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**UNIVERSITÄT  
BERN**

**ARTORG CENTER**  
**BIOMEDICAL ENGINEERING RESEARCH**

**To: Universitat Politècnica de València**

Department of Systems Engineering and Automation

Bern, March 7, 2014

**Expert: Stavroula MOUGIAKAKOU**

**Title: Uncertainty in Postprandial Model Identification in Type 1 Diabetes**

**Candidate: Alejandro José Laguna Sanz**

Dear Profs. Bondia and Rosetti,

I would like to submit my review of Mr. Alejandro LAGUNA's PhD Thesis.

My assessment includes i) my comments on the originality, quality, results and presentation of the research performed during the PhD period, and ii) my final evaluation statement.

#### **General Comments**

The scope of Mr. Alejandro LAGUNA's PhD Thesis was to design and develop a framework for optimizing the identification process for modeling and control in type 1 diabetic patients under sensor augmented pump therapy. A novel identification method based on interval models was introduced to characterize the variability of type 1 diabetic patients. Ultimate scope is to take into consideration patients variability and the associated uncertainties for the personalized insulin treatment. Glucose prediction is a complex, challenging and very intensively studied area. The proposed approach is novel and very well systematically investigated.

Mr. Alejandro LAGUNA has conducted a comprehensive, up-to-date and critical review of research in the fields of identification of model's parameters (Chapter 1). After an extensive presentation of models used for the development of an artificial pancreas (Chapter 2), he proceeds to review of the already proposed methods for model individualization in diabetes (Chapter 3).

Chapter 4 refers to optimization of the experimental design towards model identifiability enhancement. In an attempt to improve the quality of the data acquired by the glucose monitoring devices a stochastic model for simulating the error of glucose sensors is introduced (Chapter 5).

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In order to deal with issues related to identification under variability, interval models were considered (Chapter 6). The use of an interval model is novel in diabetes treatment optimization. *In silico* identification was conducted following the experiment protocol proposed in Chapter 4 and the error model proposed in Chapter 5. The identified model was able to predict satisfactorily the postprandial glucose profile.

Mr. LAGUNA preceded one step further by evaluating the proposed approach with experimental data (insulin and blood glucose reference measurements) from 12 patients under pump therapy for four different lunchtime postprandial periods each (Chapter 7). In order to evaluate the ability of the proposed method to characterize the source of uncertainty from only insulin and glucose data, two different scenarios were considered. Identification is performed using a hybrid cost index involving the envelope width and the fitting error. The presented results showed that the identified model was able to predict accurately the 5-hour postprandial glucose profile.

The work was extended by including subcutaneous insulin data (Chapter 8). For the identification a procedure similar to the one presented in Chapter 7 was followed. The results showed that despite the use of less accurate information the prediction capability of the identified model was satisfactory. Finally, Mr. LAGUNA tried identification using continuous subcutaneous glucose data. Although, as expected the prediction error was increased, the feasibility of using the proposed approach in at home setup related to artificial pancreas.

Chapter “Remarks and future work” concludes the PhD Thesis and indicates future research activities related to the artificial pancreas and diabetes technology.

### **Conclusions and Assignment**

Mr. LAGUNA’s research is of high impact and importance for type 1 diabetic patients. More specifically, the proposed approaches permit i) personalized identification in presence of variability and uncertainties, and ii) prediction of the postprandial glucose. He has followed a very systematic approach, while he has presented his results in a very well structured and comprehensive manner. Text, tables, figures, graphics and legends are excellent and meet the standards of a PhD Thesis.

In summary, the thesis is original, novel and definitely beyond the state of the art; with impact for diabetic patients and biomedical engineering; very well-structured, organized and documented.

Based on the above, I would say that the PhD Thesis submitted by Mr. LAGUNA can be **accepted without reserve**.

In case you have any additional questions do not hesitate to contact me.

Sincerely,



Dr. Stavroula Mougiakakou