GLYCAEMIA REGULATION PREDICTIVE CONTROL SYSTEMS PERFORMANCES EVALUATION

A Comparative Study of Neural and Mathematical Models

Nathanaël Cottin, Olivier Grunder and Abdellah ElMoudni
Laboratoire Systèmes et Transports, Université de Technologie de Belfort Montbéliard, rue Thierry Mieg, Belfort, France

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Abstract: Type 1 blood glucose regulation remains a complex problem to simulate. Different blood glucose control schemes for insulin-dependent diabetes therapies and systems have been proposed in the literature. This article presents an adaptative predictive control system for glycaemia regulation based on feedforward Artificial Neural Networks trained with the resilient propagation (RPROP) method. Experiments performed on a mathematical (theoretical) compensation model and our system aim to objectively compare the behaviour of each approach when both exact and perturbated data are presented. These experiments, which make use of a virtual patient, not only cover the ANN's best configuration and training parameters on exact training information, they also demonstrate the accuracy of the neural approach when up to 20% perturbated data are supplied. As a result of the experiments on perturbated data, the neural approach gives slightly better evaluations than the theoretical model. This demonstrates the neural system's ability to adapt to perturbated environments.

1 INTRODUCTION

Type 1 diabetics suffer from insulin-dependent diabetes chronic disorders. Their pancreatic β-cells do not secrete sufficient insulin, which mostly results in hyperglycaemia states. Although many researches have been conducted in the past decades, diabetics still need practical daily solutions to help them regulate they blood glucose concentration (BGC).

This work is centered on the presentation of an adaptive Neural Predictive Control (NPC) system used to infer a particular patient's blood glucose regulation metabolism. This system is validated by means of experimental comparisons against the theoretically proven closed-loop control mathematical model proposed by (Charpentier et al., 2005) used for blood glucose regulation. Not only exact raw information is used to evaluate accuracy of the experimented systems, up to 20% perturbated raw and test information allows to verify the adaptability of our NPC approach.

Compared with other works, the proposed system is designed to adapt to numerous blood glucose regulation techniques by means of pluggable modules while conforming to a common regulation process.

This article is organized as follows: next section presents some related works on closed-loop control using mathematical models and Artificial Neural Networks (ANN) to position the context of this paper. Section 3 introduces a Global Predictive Control System (GPCS) used for blood glucose regulation and its derived systems which model the theoretical and neural approaches to be compared. Next section focuses on practical experiments results based on a virtual patient with both exact and perturbated data. Conclusions draw the benefits and drawbacks of each approach and present some future works.

2 PREDICTIVE CONTROL SYSTEMS ARCHITECTURES

2.1 Global PCS

Regulating glycaemia aims to fulfill patients with either extra glucose or external insulin measurements. Regulation is handled by a Global Predictive Control System (GPCS) which takes the following parameters into account:

- Some patient's physical information, such as his age and weight (i.e. miscellaneous parameters);
- A meal identifier, used by the internal regulation

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module to perform initial tasks, before the regulation process starts;

- The glycaemia value before taking the meal (i.e. pre-meal glycaemia);
- The amount of carbohydrates the patient wishes to ingest (i.e. initial meal carbohydrates);
- The expected glycaemia value the patient needs to reach after having ingested the meal carbohydrates, assuming that short-term insulin has fully taken effect (i.e. expected post-meal glycaemia).

As a result, the system estimates the final glycaemia (i.e. evaluated post-meal glycaemia) as close as possible to the patient's expected glycaemia value. It jointly suggests a (possibly null) short-term insulin measurement to absorb the meal carbohydrates (in case of hyperglycaemia) and the total amount of carbohydrates the patient should ingest. In case an insulin measurement is predicted, this amount of carbohydrates equals the initial meal carbohydrates value. This makes sure that extra carbohydrates and insulin measurements are mutually exclusive results.

2.2 Specializations

To operate glycaemia regulation, the global system can be specialized in two PCS classes:

- Theoretical PCS (TPCS) which directly implement mathematical models for glycaemia regulation, without any regulation control loop;
- Commanded PCS (CPCS) which operate by means of an internal control-command compensation loop to suggest insulin and carbohydrates.

The CPCS overall regulation principle is depicted by figure 1. A CPCS relies on two key components:

- A *predictor*, which estimates a glycaemia positive or negative deviation given carbohydrates and insulin values. It may also take into account some patient's miscellanous information to produce a satisfactory glycaemia prediction;
- An *adaptive controller*, which modifies the current insulin or carbohydrates values based on a predicted glycaemia. The controller also determines the control loop stop condition.

The controller uses initial meal carbohydrates once. This value is then replaced with the regulated value (although the controller may have keep this initial value in case it regulates insulin).

3 EXPERIMENTS

This study compares the behaviour and the quality of the compensation results of an NPC CPCS (i.e. neural CPCS) against a TPCS. The TPCS is assumed to provide exact results: a vitual patient, that strictly conforms to the mathematical model implemented in the TPCS, is used to train the neural CPCS.

Then, some perturbations using a normal distribution are added both on training and test data. This implies that the TPCS produces errors compared with the exact data (without perturbations).
Experiments are driven on a virtual patient on both exact and perturbated raw information. This virtual patient behaves like the theoretical compensation model proposed by (Charpentier et al., 2005) in case of exact raw information. Use of this virtual patient allows to determine the neural approach accuracy against the theoretical model. Indeed, two PCS are compared:

- A *theoretical PCS* (TPCS), which implements the mathematical compensation model of the virtual patient. This PCS provides exact results when exact source raw information is used, which means that no deviation is produced;
- A *neural CPCS*, which integrates a neural predictor based on a $n-n-1$ (n refers to the number of inputs of this predictor, conforming to figure 1) feedforward ANN (Mhaskar, 2005). Input and hidden layers use the sigmoid activation function and the output layer uses the hyperbolic tangent activation function (to represent a signed deviation). This neural CPCS approximates compensation values based on the function the ANN infers.

Deviations between PCS suggestions and exact expected compensation values are expressed as follows:

- Carbohydrates deviations are expressed in grams;
- Short-term insulin deviations are expressed by a number of unitary doses.

3.1 Neural CPCS Training

The neural predictor of the neural CPCS is trained from known raw information using supervised training techniques. This set of raw information is randomly generated, though conforming to the mathematical model of (Charpentier et al., 2005).

A raw information item is basically composed of the GPCS inputs and outputs values. However, the final post-meal glycaemia value does not correspond to the neural PCS estimated glycaemia but refers to a physical measurement (performed by the patient himself or by a medical assistant).

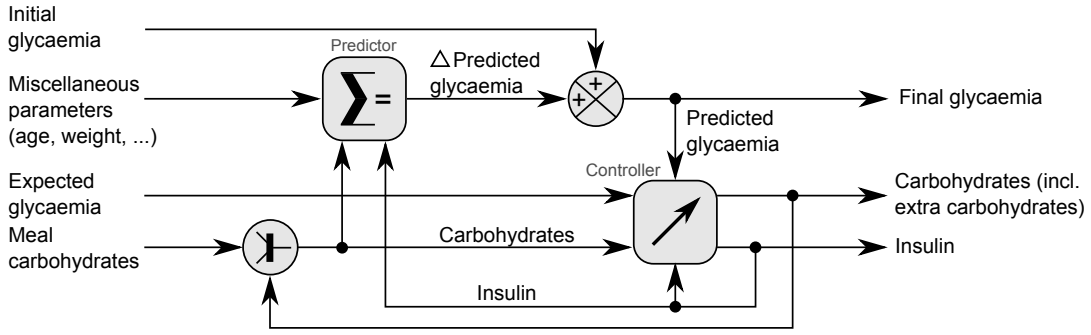

Figure 1: CPCS regulation principle.

Experiments indicate that the best configuration for the ANN is obtained for 100 training data and 3000 training epochs. Other experiments (not mentioned here) prove that using more than 200 training information does not significantly lower the average and maximum deviations indices. On the contrary, a regression phenomenon is observed (i.e. the carbohydrates and short-term insulin deviations become larger when more than 200 training information items are used).

Given a meal identifier, the corresponding ANN is trained with the selected raw information items, whose meal identifier matches the given identifier. The "resilient propagation" training algorithm (RPROP) with default parameter values suggested by (Riedmiller and Braun, 1993) is used.

One could have experimented with "well-chosen" raw information (i.e. deterministic raw information) which cover a wide range of values and provide all compensation cases, but this would have two main drawbacks:

- The experimental results would be slanted as the ANN would give insignifiant deviation values;
- This case is definitely unrealistic: a patient will never cover the whole range of possible values for all parameters (i.e. pre-glycaemia, post-glycaemia and meal carbohydrates in particular).

3.2 Results Review on Exact Data

The results of this comparison are gathered in table 1. This table indicates average and maximum regulation glucose and compensation short-term insulin deviations from exact measurements provided by the mathematical model. The neural PCS is trained with randomized exact information.

This table demonstrates that 100 training information items lead to the lowest short-term insulin average and maximum deviations (of 0.05 and 0.17 respectively). The maximum carbohydrates deviation of 1g is not significant and does not reflect upon the accuracy of the measurements. The widest insulin deviation obtained for 50 training data reflects the lack of information to train from. Use of 200 training data provides still acceptable measurements (i.e. below 0.5 doses) but a (well-known) regression phenomenon starts to become visible.

Table 1: Neural CPCS deviations from expected compensations using exact training data and 3000 epochs.

Neural PCS deviations		Training data		
		50	100	200
Carbo-hydrates	Average	0	0	0
	Max	0	1	0
Insulin	Average	0.18	0.05	0.11
	Max	0.56	0.17	0.37

3.3 Support for Perturbated Data

Previous experiments were based on exact raw information to train the ANN and validate the neural PCS behaviour. In order to ensure the validity of the neural PCS in a "real" environment, we use perturbated raw information for training to simulate devices measures deviations, patients reading errors and instable sensitivity to insulin deseases. Perturbations apply to pre-meal and post-meal glycaemia as well as meal carbohydrates on each raw information item. Each perturbation follows to a normal distribution centered on 0 with a 20% deviation maximum and a 10% average of the initial (i.e. exact) value. This means that each initial (i.e. exact) value can be modified up to $\pm 20\%$.

Table 2 gathers theoretical and neural PCS behaviours in the presence of perturbated information. The set of representative initial (exact) values being perturbated, the TPCS produces deviations from the exact measurements. The neural CPCS uses perturbated training information randomly generated. Each deviation is calculated from the exact initial values.

As table 2 states, both theoretical and neural PCS show they limits as some predicted measurements are unacceptable. This is due to the fact that perturbations

Table 2: Deviations for theoretical and neural PCS from expected compensations (with original non perturbated data) using perturbated training data and 3000 epochs.

TPCS and neural CPCS deviations		Th. PCS	Training data		
			50	100	200
Carbo-hydrates	Average	0	0	0	0
	Max	2	4	4	4
Insulin	Average	1.12	1.10	0.95	1.10
	Max	3.29	3.22	1.84	3.20

on initial values introduce a dynamic modification of the initial sensitivity to insulin which cannot be modelled by the TPCS: the mathematical formulaes lead to generate errors proportional to the deviation introduced by the perturbation. On the contrary, the neural CPCS, thanks to its neural predictor, demonstrates its ability to suggest more acceptable evaluations.

Once again, the neural CPCS trained with 100 data seems to provide the best measurements: in this case, the maximum insulin deviation is divided by a factor of 1.8 between the TPCS and the neural CPCS. The results of table 2 demonstrate that the neural CPCS suggests either comparable or more accurate values than the TPCS. The neural CPCS is able to genealize an average compensation function from perturbated training data and give good approximations, whereas the TPCS is more rigid. The neural CPCS ability to approximate the compensation function even when perturbated data are used is mostly due to the training process tuning (in terms of number of training data and maximum number of epochs) which reduces the noise generated by perturbations on training data.

4 CONCLUSIONS

An adaptive GPCS has been proposed. Theoretical and neural variants of this global system (TPCS and neural CPCS, respectively) have been presented and compared using both exact and up to 20% perturbated data. Each datum is randomly generated, though conforming to the theoretical model proposed by (Charpentier et al., 2005). As a result, the neural approach appeared to be accurate and adaptable to each patient's reaction to insulin and glucose. This study highlights that NPC techniques provide similar measurement to empirical models and are able to handle perturbations. The main drawback of NPC lies in the amount of training data required to perform an acceptable training. This can be problematic when the system does not have access to enough information. Use of predetermined ANN based on a type 1 diabetes database is investigated.

Compared with other type 1 diabetes closed-loop control systems in the literature (Takahashi et al., 2008), the Global PCS architecture is highly modular thanks to programming interfaces which allow to define its effective behaviour.

Although this study demonstrated that the neural predictor provides acceptable glycaemia deviations, complementary work is still necessary to evaluate other ANN configurations and activation functions. The neural CPCS can be used "as is". However, further testing is needed in case of meals recovery (which occurs when a patient eats while the previous meal short-term insulin has not fully taken effect). Long-term insulin regulation is currently left for future works as the corresponding controlled and mathematical models are much more complex due to the combined short-term and long-term insulin effects. Future works will also concern the definition of training data selection heuristics. These heuristics will be used to retain the most relevant training information and leave unnecessary information out.

Finally, similar experiments could also be proposed on systems which make use of Support Vector Machine (SVN) techniques in place of ANN.

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