

Acquisition System for Real-Time Monitoring of Glucose and Lactate in Recirculating Multi-Organ-on-Chip

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Summary:

This study presents a multi-channel electrochemical acquisition system for glucose and lactate biosensing in Multi-Organ-on-Chip (MOoC) platforms. A custom potentiostat-based setup achieving a theoretical current resolution of 3 pA over a ± 500 nA range. Comparative tests with a commercial system show fast (<40 s), stable, and linear responses with $R^2=0.9992$ in both glucose and lactate. The system was designed as the core instrumentation of a diabetes-focused MOoC, with flexibility for further sensor integration.

Keywords: electrochemical sensing, real-time, multi-organ-on-chip, recirculation, online acquisition

Introduction/Background

The emergence of Multi-Organ-on-Chip systems offers a powerful platform for studying complex, systemic diseases such as diabetes by recreating dynamic interactions between multiple tissues in vitro [1]. In this context, continuous and reliable monitoring of key metabolic biomarkers, such as glucose and lactate, is essential to capture organ cross-talk and metabolic regulation in real time. In particular, electrochemical biosensors are well-suited for this purpose due to their high sensitivity and compatibility with microfluidic environments. However, current MOoC platforms still largely rely on off-chip, end-point, and offline measurements, limiting temporal resolution and preventing true in situ analysis. Which is essential when MOoC are configured for fluid recirculation to better mimic closed-loop interactions between organs. This work addresses these shortcomings through the development of a customizable, multi-channel electrochemical acquisition system tailored for sensing in microfluidic MOoC applications under continuous flow and in recirculation.

Materials and Methods

Our MOoC sensing platform relies on a first-generation electrochemical glucose and lactate sensor (B.LV5, Jobst Technologies), selected for its microfluidic flow compatibility and reliability. Measurements were performed using a custom-developed acquisition system (Fig. 1) based on a digitally tunable potentiostat (-1.5 V to $+1.5$ V) and six acquisition channels. Each channel

consists of a transimpedance amplifier (TIA), a low-pass filter (LPF), and a differential input to an 8-channel, 24-bit sigma-delta ADC. The system is completed and powered with an ESP32-S3-DevKitM-1 for hardware management and USB communication. Our design is derived from the open hardware, single-channel acquisition board DStat [2] (licensed under the CERN OHL v.1.2.), although the original ATmega-based firmware and software were not retained in our implementation. Because of the ADC architecture, channels are sampled sequentially. However, the high effective sampling rate (~ 1 ms/channel) is sufficient relative to the enzymatic response time for quasi-simultaneous acquisition. The TIA with its 3-fA input bias current precision amplifier LMP7721 coupled with the 3 M Ω current/voltage gain and the low noise 24b ADC (21.8b effective resolution) gives a theoretical current resolution of ~ 3 pA over a ± 500 nA range.

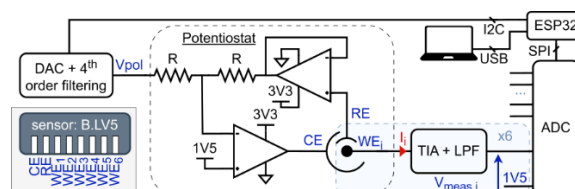


Fig. 1. Acquisition system architecture and connections to the enzymatic sensor.

Firmware was developed in C with the Espressif IoT Development Framework as core and a graphical user interface (GUI) was developed in

Python for sampling configuration, electrode selection, real-time visualization, and data logging.

Experimental setup

The system's linearity and response time were evaluated under flow (10 $\mu\text{L}/\text{min}$) at room temperature using a peristaltic pump (ISMATEC, Reglo ICC), the B.LV5 sensor, a custom microfluidic chip (cell-free), and a flow meter (Sensirion, LG16-0430D). A solution designed for hepatic gluconeogenesis experiments was used for sensor calibration. It had the following composition, SILAC RPMI 1640 Flex media (A24942-01, Fisher) supplemented with Bovine Serum Albumine 0.5% w/v, DMSO 0.5% v/v, Penicillin 100U/mL, Streptomycin 100 $\mu\text{g}/\text{mL}$, Amphotericin 0.25 $\mu\text{g}/\text{mL}$, 10 mM HEPES, 1 mM Pyruvate and 10 μM Forskolin. pH was checked as being at 7.4 before experiments. Several solutions of this medium containing varying concentrations of glucose, lactate, or a mixture of both were prepared to characterize sensor response. Punctual measurements were performed after the sensor reached steady state, with response times not exceeding 40 s across the tested range (Fig. 2A). For comparison, the same protocol was performed using the commercial acquisition system provided by the sensor manufacturer (SIX Biotransmitter).

Results

In both cases the sensor demonstrated linearity ($R^2 > 0.9966$) over the range of measurements and near identical models (Fig. 2B and 2C). A linear model was used for this concentration range, although a Michaelis–Menten model may be more appropriate for broader, non-linear ranges in enzyme-catalyzed systems or with different medium [3].

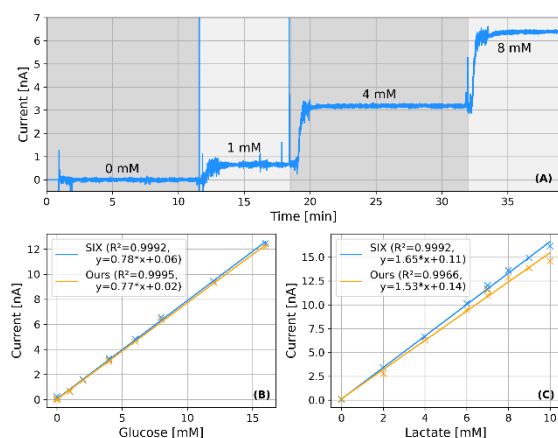


Fig. 2. (A) Glucose sensor raw response for successive glucose solutions. Linear model of the sensor response for glucose (B) and lactate (C) for two

acquisition systems: our system and the commercial reference (SIX Biotransmitter).

Conclusion and Outlook

This study presented an acquisition system for the real time monitoring of biomarkers in MOOCs. It demonstrated excellent stability and linearity in the physiological range of the tested biomarkers.

Unlike the commercial system, our potentiostat's reference tension is tunable over a -1.5 V to $+1.5\text{ V}$ range, enabling the exploration of additional electrochemical and enzymatic sensing modalities. In particular, one of our initial objectives is the development of an integrated oxygen sensor for MOOC applications.

To validate compatibility with recirculating MOOC applications, hepatic gluconeogenesis experiments in recirculation are in progress. In the medium and experimental conditions of these experiments, cell-free controls have already been performed (Fig. 3) and have allowed us to evaluate the lactate sensor drift at $0.11\text{ mM}/\text{h}$. This drift is consistent with that announced by the manufacturer ($0.15\text{ mM}/\text{h}$), which further confirms the need to calibrate these sensors for every experimental session.

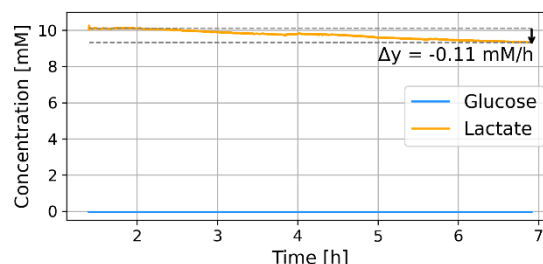


Fig. 3. Cell-free control gluconeogenesis in a recirculation loop.

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