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DIFFERENT MINIATURIZATION SYSTEMS OF ELECTRICAL BIOSENSING AND DATA ACQUISITION DURING BIOLOGICAL CELL TRANSITING WITHIN VESSEL SIZE MICROCHANNEL

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ABSTRACT

For quantitative single cell analysis within vessel size microchannel, bioimpedance technology is considered to be important for future advanced biomedical applications. However, most of bioimpedance systems takes place and is not allowed to bring to biological institute. In this paper, two miniaturization systems for electrical biosensing and data acquisition will be introduced and compared. By considering the advantages of portable systems such as easy to take and use, simplicity and inexpensive, instead of impedance spectroscopy obtained by traditional equipment, the miniaturization bioimpedance systems might be helpful for 'Lab-on-a-Chip' device to be more complex.

KEYWORDS: Bioimpedance technology, Miniaturized electrical biosensing system, Microfluidic

INTRODUCTION

For single cell analysis, optical observation is considered for its advantages such as real-time monitoring, morphology and cell population study, etc. However, this method is limited for a quantitative analysis at single cell level. Bioimpedance technology was therefore investigated. Several traditional equipment like HP 4194A and MFLI Lock-in amplifier is considered to obtain impedance spectroscopy of cells transiting within microfluidic channels. Moreover, to realize directly the bioimpedance measurements at biological institute, miniaturized system becomes necessary. In this paper, two strategies of miniaturized biosensing systems will be introduced.

THEORY

With the consideration of dielectric characterizations of hetero microfluidic system (microchannel containing cells suspension), equivalent electrical model could be achieved for each part. Under an excitation signal, the induced current could be collected and the total bioimpedance of microfluidic system could be therefore obtained [1].

EXPERIMENTAL

Firstly, a miniaturized impedance measurement AD5933 board, which sends an alternating signal with controlled frequencies series directly to the electrodes beside single microchannel, was used. After amplification, filtering and digitization processing within AD5933, real and imaginary part of the microchannel impedance was recorded to computer via a microcontroller Arduino UNO board. Secondly, a portable Analog Discovery hardware, containing a built-in signal generator and digital oscilloscopes, was used. Several types of excitations can be chosen (for example, sinusoidal signal) to measure the system bioimpedance. This signal was applied via gold springs connected to electrodes patterned on quartz substrate via a transimpedance amplifier AD847J.

RESULTS AND DISCUSSION

Before the measurements, AD5933 card calibration was necessary with a resistance which has its value approximate to the impedance modulus to be measured. Firstly, the impedance modulus spectroscopy of a known parallel RC circuit (10M Ω // 10pF) was achieved by AD5933, and verified by HP 4194A (Figure 1.A.). Secondly, single fluid restriction filled with hepatocytes medium was measured (Figure 1.B.). For both RC circuit and single

restriction, a good match of measurement curves was obtained at 30kHz. Finally, under 30kHz, real-time impedance modulus evolution was obtained for hepatocytes transiting within vessel size microchannels (Figure 1.C. and D.). Single hepatocyte transit time equals to 0.78s according to an increase of impedance modulus from 1.3M Ω to 3M Ω because of the cell presence within microchannel. Optical monitoring of cells transit was permitted at the same time (Figure 1.E.).

However, such method is limited by the non-fixed duration between two measurement points which is much more important than non-nucleated red blood cell (RBC) transit time (see Figure 1.D., duration equals to 86ms or 87ms; see Figure H., RBC transit time is around 10ms). To have a smaller constant measurement duration (or sampling frequency more important), Analog Discovery hardware was chosen. The working frequency of electrical excitation (2V) was equal to 10kHz because of the slope at lower frequencies caused by double layer capacitance at electrodes surface, and at higher frequencies caused by parasitic capacitance due to the connection via a dedicated printed circuit board containing transimpedance amplifier AD847J (feedback resistance = 100k Ω) (Figure F.) [2]. The sampling frequency was 500kHz and the transformed current signal was recorded during RBCs transiting within the restriction (Figure G. and H.). Further quantitative data processing, which provides useful information (RBC transit time, blockade amplitude and phase shift) was realized by Igor Pro software.

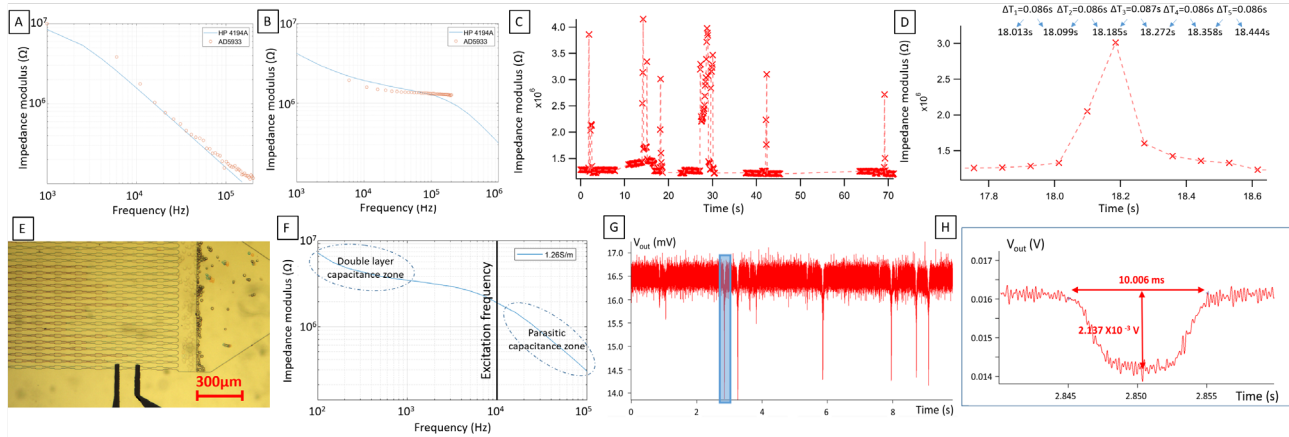


Figure 1: A. Impedance modulus spectrum of the RC circuit in parallel (10M Ω // 10pF) obtained by HP 4194A and AD5933; B. Impedance modulus spectrum of the 3rd restriction filled with hepatocytes medium (12.40mS/cm, 20.4 $^{\circ}$ C) obtained by HP 4194A and AD5933; C. Impedance modulus evolution as a function of time during hepatocytes transiting obtained by AD5933; D. Zoom zone of Fig. C. between 17.7s and 18.7s; E. Hepatocytes transiting within the restrictions network; F. Impedance modulus spectrum of the 3rd restriction filled by the RBCs conductive solution (12.64mS/cm, 20.3 $^{\circ}$ C); G. Transformed current curve as a function of time for RBCs transiting; H. Zoom zone of Fig. G. between 2.84s and 2.86s.

CONCLUSION

By considering characterizations of each miniaturization systems for electrical biosensing and data acquisition during biological cell transiting within microfluidic channel, quantitative single cell analysis could be achieved, which might be significant for drug screening and future advanced diagnostic therapies.

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