CHINESE JOURNAL OF ANALYTICAL CHEMISTRY
Volume 44, Issue 9, September 2016
Online English edition of the Chinese language journal

Available online at www.sciencedirect.com
ScienceDirect

Cite this article as: Chin J Anal Chem, 2016, 44(9), 1458–1464.

RESEARCH PAPER

Synchronous Detection of Rat Neural Spike Firing and Neurochemical Signals Based on Dual-mode Recording Instrument

XU Sheng-Wei[1,2], WANG Li[1,2], SONG Xian-Teng[1,2], ZHANG Song[1,2], WANG Mi-Xia[1], YU Ping[2,3], MAO Lan-Qun[2,3], CAI Xin-Xia[1,2,*]

[1] State Key Laboratory of Transducer Technology, Institute of Electronics, Chinese Academy of Sciences, Beijing 100190, China
[2] University of Chinese Academy of Sciences, Beijing 10090, China
[3] Center for Molecular Science, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

Abstract: A dual-mode recording system used for synchronous detection of neuroeletrical and neurochemical signals was developed, and a dual-mode synchronous detection experiment was carried out using this instrument. The device comprised a 64-channel neuroelectricity recording module with voltage resolution of 0.3 μV and a 4-channel neurochemistry recording module with current resolution of 1 pA. The software had many basic detection features as spike separation and sort, chronoamperometry, cyclic voltammetry, etc. In particular, the software could observe and analyze the dual-mode neural signals synchronously. The performance of the system was demonstrated in the single mode detection experiments. In neuroeletrical experiments, 64-channel simulate neural signals were detected and the signal-to-noise ratio (*S*/*N*) of spike recorded from cortex of Sprague-Dawley (SD) rat was 6. In the $K_3[Fe(CN)_6]$ and ascorbic acid measurement experiments, the current response of $K_3[Fe(CN)_6]$ in the range of 0.1–10 mM was obtained by cyclic voltammetry, with a correlation coefficient of 0.9889, and the current response of ascorbic acid (10 – 800 μM) by chronoamperometry increased linearly with a correlation coefficient of 0.9841. Based on the rat model of global cerebral ischemia, a dual-mode detection experiment was carried out. In the experiment, the neuroelectrical and neurochemical signals were synchronously recorded in the SD rat primary visual cortex. According to the experimental results, we got the conclusion that the concentration of ascorbic acid negatively related to the spike firing in the SD rat primary visual cortex.

Key Words: Dual-mode; Neurochemistry; Spike; Ascorbic acid; Microelectrode

1 Introduction

As one of the most important regulating system with extremely complex structure and function, nervous system is composed of a large number of nerve cells. Neurons mainly rely on neurochemical and neuroeletrical signals to complete the transmission and integration of information[1]. The neurochemical diordesrs or abnormal neuroeletrical activity will cause a variety of neurological diseases, such as Parkinson's disease, Alzheimer's disease and so on. Thus, simultaneous detection of the neuroelectrical and neurochemical information of nervous system is important for further understanding the characteristics of nerve cells[2] and researching the mechanism of nervous system and neurological diseases. In recent years, some researches on dual-mode signals detection were carried out *in vitro*[3–5] and *in vivo*[6,7], and many microelectrodes were developed to detect dual-mode signals[8–12]. However, in those studies,

Received 19 February 2016; accepted 19 May 2016
*Corresponding author. Email: xxcai@ mail.ie.ac.cn
This work was supported by the National Natural Science Foundation of China (Nos. 61527815, 31500800, 61501426, 61471342), the Key Programs of the CAS (No. KJZD-EW-L11-2), the Beijing Municipal Science & Technology Commission (Nos. Z141100000214002, Z141102003414014), and the Major National Scientific Research Plan of China (No. 2014CB744600).

DOI: 10.1016/S1872-2040(16)60959-3

experiments were carried out with discrete devices such as neural electrophysiological recording instrument, patch clamp and electrochemical workstation, which was inconvenience to the experimental operation, data observation and analysis. Therefore, it is urgent to develop dual-mode system for simultaneous detection and analysis of neurochemical and neuroeletrical signals.

In view of the above requirements, we did a lot of work previously in the field of neural signal detection technology and instruments, and a 16-channel neural signal detection system was developed[13]. In this study, we presented the design and testing of a dual-mode recording system for synchronous detection of 64-channel neuroeletrical and 4-channel neurochemical signals. Based on the previous work, the dual-mode detection performance of this system was optimized and its dual-mode synchronous analysis function was enhanced (the voltage and current resolution of the instrument were 0.3 V and 1 pA, respectively). On the basis of the rat model of global cerebral ischemia, neuroelectrical and neurochemical signals were synchronously recorded by this system in the Sprague-Dawley rat primary visual cortex.

2 Experimental

2.1 System design

The hardware block schematic of the neural signal dual-mode recording system is shown in Fig.1. This system comprised a 64-Channel neuroelectricity recording module, a 4-Channel neurochemistry recording module, Power and MCU unit and Data acquisition card. The whole equipment volume was 33 cm × 20 cm × 11 cm (length × width × height).

2.1.1 Neuroelectricity recording module

The 64-Channel neuroelectricity recording module was divided into four units, each with 16 parallel neuroelectricity channels. Every channel was composed of differential amplifier and band pass filter with 0.1–5000 Hz and connected to MEA by a Headstage which was used for impedance conversion and amplifying the input signal 10 times. The entire gain of neuroelectricity channel was 40 dB. The input signal was amplified 60 dB before it input to Data acquisition card. To meet the demand of weak signal detection, low voltage noise (2.8 nV/$\sqrt{\text{Hz}}$@1 kHz) operational amplifier AD8674 (Analog Devices) was chosen and Miller effect was used for greatly reducing thermal noise[14]. The resolution of the neuroelectricity recording module was 0.3 μV and the input noise was in the range of ±5 μV.

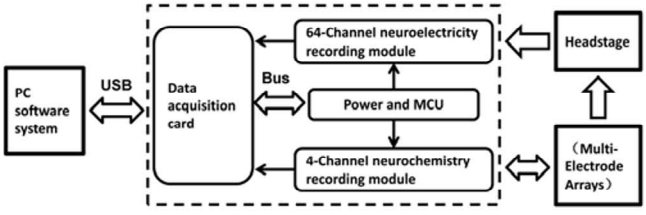

Fig.1 Hardware block schematic of the device

2.1.2 Neurochemistry recording module

The 4-channel neurochemistry recording module could synchronously detect four different chemical substances using a three-electrode electrochemical system. Each channel consisted of potentiostat, *I/V* conversion and differential amplifier. Potentiostat maintained the potential between the working electrode and reference electrode as closely as possible to the voltage of the output of DAC, which was determined by the program. *I/V* conversion, which was composed of feedback resistance and op-amp, transformed reaction current into voltage. The signal from *I/V* conversion was amplified 10 times by a differential amplifier and then input it to Data acquisition card. According that the performance of the neurochemistry channel was determined by *I/V* conversion, ultra-low input current (25 fA) ultra-low current noise (0.13 fA/$\sqrt{\text{Hz}}$@1 kHz) operational amplifier LMC6001A (National Semiconductor) was used in *I/V* conversion. Based on the principle of electromagnetic compatibility (EMC), the input pin of the LMC6001A and the pin of feedback resistance were protected from electromagnetic interference[15]. The max resolution of the neurochemistry recording module was 1 pA and the input range was ±20 μA.

2.1.3 Other modules

The Power and MCU unit mainly provided a stable DC power supply for the device. At the same time, it controlled the other modules to ensure the implementation of dual-mode synchronous detection, and it was also used as a digital function generator to output the voltage needed by the neurochemistry recording module. USB6255 OEM (National Instruments, USA) was selected as Data acquisition card, which had 16 bit resolution and an overall sample throughput of 1.25 M samples per second. The device used USB port of Data acquisition card to communicate with PC.

2.1.4 Software design

From the consideration of reliability and flexibility of software, the system used the Windows7 and Visual Studio as the programming platform, and was programmed in C#. To ensure the real-time signal processing, many techniques were used, such as multi-threaded, multi-level caching techniques. The graphical user interface (GUI) could synchronously