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A Collaborative Biomedical Engineering Undergraduate Work: An Automatic System for Blood Glucose Regulation

Graça Minas, *Member IEEE*, Filomena Soares

Abstract— **This paper is focused on the design of an automatic system to regulate blood glucose concentration. A model is developed to simulate the process. The model was based on approximating an electrochemical biosensor, for measuring the blood glucose concentration, to electrical circuits for readout, data processing and control. It was implemented using an electronics simulation software package: S-Edit and T-Spice from Tanner Tools EDA. The work was developed by a group of ten students from the fourth year of the integrated master of Biomedical Engineering course of the University of Minho in a collaborative way.**

I. Introduction

THE first self-monitoring of blood glucose (SMBG) experiences and the correspondent insulin therapy were published in 1978 in the first issue of Diabetes Care [1]. Since then, several studies and research and development activities showed that careful management of blood glucose levels delayed or even prevented diabetes complications, confirming the importance of using SMBG as a tool for preventing hypoglycemia, regulating the medication [2-7].

However, specific protocols for SMBG remain variable, in particularly regarding non–insulin-dependent patients. This is due in part to a correct test under real-world conditions of the equipment, to a correct explanation of the equipment functioning to patients and also, due to the physiological, behavioral, and social circumstances in which SMBG is carried out. A recent work from a multidisciplinary team, including endocrinologists, a health psychologist, a diabetes nurse practitioner and a patient advocate discuss within a review article how the potential of SMBG might be fully realized in today's healthcare environment [8]. The resulting recommendations cover technological, clinical, behavioral, and research considerations with the aim of achieving short- and long-term benefits.

The common open loop therapy for patients with type 1 diabetes includes daily insulin administration, based on fingerstick blood glucose measurements, diet, and physical activity conditions. An improved therapy is based on closing the loop (with no-need of patient intervention) with an automated system, consisting of a continuous blood glucose monitoring device, a control algorithm that computes the insulin infusion rate based on recent glucose concentration measurements, and an insulin infusion pump [9].

This motivation engaged the authors to simulate an automatic system to regulate blood glucose concentration, using the electronics simulation software package S-Edit and T-Spice from Tanner Tools EDA. This software includes the electronics components model of the CMOS microelectronics foundry. Therefore, when all the model blocks have been correctly simulated, a microsystem can be fabricated. This project was developed in the curricular unit, Integrated Electronics Laboratories where a collaborative learning methodology was tested. This project comprises knowledge that has being acquired in three courses of the 4th year: Biosensors, Microelectronics and Control Systems. The ten students worked in groups of two elements. Each group had a particular task definition: sensor development (biosensor electrodes), control action and actuator system (insulin pumping). At the end, the automatic system is to be assembled from the group contributions. During the semester, the students had near to 45 hours of direct contact with the teachers and 35 hours of team work. The remaining 5 hours were for evaluation.

In order to achieve the main goals proposed, the paper is organized as follows: Section 1 is focused on presenting the motivation and the challenge of the work. In section 2 it is presented some highlights regarding the teaching/learning collaborative methodology. The model development is presented in section 3. Further, in section 4, the simulation results are detailed and discussed. Finally, in section 5, there are presented the main conclusions of this study and some guidelines for the future work.

II. Teaching/Learning Methodology

It is well known that the teaching/learning process has been under a detailed analysis, and severe changes have been slowly implemented. Above all, the attitude towards the education changed. The process is now centralized in the student. This implies not only a precise definition of objectives and capabilities to be acquired, but also strategies and teaching methodologies reformulation. The student is the main actor in the learning/teaching arena; he/she should be engaged in doing something besides listening to a lecturer and taking notes.

In particular and especially important for engineer students, comes the concept "Learning by doing". It is well

Graça Minas is with the Industrial Electronics Department, University of Minho, Campus de Azurem, 4800-058, Portugal (corresponding author), phone: +351253510190; fax: +351253510189; e-mail: gminas@ dei.uminho.pt.

Filomena Soares is with the Industrial Electronics Department, University of Minho, Campus de Azurem, 4800-058, Portugal; e-mail: fsores@ dei.uminho.pt.

known that students retain better what is taught if they are able to practice [10]. Following this idea, laboratories are particular important: students can test a theory or prove the concept; here there is a strong interaction between the student and the colleagues and also with the teacher. In groups, the students construct, manipulate, modify and control the experience.

Regarding the teaching/learning methodology employed in developing this work, a collaborative task [11] was followed. Collaborative learning refers to methodologies and environments in which learners engage in a common task. Groups of students work together in searching for understanding, meaning or solutions or in creating an artifact of their learning.

III. Model Development

In order to include future developments, instead of just one electrochemical biosensor for blood glucose measurement, the students have the goal of designing an array of 16 electrochemical biosensors (Fig. 1) for further allowing the measurement of 16 biochemical parameters concentrations in blood, such as glucose, cholesterol, albumin, uric acid, among others.

In this work, one group has been developing the addressing of the electrodes array, the electrodes array and their line and column decoders. Other group has been focused on developing the transimpedance and the operational amplifiers. Other group has been dedicated to the data processing, based on a Sigma-Delta analog to digital converter. Another group has been developing the control system. Finally, the last group has been carrying out the assembly of the several blocks.

The objective of the control system is to impose a pre-defined blood glucose concentration. To accomplish this, the system must check the level of the measured electrode signal (in the present case it corresponds to the blood glucose concentration) and, if it is lower than the pre-defined reference value, it must output a signal for actuating a mechanism that injects insulin (presently, this mechanism is an external block). At the moment, this control is performed by a simple on-off algorithm. Further improvements, to be performed in the following semester of the course, include the implementation of a more robust control law: a PID type (Proportional, Integral and Derivative) control. The digital version in the form of position algorithm is to be programmed.

IV. Simulation Results

In this section the simulation results obtained by each group are presented and discussed.

A. Electrodes array and their addressing

For testing the array and its addressing, a current at each electrode has been set, simulating the measured current of the electrochemical biosensor. The addressed electrode and its corresponding current are set according to the scheme presented in Figure 2. Figure 3 shows the current signals at each addressed electrode where it can be seen that this task was the must well developed by the students and it outputs the specified current. The main difficulty of this task was the implementation of the transmission gate (composed by the two MOSFETs) of each cell, once they have difficulties in understanding the necessity of a transmission gate inside the cell.

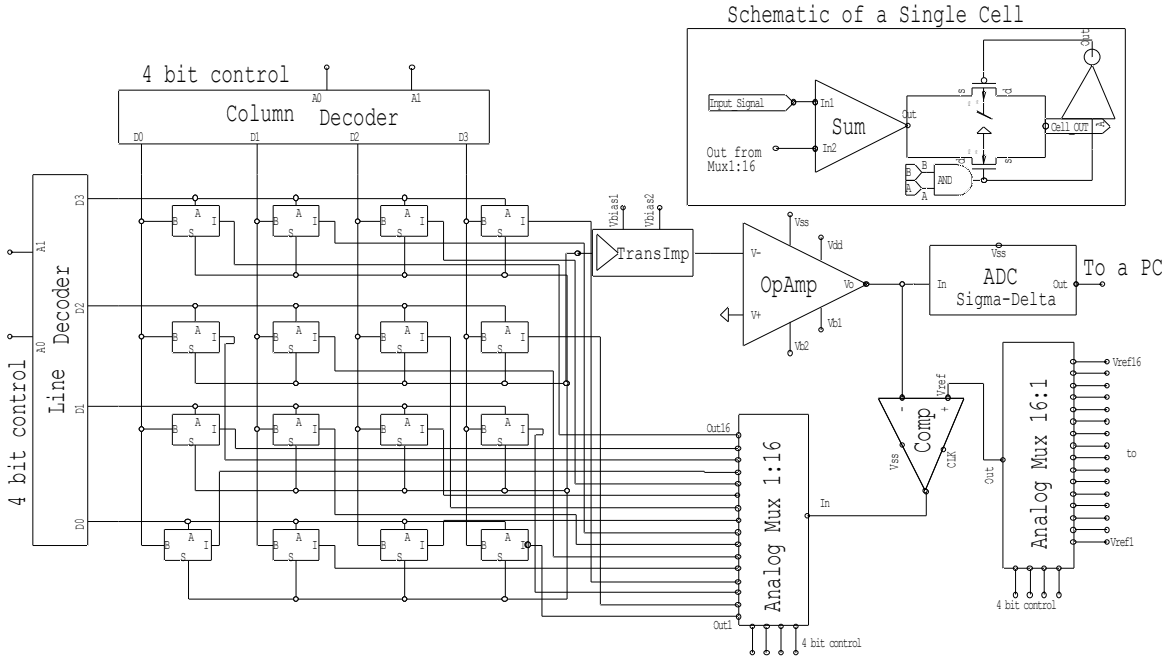


Fig. 1. Schematic of the complete system. The analog multiplexer 1:16 connected to the comparator output performs an algebraic sum to the cell, simulating that the actuation mechanism injected insulin (that mechanism is not implemented yet).

Addressing				
S1	S2	S3	S4	Electrode
0	0	0	0	1
0	0	0	1	2
0	0	1	0	3
0	0	1	1	4
0	1	0	0	5
0	1	0	1	6
0	1	1	0	7
0	1	1	1	8
1	0	0	0	9
1	0	0	1	10
1	0	1	0	11
1	0	1	1	12
1	1	0	0	13
1	1	0	1	14
1	1	1	0	15
1	1	1	1	16

Cell scheme

	C1	C2	C3	C4
L1	16	8	12	4
L2	14	6	10	2
L3	15	7	11	3
L4	13	5	9	1

Current (A)

	C1	C2	C3	C4
L1	300u	60u	100u	20u
L2	200u	40u	80u	5u
L3	250u	50u	90u	10u
L4	150u	30u	70u	0.1u

Fig. 2. Addressing table, the corresponding addressed cells in the array and their current.

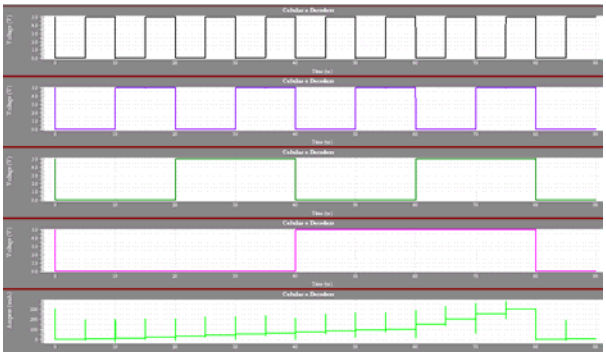
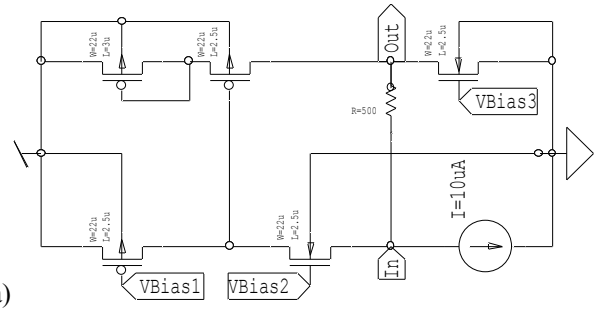


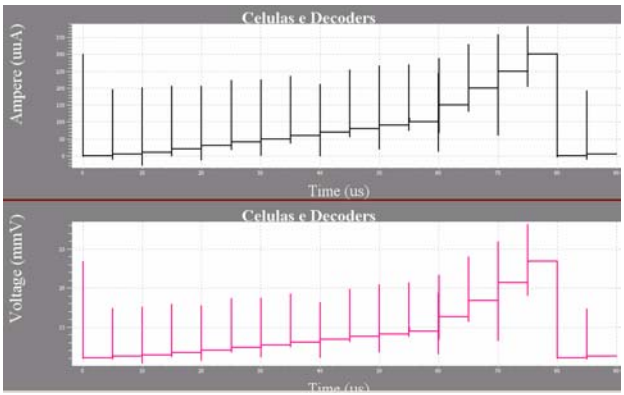
Fig. 3. Signals for addressing the electrodes array and their output.

B. *Transimpedance and operational amplifiers*

A transimpedance amplifier is needed for converting the output current of the electrode array in a voltage. Its schematic and its input and output signals are presented in Fig. 4. Due to the simple configuration, this amplifier does not output enough voltage for data processing. Therefore an operational amplifier has been connected to it. Figure 5 shows the used operational amplifier. It is a rail-to-rail operational amplifier with the following characteristics: CMRR = 81dB; Slew-Rate = 8.57 V/µs; open loop gain = 66 dB; offset voltage = 30 mV; frequency@unit gain = 2.3MHz; power consumption = 374 mW. This task was the must time consuming task for output an op amp with the reported characteristics. The main difficulties were to set the MOSFETs widths for the required offset voltage. Indeed they only get 30 mV instead of the 20 mV asked.



(a)



(b)

Fig. 4. (a) Schematic of the transimpedance amplifier and (b) its operation showing the output voltage as a function of the input current.

C. *Analog to digital converter*

The A/D conversion is performed by using a one bit first order Sigma-Delta modulator (Fig. 6). The circuit consists of the following sections: an integrator and a one bit A/D converter in the forward path, and a one bit D/A converter in the feedback path of a single feedback loop system. The integrator provides the delay needed. The one bit A/D converter is a latched comparator that converts an analog signal into either a high or a low. The one bit D/A converter (two voltage controlled switches) uses the comparator output to determine if a high or a low is summed with the input. Therefore, the complete model has a bit stream output and allows its use in small data acquisition and control systems. That bit stream is proportional to the electrical current measured by the biosensor electrodes. Figure 7 shows the performance of the Sigma-Delta modulator. As it can be seen as the input voltage increases the output of the modulator is more time at the high level.

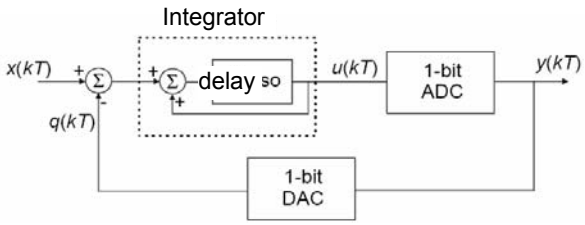


Fig. 6 Block diagram of the one bit first order Sigma-Delta modulator.

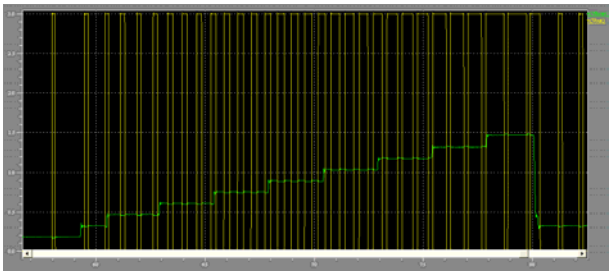


Fig. 7. Input (green) and output (yellow) signals of the Sigma-Delta converter.

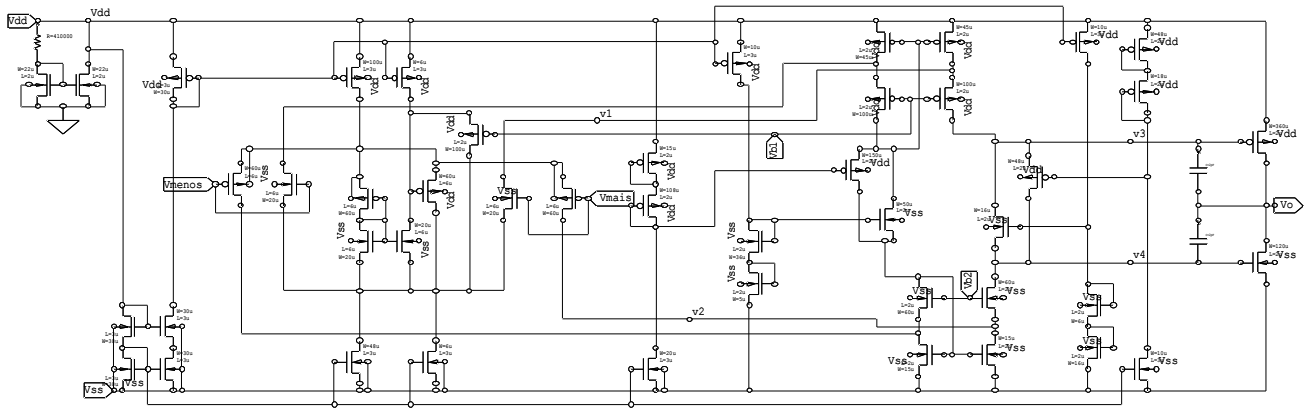


Fig. 5. Schematic of the operational amplifier

D. *On-Off Control*

The On-Off control is performed by a comparator with hysteresis which reference voltage (Vref) was set to the voltage that is equivalent to the boundary of glucose concentration. Thinking in the 16 biosensors array the comparator input (Vref) will have an analog multiplexer 16:1 (see Fig. 1) which output corresponds to the reference voltage of the biochemical parameter in analysis. Figure 8 shows the schematic of the comparator. The mosfets that are in the pink zone form the pre-amplifier circuit, which allow amplifying the input voltages enabling a higher discrimination of the lower voltages in the decision circuit (green one). The decision circuit (green) is the heart of the comparator and it should discriminate voltages signals in the order of mV. The output buffer (yellow) allows converting the decision circuit output to rail-to-rail voltage levels. The main difficulty was the analog multiplexer's design, once they were familiar only with digital multiplexers.

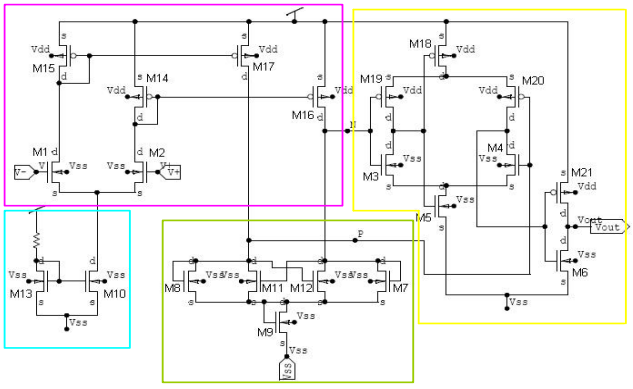


Fig. 8. The comparator that acts as the control element.

V. Conclusions

This paper presented a project work developed in a collaborative way by ten students from the fourth year of the integrated master of Biomedical Engineering course of the University of Minho. The several blocks of the developed model, based on the approximation of an electrochemical biosensor for measuring the blood glucose concentration, were implemented and tested. However, at the moment the students are connecting all the blocks for having the desired results of the overall system. At the end of the school year this task will be concluded and the results presented at the conference. Moreover, the several blocks implemented met the criteria specified except for the offset of the operational amplifier.

The project results and the positive opinion of the students motivated the authors to continue with this teaching/learning methodology. In this experience, not only the students had to work together, developing specific tasks, following a common objective, but also, they had to put in practice the knowledge acquired in three courses of the 4th year: Biosensors, Microelectronics and Control Systems.

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