**Title:**

Identification of interval postprandial models for glucose control in type 1 diabetes

**Abstract:**

Postprandial characterization of patients with type 1 diabetes is crucial for the development of an automatic glucose control system (Artificial Pancreas). Uncertainty sources within the patient, and variability of the glucose response between patients, are a challenge for individual patients model identification leading to poor predictability with current methods. Also, continuous glucose monitors, which have been the springboard for research towards a domiciliary artificial pancreas, still introduce large measurement errors, greatly complicating the characterization of the patient.

In this thesis, individual model identification characterizing intra-patient variability from domiciliary data is addressed. First, literature models are reviewed. Next, we investigate the collection of data, and how can it be improved using optimal experiment design. Data gathering improvement is later applied to an ambulatory clinical protocol implemented at the Hospital Clínic Universitari de València, and data are collected from twelve patients following a set of mixed meal studies. With regard to the uncertainty of the glucose monitors, two continuous glucose monitoring devices are analyzed and statistically modeled. The models of these devices are used for *in silico* simulations and the analysis of identification methods.

Identification using intervals models is then performed, showing an inherent capability for characterization of both the patient and the related uncertainty. First an *in silico* study is conducted in order to assess the feasibility of the identifications. Then, model identification is addressed from real patient data, increasing the complexity of the problem. As conclusion a new method for interval model identification is developed and successfully validated from clinical data.

**Methodology**

In this thesis, methods for optimal experiment design, statistical modeling, and interval identification are applied as detailed below.

* Experiment design:
  + Fisher Information Matrix Identifiability – To compute identifiability of the model, which will be the index to maximize when designing
  + Scatter Search for Matlab Optimization – Fast optimization method for large non-linear models
  + Optimal Experiment Design for parametric models as described in “Walter, E. & Pronzato, L. Identification of parametric models. Springer Heidelberg, 1997 “
* Statistical modeling:
  + Delay from cross-correlation of two signals – In order to characterize the delay distributions of the monitors
  + AR model fitting – For determining the time correlation of the signals
  + Simulation of time-correlated non-gaussian sequences as described by “Silveira Santos, J. & Daoud Yacoub, M. Coloring Non-Gaussian Sequences IEEE Transactions on Signal Processing, Institute of Electrical and Electronics Engineers, 2008, 56, 5817-5822”
  + Statistical Distribution Fitting – Including Logistic distribution, Weibull distribution, Log-Normal distribution, and Normal distribution
* Interval identification:
  + Interval analysis and Guaranteed simulation methods – For developing the interval models of the diabetic patients
  + Multi-objective Optimization – For creating Pareto fronts with two objectives: the interval width and the data fitting index
  + Covariance Matrix Evolutionary Optimization – Very fast single objective optimization for the data fitting of a compound index or when width of the interval is fixed

**Objectives:**

The main objectives of the thesis are:

* To simplify and improve identification methods for the Artificial Pancreas
* To address the problem of intra-patient variability in model identification
* To provide useful prediction tools for the Artificial Pancreas

**Means and Assets:**

* Computer Dell Precision T3500 for the computing tasks
* Data for identifications and sensor modeling were obtained in collaboration with the Hospital Clínic Universitari de València. Data consisted in 4 postprandial periods for 12 patients, where inputs where standardized and measured. Insulin was also measured in laboratory. Glucose reference was measured in laboratory, and data from 2 commercial devices was also obtained.
* The commercial devices studied were the Dexcom® Seven® Plus and the Medtronic® Paradigm® VEO™.
* This thesis was founded by the CICYT projects INSULAID2 and ClosedLoop4Meals

**Schedule:**

1st year: Master’s courses and familiarization with models.

2nd year: Optimal experiment design and implementation of clinical study.

3rd year: Analysis of the results from experiments. Statistical modeling of sensors. *In silico* studies and development of identification methods.

4th year: Application of methods to real data and validation of models. Manuscript writing.

**Previous and current work:**

This work is based on the diabetes group of the Institut Tecnologic d’automàtica I informàtica industrial of the Universitat Politècnica of València. The group has been working in the context of artificial pancreas for the last 8 years.

The author of this work already advanced some preliminary identification results in his Master’s thesis: “Laguna Sanz, A. J. Model Identification from Ambulatory Data for Post-Prandial Glucose Control in type 1 Diabetes Departament d'Enginyeria de Sistemes i Automàtica, 2010”

Currently (11/12/2012) the development of this thesis is in its last stage in model validation and writing of the manuscript.

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