LONG-TERM STABLE AND MICRO-SIZED ON-CHIP REFERENCE ELECTRODE WITH BIOCOMPATIBLE COATING

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ABSTRACT

Achieving high-resolution analysis with electrochemical sensing modalities necessitates the use of microelectrode arrays (MEAs). Ag/AgCl quasi-reference electrodes integrated with MEAs have shown in many studies. To fabricate on-chip Ag/AgCl quasi-reference electrodes, electrochemically deposition and printing have been utilized. However, these methods are not scalable and require unnecessary circuitry for complementary metal-oxide-semiconductor (CMOS) chips, respectively. Moreover, for long-term measurement of living cells, the biocompatible coating is needed for Ag/AgCl quasi-reference electrode. Here, we present highly miniaturized, scalable Ag/AgCl quasi-reference electrodes, which offer compatibility with MEAs and CMOS, long-term stable open-circuit voltage (OCV), and biocompatibility.

KEYWORDS: Electrochemical sensing, Microelectrode arrays (MEA), Reference electrode, Cell culture assay

INTRODUCTION

Electrochemical sensing has drawn increasing attention with its unparalleled advantages to support label-free, real-time, and non-invasive analysis at tissue/cellular/molecular levels. Hence, electrochemical sensing has been widely employed in Point-of-Care (PoC) diagnostic devices, wearable electronics, cell-based assays, and molecular detections. Recently, MEAs gain substantial interest in lab-on-a-chip (LoC) systems to electrochemically evaluate cell culture in high spatiotemporal resolution. Most existing MEAs use pseudo non-Ag/AgCl reference electrodes, conventional bulky Ag/AgCl electrodes, or Ag/AgCl quasi-reference electrodes. However, the commonly used reference electrodes are either bulky (as off-the-shelf electrodes), leading to various limitations of scalability, crosstalk, drifts, and analyte volume (Figure 1a). Unlike the conventional bulky reference electrodes, Ag/AgCl quasi-reference electrode can be integrated with MEAs and provide working electrodes with the same reference voltage. To fabricate on-chip Ag/AgCl quasi-reference electrodes, electrochemical deposition and printing have been utilized. However, electrochemical deposition requires unnecessary circuitry for CMOS chips, and the printing suffers from its limited scalability. Moreover, the direct exposure of Ag/AgCl quasi-reference electrode to solution should be prevented because Ag^+ ions can damage the viability of living organisms [1]. To resolve the aforementioned problems, we fabricated Ag/AgCl quasi-reference electrode using a standard photolithography procedure and coated the fabricated reference electrode with a biocompatible material, PEDOT:PSS.

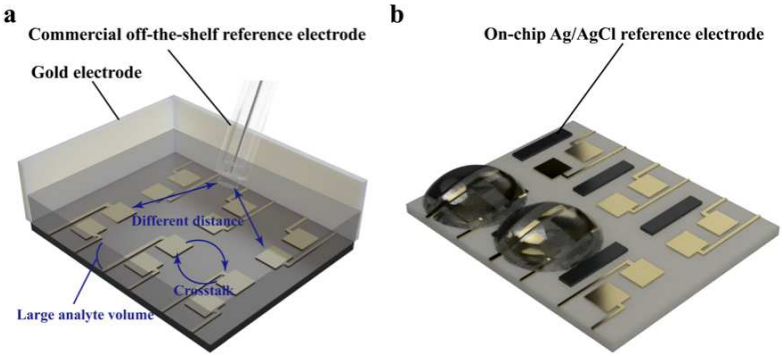

Figure 1: (a) Commercial off-the-shelf reference electrode with MEA. (b) On-chip Ag/AgCl reference electrode with MEA.

EXPERIMENTAL

We fabricated 500μm×500μm silver electrode arrays using standard photolithography procedures. Then, the silver electrode arrays were immersed in 0.05 M $FeCl_3$ solution to convert silver to AgCl. Finally, PEDOT:PSS is spin-coated on top of the Ag/AgCl reference electrodes for protection and biocompatibility. The microscopic image and cross-sectional SEM image were captured to verify the uniformity of AgCl and PEDOT: PSS coating. The OCV curves of the fabricated reference electrodes, commercial reference electrode (World Precision Instrument, DRIEF-2), and 500μm × 500μm gold electrode was measured in 250ml 0.1×DPBS solution for every 5 minutes over 20 days using a potentiostat (BioLogic, VMP-300).

RESULT AND DISCUSSION

Figure 2a and 2b present a comparison between the size of the fabricated Ag/AgCl reference electrodes and that of the commercial electrode. The area of the fabricated reference electrodes is orders-of-magnitude smaller than that of the commercial electrode. Cross-sectional SEM images show that AgCl and PEDOT: PSS coating are uniformly covered in spite of the micro size of the reference electrodes.

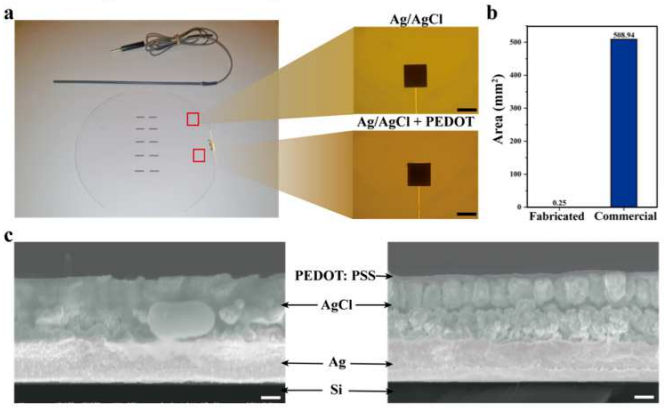

Figure 2: (a) Optical and microscopic images of fabricated and commercial reference electrodes for comparison of the electrode size (scale bar = 400 μm). (b) Comparison of the area between fabricated and commercial electrodes. (c) SEM images of fabricated reference electrode (Left: Ag/AgCl and Right: Ag/AgCl + PEDOT, Scale bar = 600 nm.

The long-term OCV measurement results are shown in Figure 3a. There was a small difference between the OCV of Ag/AgCl and that of the PEDOT: PSS coated Ag/AgCl reference electrode. This result means that the PEDOT: PSS coating does not significantly affect OCV. The OCV of the fabricated reference electrodes and commercial reference electrodes kept decreasing over time and then settled. The degradation rate of OCV was lower in the commercial electrode compared to the fabricated reference electrodes (Figure 3b). However, the degradation rate of OCV became similar after 17 days. The fabricated Ag/AgCl electrodes with/without PEDOT:PSS coating have similar OCV drifts. , which are much less than the OCV of the gold electrodes. The standard deviation of OCV was calculated based on daily measurement results (Figure 3c and 3d). The OCV standard deviation of the gold electrode was over 9 mV for 20 days. In contrast, the OCV standard deviation of fabricated reference electrodes and the commercial reference electrode was lower than 3.5 mV for 20 days. These results indicate that the fabricated Ag/AgCl reference electrodes with/without PEDOT:PSS coating, like the commercial electrode, are very stable with less drifts and variations in the long term.

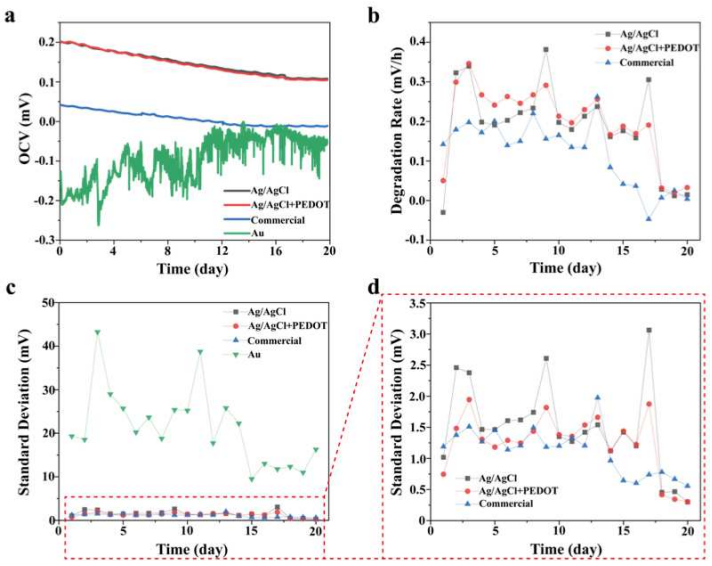

Figure 3: (a) OCV records measured every 5 minutes over 20 days. (b) OCV degradation rate of different reference electrodes. (c) Standard deviation of OCV of different reference electrodes. (d) Magnified graph of standard deviation of OCV.

CONCLUSION

The fabricated micro-sized Ag/AgCl reference electrodes showed a lower standard deviation of OCV than Au pseudo reference electrodes. More importantly, the fabricated Ag/AgCl reference electrodes with/without PEDOT: PSS biocompatibility coating exhibited a long-term stable OCV similar to the commercial bulky reference electrode. Hence, the fabricated miniatured Ag/AgCl reference electrodes can be employed in CMOS as well as high-density MEAs with microfluidics or droplet manipulation platforms to achieve highly paralleled screenings with ultra-low analyte volumes.

REFERENCES

[1] H. Wang, N. Law, G. Pearson, B. E. Dongen, R. M. Jarvis, R. Goodacre, and J. R. Lloyd, "Impact of Silver (I) on the Metabolism of Shewanella oneidensis", *J. Bacteriol.*, 192, 1143-1150, 2010

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