fuzzy rules extracted from the generated rules in the lattice model where *rhoa* = 0.9, as shown below. There are a total of 29 rules, 14 pointing to class Low and 15 pointing to class High. Four attributes are used in predicting the class GTM. It is possible to extend the model to include more attributes and more class labels. The fuzzy rules map the values of attributes in pairs of min–max ranges, via some non-relationship.

$$\mathcal{L}_{\varrho=0.9}=\begin{bmatrix} 0.3895|a_1|0.4167\cup 2.0|a_2|14.0\cup 0.1361|a_3|0.1979\cup 2.0|a_4|4.0\Rightarrow class=High|95.6\% \\ 0.3014|a_1|0.3194\cup 14.0|a_2|15.0\cup 0.1146|a_3|0.2083\cup 3.0|a_4|4.0\Rightarrow class=High|97.3\% \\ \vdots \\ 0.9972|a_1|1.0569\cup 14.0|a_2|16.0\cup 0.6118|a_3|0.6563\cup 7.0|a_4|8.0\Rightarrow class=Low|97.1\% \\ 1.0021|a_1|1.0090\cup 13.0|a_2|15.0\cup 0.5694|a_3|0.6076\cup 9.0|a_4|11.0\Rightarrow class=Low|94.8\% \end{bmatrix}$$

In the performance comparison, FLR is rated slightly lower than ANN in performance with $\Delta 0.01$ in accuracy and $\Delta 0.02$ in Kappa statistics. The performance trade-off is justified by the benefit of

transparent and descriptive fuzzy rules generated by FLR. In general, ANN, FLR and Ripper models that potentially can generalize a decision model with rules (rule generation from ANN is possible, though implicitly) can attain almost equally high accuracies and Kappa values with their difference less than 0.0707. On the other hands, BayesNet, LR and SVM may not qualify in inducing a model for accommodating the very non-linear relations between insulin applications and the blood glucose predictions. Despite the fact that relatively low Kappa statistics are yielded from these models, they show a noticeable discrepancy between the accuracy and Kappa statistics. For instance, SVM obtained an accuracy of 0.76 whereas the Kappa statistic is only 0.5146. With a Kappa value about 50%, the consistency of the results would be as good as by random chance, which translates to the poor generalization of the model fitting for different datasets. FLR, nevertheless, has an outstanding advantage of producing fuzzy rules with reasonable performance, among the other candidate.

6. Conclusion

A well-known research challenge in the maintenance therapy for insulin-dependent diabetes mellitus (IDDM) patients is selecting the right insulin dose and timing for the patients. Although it is a well-known medical practice that the blood glucose level for most IDDM patients should be kept within 80–140 mg/dL, the target range for each individual may differ and the course of insulin injections can be quite patient-specific that depends on one's lifestyle and individual health conditions. For this reason, predictive models have been developed in the past in order to predict the blood glucose concentration and/or modeling the effects of insulin on the progress of the prognosis. These cores of these models, which are either data mining kernels or time-series forecasting algorithms, however run short of achieving a very accuracy result. In this paper, we proposed a methodology that combines a series of time-transformation task, model size calibration and decision-model induction using Predictive Apriori (PA) and Fuzzy Lattice Reasoning (FLR). Fuzzy Lattice is an emerging computational intelligence paradigm based on lattice theory (Grana, 2008). It can process disparate types of lattice-ordered hyperbox data, and model uncertain information among them based on the concept of a fuzzy partial-order relation (Nanda, 1989). Firstly, decision rules that describe the conditions that lead to hyper- and hypoglycemia are harvested. This is done by Predictive Apriori algorithm. For rules that characterize normoglycemia which is known as the so-called 'grey area' or 'fuzzy zone' whose buffer range is still controversial and patient-specific, FLR is used. Instead of stating explicitly when, which type and how much insulin injections should be applied to an individual patient, FLR works in another way by checking the current pattern of insulin applications and it tries to predict a consequence in terms of class labels. Users can therefore continuously gauge how well the current therapy is going based on the predicted outcomes. FLR has an edge over the other machine learning algorithms for its ability to generate descriptive fuzzy rules that would be suitable for predicting the target blood glucose levels, via a series of fuzzy tests over the insulin types and doses received in prior. FLR is flexible in the inclusion of several or more testing factors such as types of insulin, the dosages, and the frequencies as well as other contributing factors like exercises and illness. For calibration, a vigilance parameter called *rhoa*, can be used to control the size of the lattice, hence the amount of rules required. Experiments were conducted via computer simulation on the IDDM dataset, which demonstrated optimal value of *rhoa* can be obtained resulting in good multi-faceted performance – high accuracy and Kappa statistics, reasonable balance of rule distribution over the prediction target classes. The proposed fuzzy rule generation model based on FLR has been compared through the simulation experiment that outperformed the other classical machine learning models in overall performance, except Artificial Neural Network. Albeit the aspect of performance, a large potential in the benefits of fuzzy rules derived from FLR is available to be exploited for IDDM therapy design and management. This paper contributed as a pioneer and cornerstone for applying fuzzy lattice computing on IDDM, with successful preliminary results.

Acknowledgments

The authors are thankful for the financial support from the research Grant "Adaptive OVFDT with Incremental Pruning and ROC Corrective Learning for Data Stream Mining," Grant no. MYRG073(Y2-L2)-FST12-FCC, offered by the University of Macau, FST, and RDAO.

References

Acharya, A., & Modi, S. (2011). An algorithm for finding frequent itemset based on lattice approach for lower cardinality dense and sparse dataset. *International Journal on Computer Science and Engineering, 3*(1), 371–378. ISSN 0975-3397.

Ackerman, E., Gatewood, L., Rosevear, J., & Molnar, G. (1965). Model studies of blood-glucose regulation. *Bulletin of Mathematical Biophysics, 27*(special issue), 21–37.

Akmal, S. M, Ismail, K., & Zainudin, S. (2011). Prediction of diabetes by using artificial neural network. In *Proceedings of 2011 international conference on circuits, system and simulation* (Vol. 7, pp. 299–303).

American Diabetes Association. (2007). Standards of Medical Care in Diabetes-2007, Diabetes Care, Vol. 30, January.

Athanasiadis, I. N. (2007). The fuzzy lattice reasoning (FLR) classifier for mining environmental data. In V. G. Kaburlasos & G. X. Ritter (Eds.), *Computational intelligence based on lattice theory* (pp. 175–193). SpringerVerlag.

Bennett, D. L., & Gourley, S. A. (2004). Asymptotic properties of a delay differential equation model for the interaction of glucose with plasma and interstitial insulin. *Applied Mathematics and Computation, 151*, 189–207.

Cescon, M., Dressler, I., Johansson, R., & Robertsson, A. (2009). Subspace-based identification of compliance dynamics of parallel kinematic manipulator. In *IEEE/ASME international conference on advanced intelligent, mechatronics* (pp. 1028–1033).

Dassau, E., Cameron, F., Lee, H., Bequette, B. W., Zisser, H., Jovanovic, L., et al. (2010). Real-Time hypoglycemia prediction suite using continuous glucose monitoring: A safety net for the artificial pancreas. *Diabetes Care, 33*(6), 1249–1254. http://dx.doi.org/10.2337/dc09-1487.

De Gaetano, A., & Arino, O. (2000). Mathematical modelling of the intravenous glucose tolerance test. *Journal of Mathematical Biology, 40*, 136–168.

Delia Corte, M., Romano, S., Voeghelin, M. R., & Serio, M. (1970). On a mathematical model for the analysis of the glucose tolerance curve. *Diabetes, 19*(6), 445–449.

Fong, S., & Cerone, A. (2012). Attribute overlap minimization and outlier elimination as dimensionality reduction techniques for text classification algorithms. In Journal of emerging technologies in web intelligence (JETWI), August (Vol. 4, issue 3, pp. 259–263). Oulu, Finland: Academy Publisher. ISSN 1798-0461.

Ginsberg, B. H. (2009). Factors "Affecting blood glucose monitoring: Sources of errors in measurement". *Journal of Diabetes Science and Technology, 3*(4), 1–11.

Gogou, G., Maglaveras, N., Ambrosiadou, B. V., Goulis, D., & Pappas, C. (2001). A neural network approach in diabetes management by insulin administration. *Journal of Medical Systems, 25*(2), 119–131.

Grana, M. (2008). Lattice computing: Lattice theory based computational intelligence. In Matsuhisa, T., & Koibuchi, H. (Eds.) *Proceedings of Kosen workshop on mathematics, technology, and education (MTE), Irabaki National College of Technology, 15–18 February* (pp. 19–27). Ibaraki, Japan.

Han, J. C., Rodriguez, J. C., & Beheshti, M. (2009). Discovering decision tree based diabetes prediction model. In *Proceedings of ASEA* (Vol. 30, pp. 99–109).

Hinshaw, L., Man, C. D., Nandy, D. K., Saad, A., Bharucha, A. E., & Levine, J. A., et al. (2013). Diurnal pattern of insulin action in type 1 diabetes – Implications for a closed loop system. In *Diabetes, the American diabetes association, February 27*, PMID: 23447123.

Kaburlasos, V. (2006). Towards a unified modeling and knowledge-representation based on lattice theory, computational intelligence and soft computing applications. *Studies in Computational Intelligence*, 27.

Kaburlasos, V. G., Athanasiadis, I. N., & Mitkas, P. A. (2007). Fuzzy lattice reasoning (FLR) classifier and its application for ambient ozone estimation. *International Journal of Approximate Reasoning, 45*(1), 152–188.

Kaburlasos, V. G., & Petridis, V. (1997). Fuzzy lattice neurocomputing (FLN): A novel connectionist scheme for versatile learning and decision making by clustering. *International Journal of Computers and their Applications, 4*(3), 31–43.

Kalpana, M., & Senthil Kuma, A. V. (2012). Design and implementation of fuzzy expert system using fuzzy assessment methodology. *International Journal of Science and Applied Information Technology, 1*(1), 39–45.

Khezeli, Y. J., & Nezamabadi-pour, H. (2012a). Fuzzy lattice reasoning for pattern classification using a new positive valuation function. *Advances in Fuzzy Systems, 2012*, 1–8. Article ID 206121.

Khezeli, Y. J., & Nezamabadi-pour, H. (2012b). Fuzzy lattice reasoning for pattern classification using a new positive valuation function. *Advances in Fuzzy Systems, 2012*, 1–8. http://dx.doi.org/10.1155/2012/206121. Article ID 206121.

Li, J., & Kuang, Y. (2001). Analysis of IVGTT glucose–insulin interaction models with time delay, discrete and continuous dynamical systems. *Discrete and Continuous Dynamical Systems – Series B, 1*(1), 103–124.

Liu, H., Xiong, S., & Fang, Z. (2011). FL-GrCCA: A granular computing classification algorithm based on fuzzy lattices. *Computers and Mathematics with Applications, 61*(1), 138–147.

Maciejowski, J. M. (2002). *Predictive control with constraints*. Harlow, UK: Prentice-Hall, Pearson Education Limited. ISBN 0-201-39823-0 PPR.

Makroglou, A., Li, J., & Kuang, Y. (2006). Mathematical models and software tools for the glucose–insulin regulatory system and diabetes: An overview. *Applied Numerical Mathematics, 56*, 559–573.

Mukhopadhyay, A., De Gaetano, A., & Arino, O. (2004). Modelling the intra-venous glucose tolerance test: A global study for a single-distributed-delay model, discrete and continuous dynamical systems. *Discrete and Continuous Dynamical Systems – Series B, 4*(2), 407. May.

Nanda, S. (1989). Fuzzy lattices. *Bulletin Calcutta Mathematical Society, 81*, 1–2.

Otto, E., Semotok, C., Andrysek, J., & Basir, O. (2000). An intelligent diabetes software prototype: Predicting blood glucose levels and recommending regimen changes. *Diabetes Technology and Therapeutics, 2*(4), 569–576. Winter.

Richard, M., Youqing, W., Eyal, D., Robert, K., Jr., Donald, M., Howard, Z., et al. (2010). Proposed clinical application for tuning fuzzy logic controller of artificial pancreas utilizing a personalization factor. *Journal of Diabetes Science and Technology, 4*(4), 913–922.

Scheffer, T. (2001). Finding association rules that trade support optimally against confidence. In *Proceedings of the 5th European conference on principles and practice of knowledge discovery in databases (PKDD'01)* (pp. 424–435).

Ståhl, F., & Johansson, R. (2009). Diabetes mellitus modeling and short-term prediction based on blood glucose measurements. *Mathematical Biosciences, 217*, 101–117.

Viera, A. J., & Garrett, J. M. (2005). Understanding interobserver agreement: The kappa statistic. *Family Medicine, Research Series, 37*(5), 360–363.

Wang, H., Li, J., & Kuang, Y. (2009). Enhanced modelling of the glucose–insulin system and its applications in insulin therapies. *Journal of Biological Dynamics, 3*(1), 22–38.

Zhang, Y., Fong, S., Fiaidhi, J., & Mohammed, S. (2012). Real-time clinical decision support system with data stream mining. *Journal of Biomedicine and Biotechnology, Hindawi, 2012*, 1–8. Article ID 580186.

Zimmermann, A., Lopes, N., Polleres, A., & Straccia, U. (2012). A general framework for representing, reasoning and querying with annotated semantic web data. *Journal of web semantics: Science, services and agents on the World Wide Web* (Vol. 11, pp. 72–95). New York: Springer.