CHINESE JOURNAL OF ANALYTICAL CHEMISTRY
Volume 44, Issue 7, July 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(7), 1148–1154.

RESEARCH PAPER

Development of Portable Device for Point-of-Care Testing of Tumor Marker

FAN Yan[1,2,3], WANG Yang[1,2], LIU Jun-Tao[1,2], LUO Jin-Ping[1,2], XU Hui-Ren[1,2], XU Sheng-Wei[1,2], 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] Intelligence and Information Engineering College of Tangshan University, Tangshan 063000, China

Abstract: By combining electrochemical detection technique and electronic technique, a portable device which adopted differential pulse voltammetry (DPV) measurement was developed to meet the needs of high sensitivity and on-site rapid detection of tumor marker. The voltage and current resolution of portable device were 0.8 mV and 1 nA, respectively. Combined with home-made microfluidic paper-based analytical device, carcinoembryonic antigen (CEA) was detected by portable device. Experimental results revealed that the DPV peak currents showed good linear relationship with the logarithm of CEA concentration in the range of 1–500 μg L^{-1}. The corresponding correlation coefficient was 0.998 and the limit of detection was 10 ng L^{-1}. According to the principle of specific binding of antibody and antigen with electrochemical detection, CEA concentration could be calculated automatically according to the linear equation. The portable device with the features of high sensitivity and low detection limit could be widely used in the point-of-care testing of tumor marker.

Key Words: Carcinoembryonic antigen; Electrochemical detection; Differential pulse voltammetry; Portable; Point-of-care testing

1 Introduction

Lung cancer is one of the most malignant tumors and seriously threatens the health of human, with the incidence and mortality rates occupying the first position in malignant tumors. Lung cancer has no clinical symptoms in the early stage, but once diagnosed, it is already at advanced stages and very easy to spread and metastasize. A large number of clinical studies reveal that the prognosis of lung cancer is closely related to clinical stages. The five-year survival rate for lung cancer patients at the early stages is 70%, while it has very low five-year survival rate for lung cancer patients at the advanced stages[1,2]. As a result, the early finding, diagnosis and treatment of lung cancer have great clinical significance.

Many clinical methods have been developed for the detection of tumor markers, such as enzyme-linked immunoassay (ELISA)[3], radioimmunoassay (RIA)[4], electrochemiluminescence immunoassay (ECLIA)[5], chemiluminescence immunoassay (CLIA)[6] and fluoroimmunoassay (FIA)[7]. Although these methods are very sensitive, but they are not suitable for on-site rapid detection of tumor marker because these methods require large serum sample, long analysis time, high cost and complicated process. With the development of biochip technology, electrochemical immunoassay which combines electrochemical detection technique and immunological technique has attracted more and more attention of researchers in recent years[8–11]. The electrochemical immunoassay method is very suitable for on-site rapid detection of tumor marker with the advantages of low serum sample, short analysis time, low cost, high

Received 29 January 2016; accepted 1 March 2016
*Corresponding author. Email: xxcai@mail.ie.ac.cn
This work was supported by the National Natural Science Foundation of China (Nos. 61527815, 61471342, 31500800, 61501426), the National Basic Research Program of China (No. 2014CB744600), the Beijing Science and Technology Plan of China (Nos. Z141100000214002, Z141100003414015), and the Key Programs of the Chinese Academy of Sciences (No. KJZD-EW-L11-2).

DOI: 10.1016/S1872-2040(16)60947-7

sensitivity, high accuracy, simple process and good repeatability. Now it has been applied in laboratory by using large electrochemical workstations with high detection accuracy, but it is costly and inconvenient to carry. Thus it has great practical value to develop portable devices for the on-site rapid detection of tumor marker.

In this study, a portable device was developed for on-site rapid detection of tumor marker on the basis of the above research background. Combing with microfluidic paper-based analytical device (μPADs), the portable device could rapidly and quantitatively detect carcinoembryonic antigen (CEA) with high sensitivity.

2 System design

The portable system is consisted of electrochemical detection module, STM32 main control module, memory and display module and UART communication module. The hardware block schematic of system is shown in Fig.1.

2.1 Electrochemical detection module

The concentration of tumor marker (~μg L^{-1}) was detected by electrochemical method according to the principle that the specificity binding of different concentrations of antigen-antibody complexes could cause the change of electrochemical detection current[9]. The current signal was too weak (nA to μA) to measure, thus it should be converted to easily measured voltage signal. Electrochemical detection module included differential pulse voltammetry (DPV) working voltage waveform generating circuit and current-voltage conversion circuit. DPV working voltage waveform generating circuit was designed according to the working principle of potentiostat. By using "virtual short" and "virtual-off" feature, it was formed as a voltage follower to provide a program-controlled working potential which was not affected by electrochemical detection current[12,13]. Current-voltage conversion circuit formed as T-type feedback network[14] was used to convert current signals to easily measured voltage signals that were passed to ADC module for following data calculation.

2.2 STM32 main control module

STM32 main control module adopted a 32-bit microprocessor chip STM32F103RCT6 with the ARM Cortex-M3 kernel as the central control chip which consisted of three 18-channel, 12-bit analog-to-digital converter (ADCs) and a 12-bit digital-to-analog converter (DAC). The voltage and current resolution were 0.8 mV and 1 nA, respectively, which could meet the accuracy demand of electrochemical detection of tumor marker.

2.3 Memory and display module

Memory module made use of serial CMOS EEPROM chip AT24C02, whose memory size was 2 kb composed of 256 8-bit bytes, to store the detection results of tumor maker. 2.4-inch OLED with reaction speed around 10 μs was used in display module to display the detection results, possessing the features of low power, ultra wide angle of view and autoluminescence.

2.4 UART communication module

UART communication module transmitted detection results of tumor marker to PC via USB and saved these results for further data analysis and processing.

2.5 Working principle of portable device

Working principle of portable device are described as follows. STM32 main control module was programmed to generate digital DPV signals. The digital DPV signals were converted to analog signals by internal DAC integrated within the STM32F103RCT6 chip, then transferred to DPV working voltage waveform generating circuit and applied to each electrode of μPADs. Weak electrochemical current signals were generated under applied analog voltage and converted to voltage signals through current-voltage conversion circuit.

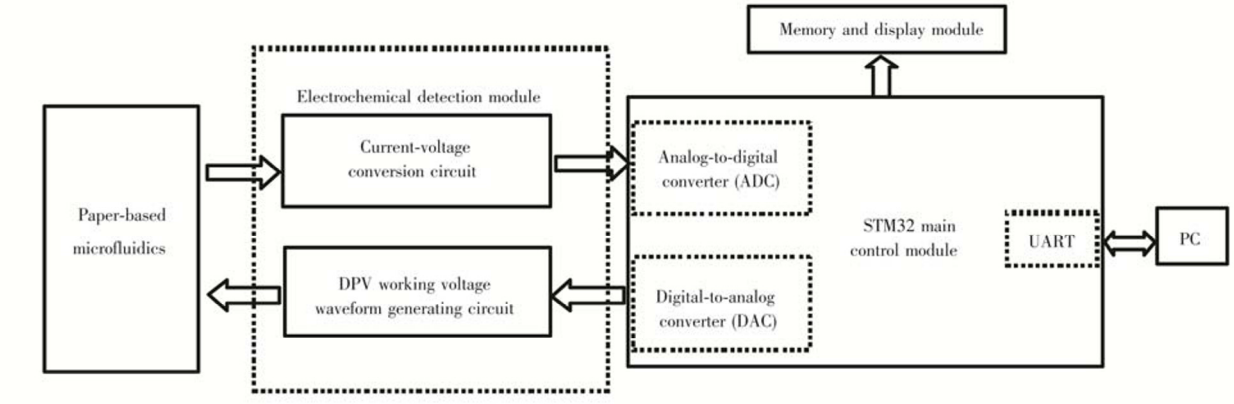

Fig.1 Hardware block schematic of portable device for carcinoembryonic antigen (CEA) detection