The 21st Korean MEMS Conference

제21회 한국 MEMS 학술대회

2019.4.4(목) ~ 4.6(토), 제주 KAL호텔

| 논문원고접수 |

2018년 12월 3일(월) ~ 12월 31일(월)

| 논문심사결과 통보일 |

2019년 2월 11일(월)까지 홈페이지 (http://www.micronanos.org)에 공지 및 책임저자에게 이메일로 통보

| 초록 및 논문접수처 |

http://www.micronanos.org

| 논문범위 |

1. Materials, Fabrication, and Packaging Technologies
2. Fundamentals in MEMS/NEMS
3. Micro/Nanofluidics and Lab-on-a-Chip
4. Bio/Medical Micro/Nano Devices
5. Micro/Nano Sensors and Actuators
6. RF/Optical Micro/Nano Devices
7. Micro/Nano Energy Devices
8. Flexible and Printed Devices
9. MEMS/NEMS Applications and Commercialization

주최 : (사)마이크로나노시스템학회 (E-mail : master@micronanos.org, 전화 : 02-749-6482)

FP-2-27	로즈룸	Dimension effect of Interdigitated Electrode Array on Impedance Measurement of Drug-induced Cardiomyocytes	부자	이동원	부자	Chonnam National University
FP-2-28	로즈룸	Fabrication of pseudo-Palladium nanostructures and its application to hydrogen gas sensor	김상훈	윤광석	김상훈	서강대학교
FP-2-29	로즈룸	습한 조건에서 MoS2의 NO2 반응 및 회복 특성 분석	강윤성	김종백	강윤성	연세대학교
FP-2-30	로즈룸	완벽하게 정렬된 균일한 나노갭을 이용한 스위치형 팔라듐 수소 가스 센서 Switching Type Palladium Hydrogen Sensor with Perfectly Aligned and Highly	정명근 Jaeshin Lee	윤준보	정명근	한국과학기술원
FP-2-31	로즈룸	Hierarchical Mesoporous SnO2 nanospheres on Reduced Graphene Oxide for Ammonia Sensor applications	아룬	이동원	아룬	Chonnam National University
FP-2-32	로즈룸	Delta-E Measurement of Fe-based Magnetostrictive Amorphous Films using Aluminum Nitride MEMS Resonator	정순인	김회준	정순인	대구
FP-2-33	로즈룸	이중 채널 마이크로 공진기를 이용한 액상 시료 물성 동시 측정	이재섭	이정철	이재섭	한국과학기술원
FP-2-34	로즈룸	시뮬레이션을 통한 마이크로구조 압전 센서 성능의 매개 변수 영향 연구 A Parametric Study on the Performance of Microstructured PVDF Piezoelectric	이서연	류원형	이서연	연세대학교
FP-2-35	로즈룸	Suspended ZnO nanorod bridge network-based gas sensor	이승욱	신흥주	이승욱	울산과학기술원
FP-2-36	로즈룸	다공성 유연물질과 3차원 마이크로 압출공정을 이용한 고효율 트리보센서 제작	소새롬	박상후	박석희	한국생산기술연구원
FP-2-37	동백룸	DMF device with SU-8 based dielectric layer/micro-pillar for sorting micro-particles	이재용	공성호	공성호	경북대학교
FP-2-38	동백룸	The development of the method for differential count between neutrophils and lymphocytes by signal analysis (신호 분석을 통한 호중구 및 림프구 감별 계수 방법	안재현	양성	안재현	광주과학기술원
FP-2-39	동백룸	3차원 다공성 골드폼 전극을 이용한 프로칼시토닌(PCT) 검출 전기화학 센서	정유경	양성	정유경	광주과학기술원
FP-2-40	동백룸	대면적 상보 플라즈모닉 구조를 이용한 저(低)색누화 가변 광학 필터 제작	안명수	정기훈	안명수	한국과학기술원
FP-2-41	동백룸	UV 펄스 레이저 기반 환원 그래핀 패터닝에 관한 연구 A study on reduced graphene oxide patterning with a UV pulse laser	이준욱	이준욱	이준욱	부산대학교 3차원혁신제조센터
FP-2-42	동백룸	압전구동기를 이용한 Otto 구조 기반의 표면 플라즈몬 공명 측정	이연수	김정무	이연수	전북대학교
FP-2-43	동백룸	다공성 전극기반 마이크로유체 미생물 연료전지 Microfluidic microbial fuel cell with porous electrode	양계도	안유민	양계도	한양대학교
FP-2-44	동백룸	Comparison of super capacitors made of double-layered nano-structures in fiber shape	장정	윤광석	장정	서강대학교
FP-2-45	동백룸	역전기투석 발전 시스템의 출력 향상을 위한 고분자-세라믹 복합 이온교환막 개발 (Development of polymer-ceramic hybrid ion exchange membrane for power	정동현	서영호	한의돈	강원대학교
FP-2-46	동백룸	Microfluidic membraneless redox flow battery using electroactive electrolyte	박형주	김성재	박형주	서울대학교
FP-2-47	동백룸	Bi4Ti3O12/PVDF Composite based Piezoelectric Nanogenerator for Biomechanical Energy Harvesting	Nirmal Prashanth	Sang-Jae Kim	Nirmal Prashanth	제주대학교
FP-2-48	동백룸	3D Printed Rolling Circle Amplification Device for On-site Colorimetric Detection of Mercury Ion	임지원	임지원	임지원	한국식품연구원
FP-2-49	동백룸	Paper-based Flexible NO2 Sensor Using Carbon Nanotube-WS2 Hybrid as Sensing Material	추남선	조일주	추남선	한국과학기술연구원
FP-2-50	동백룸	불활성 기체 가열법을 이용한 스핀 코팅된 은 박막의 열 소결	신권용	이상호	이상호	한국생산기술연구원
FP-2-51	동백룸	Development of colorimetric sensor for detection of toxic gases based on inkjet printing	김다미	김상효	김다미	가천대학교
FP-2-52	동백룸	Real-time quantification using hybrid paper-polymer centrifugal optical devices	김세진	김상효	김세진	가천대학교

Dimension effect of Interdigitated Electrode Array on Impedance Measurement of Drug-induced Cardiomyocytes

[1]Pooja Kanade, [1]Nomin Erdene Oyunbaatar, [1]Dong Weon Lee*
[1]MEMS and Nanotechnology Laboratory, Department of Mechanical Engineering, Chonnam National University, Gwangju 61186, Korea
E-mail: mems@jnu.ac.kr

약물 처리된 심근세포의 임피던스 측정에서 Interdigitated 전극의 구조 효과

[1]Pooja Kanade, [1]Nomin Erdene Oyunbaatar, [1] 이동원*,
[1] 전남대학교 기계공학과

Abstract

Interdigitated Electrode Arrays (IDEs) have been extensively used to measure electrophysiology of cardiac cells. Recently, our team developed a novel device that consists of an IDE integrated on a micro-cantilever. We had fabricated IDEs of different dimensions on the top of the cantilever. This current study reports the relationship between the dimensions of the IDE and the output impedance. This study highlights the relationship between various parameters of a cell culture medium and their electrical equivalent. It was found that lower values of electrode length lead to lower impedance. Also, increase in cross-section of IDE leads to decrease in impedance. Further, the impedance changes due to Verapamil drug, a Calcium ion channel blocker, was tested. This study shows that IDEs are an important tool for measuring the electrophysiological properties of cardiomyocytes. IDEs can also be used for screening of drugs and their toxic effects on cardiomyocytes.

Keywords: ***Cardiomyocytes (심근세포), Impedance (임피던스), Interdigitated Electrode Array (Interdigitated 전극 패턴)***

1. Introduction

Some of the leading causes of untimely deaths worldwide are diseases related to the heart and its irregular functioning [1]. A significant amount of research is going on for understanding the mechanical and electrophysiological characteristics of cardiomyocytes and their corresponding behavior owing to cytotoxicity caused by various drugs [2]. IDEs have been used to measure the impedance of the cells and their culture, that enables us to understand the growth and contraction forces of cardiomyocytes [3]. This is a non-invasive technique and real-time information of the cell can be obtained for a range of frequencies.

Recently, our team had developed a novel device for analyzing the growth and contraction forces of cardiomyocytes simultaneously with deflection force occurring because of the cardiomyocytes. This device can measure deflection of the cantilever as well as measure impedance from the IDEs simultaneously. This latest study focuses on changing the dimensions of the IDEs and observing changes in the output impedance to improve the accuracy of the experimental results.

2. Description of the Method and Results

2.1 Description of the Method

We fabricated a cantilever device that was used as a base layer for IDE. Multiple devices have been fabricated with varying the dimensions of electrode. IDEs with width of 5μm, 10μm and 15μm were fabricated. The IDE was fabricated with gold as electrodes on the photosensitive polymer base layer of cantilever. Figure 1 shows the optical image of IDE patterns of various widths. Neonatal rats' cardiac cells are cultured on the device for analyzing the bending displacement and impedance. Figure 2 shows the device in cell culture medium and distribution of cardiomyocytes on IDE.

2.2 Results

Figure 3 shows the schematic of distribution of cardiomyocytes on the IDE, along with the equivalent circuit. R_s is the resistance of bulk solution and wire connection, C_{p1} and R_{p1} are resistance and capacitance at electrode and cardiomyocyte interface respectively, C_{p2} and R_{p2} are resistance and capacitance between the uncovered electrode and solution respectively.

Capacitance and solution resistance can be calculated from the following equation [3]:

$$K = R_s\sigma = \frac{\varepsilon_0\varepsilon_r}{C_{p1}} \quad (1)$$

where K is the cell constant of the IDE assembly, R_s is the solution resistance, σ is the conductivity of solution, ε_0 is permittivity of vacuum, ε_r is relative permittivity of solution and C_{p1} is the capacitance between electrode and solution.

Cell constant can be calculated from the following equation [3]:

$$K = 2\frac{\sqrt[3]{S/W}}{L(N-1)} \quad (2)$$

where S is inter-trace distance, W and L are finger width and length and N is number of fingers in IDE.

Figure 4(a) shows the impedance curves of IDEs of various dimensions on day 8 after cell seeding. As is evident from the graph, the net impedance of the system is decreasing at high frequencies on increasing the electrode width. Table 1(a) gives details of the IDE patterns that have been used in this study. The cell constant K is also calculated. We can see that the cell constant is more dependent on the electrode length and is inversely proportional to it. Table 1(b) shows the values of each component of the equivalent circuit on day 8 of cell seeding. Equivalent impedance values Z_1 and Z_2 are also calculated from R_1-C_1 and R_2-C_2 respectively, at 100 kHz frequency. 100 kHz was chosen to calculate the impedance because IDEs were found to have a slightly more linear impedance at higher frequencies. The value of Z_2 is slightly increasing at 10μm and then decreasing at 15μm. The major contributing factor in this is the electrode width, because of which the cross-sectional area changes.

Figure 4(b) shows the impedance change on addition of 150nM Verapamil drug, which is a calcium ion channel blocker. As we compare both Figures 4(a) and 4(b), we observe that the impedance is linear over a higher range of frequencies on addition of Verapamil. The resistive component begins to dominate from ~5kHz, whereas in absence of drug, it begins at above 10kHz. We can see that IDE of width 5µm has a resistive component that dominates more than the capacitive component – over a higher range of frequencies, which is evident from the linearity of the graphs. Also, it has a lower *K* value which is desirable (Table 1(a)). Hence, based on the current configuration, we can conclude that the IDE of width 5µm is preferable.

From this study, we can successfully conclude that IDE is an important tool to study electrophysiological properties of cardiac cells. IDEs can also be used to study the effect of various drugs on cardiomyocytes.

Acknowledgments

This study was supported by a grant of the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea(HI13C1527).

References

[1] E. Benjamin, M. Blaha, S. Chiuve, Heart Disease and Stroke Statistics-2017 Update: A Report from the American Heart Association, *Circulation*, 135, 10: e146 - e603 (Mar 2017).
[2] N. Mazlan, M. Ramli et al., Interdigitated Electrodes as Impedance and Capacitance Biosensors: A Review, *AIP Conference Proceedings,* 1885, 020276 (Sept 2017).
[3] F. Qian, C. Huang, Y. Lin et al., Simultaneous electrical recording of cardiac electrophysiology and contraction on chip, *Lab on a Chip*, 17, 1732 (Apr 2017).

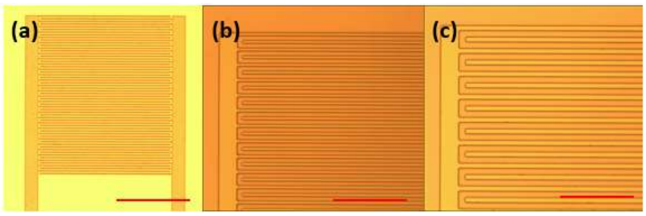

Fig. 1. Optical image of IDEs with widths (a) 5nm, (b) 10nm and (c) 15 nm. Scale bar: 500µm

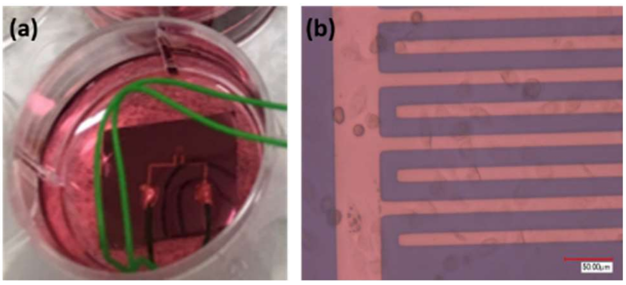

Fig. 2. (a) Image of device in cell culture medium (b) distribution of cardiomyocytes on IDE

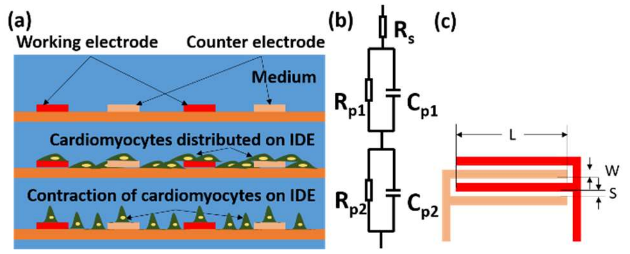

Fig. 3. Schematic of distribution of cardiomyocytes on IDE (b) equivalent circuit (c) schematic of IDE

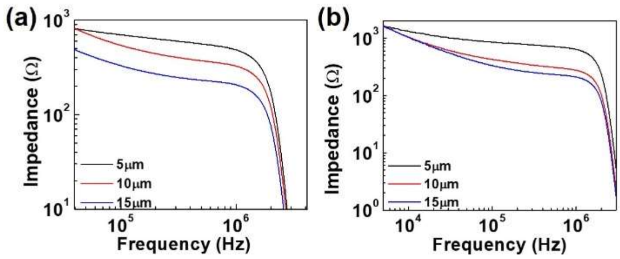

Fig. 4. (a) Impedance data of IDEs of 5µm, 10µm, 15µm on day 8 after cell seeding (b) Impedance data on addition of 150nM Verapamil drug

Table 1. IDE results

(a) IDE dimensions and calculated *K* value

IDE #	No. of fingers (*N*)	Finger length, *L* (um)	Finger width, *W* (um)	Interspace, *S* (um)	Electrode length (mm)	*K* (1/cm)
1	60	495	5	5	150	0.68
2	30	990	10	10	297	0.70
3	30	985	15	15	443	0.70

(b) Parameters extracted from equivalent circuit model on day 8 after cell seeding

Width	R_s (Ω)	R_{p1} (Ω)	C_{p1} (µF)	R_{p2} (Ω)	C_{p2} (µF)	Z_1 at 100 kHz (Ω)	Z_2 at 100 kHz (Ω)
5 µm	7.11E+02 ±3.67	4.09E+04 ±2.32	8.44E-08 ±1.03	3.15E+03 ±3.24	5.11E-08 ±3.71	18.85	31.14
10 µm	4.96E+02 ±5.94	4.15E+04 ±1.47	6.12E-08 ±1.18	4.30E+03 ±3.45	4.35E-08 ±3.11	26	36.58
15 µm	4.17E+02 ±7.59	8.41E+04 ±2.56	5.36E-08 ±0.93	4.59E+03 ±3.79	5.38E-08 ±3.20	29.69	29.58

The 21st Korean MEMS Conference, 2019.04.04 – 2019.04.06, Jeju, South Korea

전남대학교 CHONNAM NATIONAL UNIVERSITY

MNTL

Dimension effect of Interdigitated Electrode Array on Impedance Measurement of Drug-induced Cardiomyocytes

약물 처리된 심근세포의 임피던스 측정에서 Interdigitated 전극의 구조 효과

[1]Pooja Kanade, [1]Nomin Erdene Oyunbaatar, [1]Dong-Weon Lee*

[1]MEMS and Nanotechnology Laboratory, Department of Mechanical Engineering, Chonnam National University, Gwangju 61186, Korea, E-mail: mems@jnu.ac.kr

ABSTRACT

Interdigitated Electrode Arrays (IDEs) have been extensively used to measure electrophysiology of cardiac cells. Recently, our team developed a novel device that consists of an IDE integrated on a micro-cantilever. We had fabricated IDEs of different dimensions on the top of the cantilever. This current study reports the relationship between the dimensions of the IDE and the output impedance. This study highlights the relationship between various parameters of a cell culture medium and their electrical equivalent. It was found that lower values of electrode length lead to lower impedance. Also, increase in cross-section of IDE leads to decrease in impedance. Further, the impedance changes due to Verapamil drug, a Calcium ion channel blocker, was tested. This study shows that IDEs are an important tool for measuring the electrophysiological properties of cardiomyocytes. IDEs can also be used for screening of drugs and their toxic effects on cardiomyocytes.

Keywords: *Cardiomyocytes (심근세포), Impedance (임피던스), Interdigitated Electrode Array (Interdigitated 전극 패턴)*

INTRODUCTION

What is an IDE ?

- Interlocked planar microelectrode arrays
- Interdigitated configuration typically enhances sensitivity and detection limits.
- Used to measure impedance spectroscopy of a system – a label-free, non-invasive, real-time monitoring technique that can detect subtle cellular changes

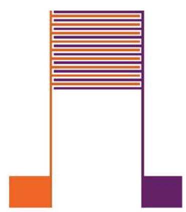

Figure 1: Schematic of an IDE

Electrical and mechanical responses of cardiomyocytes have not been measured simultaneously till date

Motivation

Optimize dimensions of IDE so that it can be integrated with the cantilever – a device that can simultaneously measure mechanical and electrophysiological properties of cardiac cells

OBJECTIVE

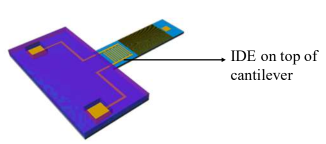

Figure 2: Schematic of the target device of IDE integrated with cantilever

- Integrate interdigitated electrode array (IDE) with cantilever
- Optimize dimensions of the IDE (width, spacing and no. of fingers)
- Study the changes in impedance of cardiac cells on addition of drugs such as Verapamil

FABRICATION STEPS

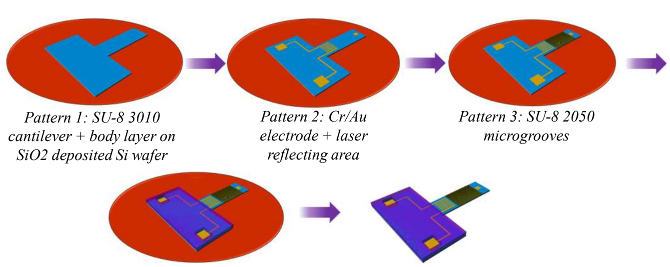

Figure 3: Fabrication process flow of the IDE-cum-cantilever device

FABRICATED DEVICE

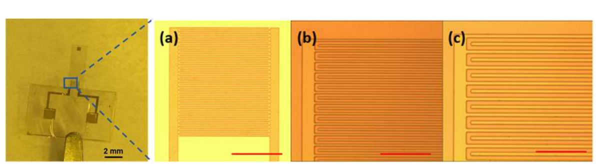

Figure 4: Optical image of IDEs with widths (a) 5μm, (b) 10μm and (c) 15μm. Scale bar: 500μm

WORKING PRINCIPLE

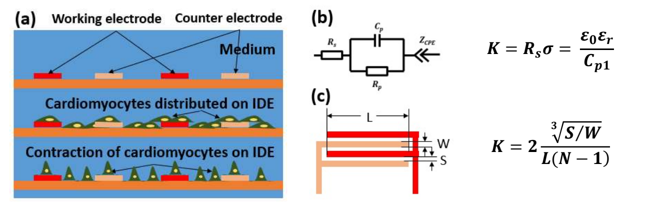

Figure 5: Schematic of distribution of cardiomyocytes on IDE (b) equivalent circuit (c) schematic of IDE

RESULTS

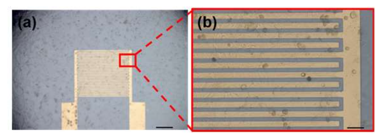

Figure 6: (a) Optical image of device in cell culture medium (b) distribution of cardiomyocytes on IDE on day 8. Scale bar = 50μm

IDE #	No. of Fingers (N)	Finger Length L (μm)	Finger Width W (μm)	Interspace S (μm)	Electrode Length (mm)	K (1/cm)
1	60	495	5	5	150	0.68
2	30	990	10	10	297	0.70
3	30	985	15	15	443	0.70

Table 1: IDE dimensions and calculated cell constant (K) value

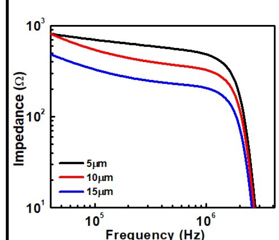

Figure 7: Impedance data of IDEs of 5μm, 10μm, 15μm on day 8 after cell seeding

- Cell constant of IDE #1 is the lowest. The impedance of this device is also more linear over a higher range of frequencies.
- The cell constant is more dependent on the electrode length and is inversely proportional to it.
- The net impedance of the system is decreasing at high frequencies on increasing the electrode width.

Width	Rs (kΩ)	Rp (kΩ)	Cp (nF)	Q (nF)	n	Z at 100 kHz (Ω)
5 μm	0.517 ± 0.02	0.723 ± 0.178	417.8 ± 114.3	622 ± 23.95	0.702 ± 0.006	699.1
10 μm	0.611 ± 0.061	8.136 ± 0.497	33.78 ± 2.216	596.7 ± 65.76	0.706 ± 0.019	543.7
15 μm	0.206 ± 0.022	9.702 ± 1.988	236.7 ± 23.7	391.9 ± 27.0	0.724 ± 0.006	330.3

Table 2: Parameters extracted from equivalent circuit model on day 8 after cell seeding

Drug Toxicity Results

- Verapamil is a calcium ion channel blocker drug, that is known to affect electrophysiological properties of cardiac cells.
- Impedance is linear over a higher range of frequencies on addition of Verapamil.
- IDE of width 5μm has a resistive component that dominates more than the capacitive component – over a higher range of frequencies. Hence, it is more preferable.

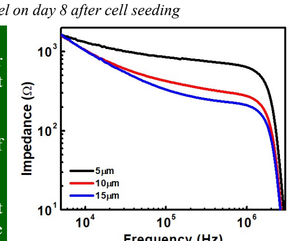

Figure 8: Impedance data on addition of 150nM Verapamil drug

CONCLUSION

- #1 type IDE of width and spacing of 5μm is more preferable to use for impedance measurement, as the impedance is more linear over a higher range of frequencies.
- IDE is an important tool to study electrophysiological properties of cardiac cells.
- This device can be used to study the effect of various drugs on cardiomyocytes.

Acknowledgment

This study was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. 2017R1E1A1A01074550).

References

[1] E. Benjamin et al., Circulation,135, 10: e146- e603 (Mar 2017)
[2] N. Mazlan, et al., AIP Conference Proceedings, 1885, 020276 (Sept 2017)
[3] F. Qian, et al., Lab on a Chip, 17, 1732 (Apr 2017)