INVESTIGATION OF USING POTENTIOSTATS AND MICROFLUIDIC DEVICES FOR CONTINUOUS IONS DETECTION

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To my beloved family

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Abstract

In the light of the importance of the bedside patient monitoring system, a miniaturized, flexible, versatile, disposable and cost effective bedside patient continuous monitoring system is essential. Therefore, this research addresses the development of a cost effective and miniaturize continuous monitoring system. For electrochemical analysis, three potentiostats were used: EmStat, CheapStat and in house UTMStat. For lab-on-chip system, two models were proposed and their electrochemistry and pumping characteristics were studied. The 2 layers detection zone was developed through fused filament technology and replication moulding technique with a screen printed electrode attached together. It achieved the maximum flow rate of 0.30405 ml/min with resonance frequency of 20 Hz in micropump reverse direction. With the maximum frequency, the highest oxidation peak current of 15.86176 μA in cyclic voltammetry measurement was achieved by 10 mM ferrocyanide ions at potential 0.25 V. The monolithic microfluidic device was developed through sticker masks fabrication and replication moulding technique with two screen printed electrodes attached beneath the inlets and the outlets of the micropump. It achieved the maximum flow rate of 0.19693 ml/min with resonance frequency of 10 Hz in micropump forward direction. With the maximum frequency, the highest oxidation peak current of 28.32518 μA in cyclic voltammetry measurement was achieved by 10 mM ferrocyanide ions at potential 0.32 V. Additionally, the electrochemical investigation was extended by measuring the cyclic voltammetry measurements of chloride ions from a mixture by using EmStat and CheapStat. The highest oxidation peak was observed at 61.26875 μA and 1.04400 μA by using EmStat and CheapStat respectively at potential 0.13 V. Specifically, the monolithic microfluidic device is well integrated in lab-on-chip system with the advantage of miniaturize with the dimensions of 41 mm x 26 mm, cost effective by using sticker masks fabrication and replication moulding technique, disposability since it is inexpensive and meant for biomedical analysis, flexibility where it can be used for other ions detection just by changing the screen printed electrode and can measure the data during pumping. This research successfully provides an alternative approach for continuous monitoring of ferrocyanide and chloride ions detection via cyclic voltammetry and amperometry measurements.

ABSTRAK

Mengambil kira kepentingan sistem pemantauan sisi katil pesakit, sistem pemantauan pesakit secara berterusan yang bersaiz kecil, fleksibel, serba boleh, boleh guna dan kos efektif adalah penting. Oleh itu, kajian ini menunjukkan pembangunan sistem pemantauan secara berterusan yang murah dan bersaiz kecil. Untuk analisis elektrokimia, tiga potentiostats telah digunakan: EmStat, CheapStat dan “in house” UTMStat. Untuk sistem “makmal dalam cip”, dua model telah dicadangkan dan ciri-ciri elektrokimia dan mengepam telah dikaji. 2 lapisan zon pengesanan telah dibangunkan melalui teknologi “fused filament” dan teknik acuan replikasi dengan satu elektrod skrin bercetak yang disertakan. Peranti ini mencapai kadar aliran tahap maksimum pada 0.30405 ml/min dengan frekuensi resonans 20 Hz dalam arah berlawanan. Menggunakan frekuensi maximum, pengoksidaan puncak arus yang tertinggi sebanyak 15.86176 μA dalam pengukuran voltammetri berkitar dicapai oleh 10 mM ion “ferrocyanide” pada potensi 0.25 V. Peranti “microfluidic” monolitik dibangunkan melalui fabrikasi “sticker mask” dan teknik acuan replikasi dengan dua elektrod skrin bercetak yang disertakan di bawah salur masuk dan salur keluar micropump itu. Peranti ini mencapai kadar aliran tahap maksimum pada 0.19693 ml/min dengan frekuensi resonans 10 Hz dalam arah ke hadapan. Menggunakan frekuensi maximum, pengoksidaan puncak arus yang tertinggi sebanyak 28.32518 μA dalam pengukuran voltammetri berkitar dicapai oleh 10 mM ion “ferrocyanide” pada potensi 0.32 V. Selain itu, siasatan elektrokimia dilanjutkan dengan pengukuran voltammetri berkitar ion klorida daripada campuran dengan menggunakan EmStat dan CheapStat. Pengoksidaan puncak arus yang tertinggi diperhatikan di 61.26875 μA dan 1.04400 μA dengan menggunakan EmStat dan CheapStat masing-masing pada potensi 0.13 V. Secara khusus, peranti “microfluidic” monolitik yang dibentangkan adalah disepadukan dalam sistem “makmal dalam cip” dengan kelebihan bersaiz kecil dengan dimensi 41 mm x 26 mm, kos efektif dengan menggunakan fabrikasi “sticker mask” dan teknik acuan replikasi, “pakai buang” kerana ia adalah murah dan bertujuan untuk analisis bioperubatan, fleksibiliti di mana ia boleh digunakan untuk pengesanan ion-ion lain hanya dengan menukar elektrod skrin bercetak dan dapat mengukur data semasa mengepam. Kajian ini telah berjaya menyediakan satu pendekatan alternatif untuk pemantauan ion “ferrocyanide” dan klorida secara berterusan melalui ukuran voltammetri berkitar dan amperometri.

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LIST OF ABBREVIATIONS

LOC	-	Lab on a chip
PDMS	-	Poly(dimethylsiloxane)
SLA	-	Stereolithography
WE	-	Working electrode
CE	-	Counter electrode
RE	-	Reference electrode
CCS	-	Carbon capture and storage
PVC	-	Polyvinyl chloride
3D	-	3 dimensional
DNA	-	Deoxyribonucleic acid
RNA	-	Ribonucleic acid
CMOS	-	Complementary metal-oxide semiconductor
BiCMOS	-	Bipolar and CMOS
NI	-	National instruments
SPE	-	Screen printed electrode
FFF	-	Fused filament fabrication
FDM	-	Fused deposition modeling
UV	-	Ultraviolet
SLS	-	Selective laser sintering
REM	-	Replica moulding
3DP	-	3D printing
ESI-MS	-	Electrospray ionisation mass spectrometer
PLA	-	Polylactic acid
ABS	-	Acrylonitrile butadiene styrene
USB	-	Universal serial bus
GUI	-	Graphical user interface
SMD	-	Surface mount device

PCB	-	Printed circuit board
PC	-	Personal computer
MSB	-	Most significant bit
LSB	-	Least significant bit
BMP	-	Bitmap
ISR	-	Interrupt service routine
CSV	-	Comma separated values
AC1.W2.RS	-	SPE with platinum WE and CE and silver RE
GCODE	-	G programming language
AC1.W3.R1	-	SPE with silver WE, platinum CE and Ag/AgCl RE
DXF	-	Drawing interchange format
NHE	-	Normal hydrogen electrode
SBF	-	Simulated body fluid

LIST OF SYMBOLS

$i_{lim-lev}$	-	Limiting current
n	-	Number of electron transfer
F	-	Faraday's constant
C_{bulk}	-	Concentration of the bulk solution
D_0	-	Diffusion coefficient
V_f	-	Volume flow rate
h	-	Height
d	-	Width
w	-	Rotation rate
x_e	-	Length of the band electrode
NO_2	-	Nitrogen dioxide
CO_2	-	Carbon dioxide
SO_2	-	Sulfur dioxide
NO	-	Nitrogen oxide
H^+	-	Hydrogen ion
K^+	-	Potassium ion
Ca^{2+}	-	Calcium ion
Na^+	-	Sodium ion
O_2	-	Oxygen
H_2O_2	-	Hydrogen peroxide
Cl^-	-	Chloride ion
$[Fe(CN)_6]^{4-}$	-	Ferrocyanide ion
$[Fe(CN)_6]^{3-}$	-	Ferricyanide ion
Ag	-	Silver
Ag^+	-	Silver ion
$E(NHE)$	-	Potential with respect to NHE

$E(Ag/AgCl)$	-	Potential with respect to Ag/AgCl
e^-	-	Electron

Chapter 1

INTRODUCTION

1.1 Research Background

Monitoring chemicals and biomarkers is essential to predict patients' critical conditions during surgical procedures and following these in intensive care units. Monitoring biomarkers provides information of any abnormalities occurring in metabolic pathways, and hence offer further understanding or can potentially be an early diagnosis for a number of illnesses. For example, hypoxia can be detected by a decrease in glucose and an increase in lactate, typically of a lack of oxygen during the biochemical pathways.

Biomarkers are typically detected in human fluids such as blood, serum, urine or cerebral spinal fluid and interstitial space. This brings a challenge when monitoring biomarkers through the conventional method by using an expensive and large piece of equipment. With this equipment, it is hard to provide health care for the rural population due to its low socio-economic income [5], transportation and distance challenges. In addition, current ions analyzer is normally located in the central laboratories which requires specialized technicians to operate on the machine, offers delayed diagnosis and not disposable. Besides, during the process, mix-ups sometimes occur when samples are sent to laboratories.

Therefore, there are numerous efforts in developing an affordable miniaturized bedside patient continuous monitoring system. One of the approaches is through lab on chip (LOC) device due to its unique ability in micro-scale sample handling, mixing, separation, detection, user friendly and inexpensive [6–9]

Many reported continuous monitoring system, nevertheless, utilizes external regulated pressure source or by syringe pumps or even through manual pipetting. This approach has constrained the purpose of portability of LOC. Consequently, to mitigate such drawbacks, the integration of the micropump and the reaction zone is crucial.

Potentiometric system has always been related to electrochemical detection method [10] in LOC. The combination of electrochemical cell and a potentiostat circuit forms a potentiostatic system. Potentiostat is a feedback control system [11] which adjusts the voltage across the WE (working electrode) - CE (counter electrode) pair to maintain the preset potential between the WE and RE (reference electrode) of an electrochemical cell [12].

Besides clinical diagnosis [13–22], continuous monitoring system has also been applied in water quality control [23–27], pharmaceutical product [28–32], corrosion quality control [33–37], environmental emission [38–42] and other fields [43–47].

1.2 Problem Statement

In view of the importance of the bedside patient monitoring system, a miniaturized continuous monitoring system with flexibility, versatility and disposable is much needed. An external pressure source is utilized in most of the applications of the current continuous monitoring system to deliver the sample to the detection zone [2, 13, 14]. But, there are few drawbacks in this approach which has restricted the system's mobility due to the additional manual procedures or exterior components for measurement setup are needed. Moreover, the losses because of the friction and shear stress of the tubing wall might be introduced by the connection between the pressure source and the electrochemical detection zone [1].

In addition, as stated in [4], current method is expensive where commercially available laboratory potentiostats sold for more than a thousand dollars. Besides, current medical practice is still relying on the expensive and large piece of equipment which generally located in the central laboratories that require specialized technicians, offers delayed diagnosis and not disposable. In a lab on chip design, disposability is a main aspect that should be highlighted to confirm that the sample is unpolluted as the continuous patient monitoring system is meant for biomedical analysis. To eliminate the sterilizing procedure and to confirm the hygiene condition, the device needs to be disposed.

1.3 Research Objectives and Scope of the Thesis

The primary objective of this project is to develop an in channel electrochemical detection for continuous flow lab on chip application. The specific goals can be further expressed as:

1. To develop electrochemical detection system for continuous monitoring of ions.
2. To evaluate the performance of the developed device in a continuous monitoring system.

To accomplish these objectives, two different models are proposed and their electrochemistry and pumping characteristics are studied. The first model is to demonstrate the effect of pinching right above the electrochemical detection zone. The electrochemical detection zone is developed in two different thickness of poly (dimethylsiloxane) (PDMS) polymer layers with fused filament technology and replication moulding technique with a screen printed electrode attached together.

Structurally, the inlet and outlet of the micropump were modified based on the electrode surface where the screen printed electrodes were place beneath. To ease the fabrication technique and to have smoother mould surface, the electrochemical detection zone approaches sticker mask fabrication and as mentioned above replication moulding technique with two screens printed electrodes attached together. This new design of the electrochemical detection zone is introduced in the second model.

1.4 Thesis Outline

A review of the continuous monitoring system development is given in Chapter 2. Then in Chapter 3, the methods in developing of potentiostat, 2 layers detection zone and monolithic microfluidic are described. In Chapter 4, the examinations of potentiostat, continuous monitoring systems for 2 layers detection zone and monolithic microfluidic are discussed. Finally, an outlook on future project development is concluded in Chapter 5.

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