Topic No. 6.10
Oral or Poster

Abstract Reference No: 0037

THE HYBRID CANTILEVER OF CONDUCTIVE GRAPHENE AND SU-8 FOR IMPROVING THE MATURITY AND ELECTRICAL COUPLING OF CARDIOMYOCYTES

Longlong Li[1], Jong-Yun Kim[1, 2], and Daeyun Lim[3], and Chil-Hyoung Lee[3], and Dong-Weon Lee[1, 2, †]

[1] *MEMS Nanotechnology Laboratory, Department of Mechanical Engineering, Chonnam National University, Gwangju 61186, Republic of Korea*

[2] *Advanced Medical Device Research Center for Cardiovascular Disease, Chonnam National University, Gwangju 61186, Republic of Korea*

[3] *Green Energy & Nano Technology R&D group, Korea Institute of Industrial Technology, Gwangju 61012, Republic of Korea*

[†] *mems@jnu.ac.kr*

Abstract

This study presents a novel cantilever platform designed to enhance cell maturation and connectivity for cardiotoxicity screening applications. The platform utilizes a combination of SU-8 and graphene transferred onto a micron-grooved SU-8 cantilever surface using Thermal Release Tape (TRT). The transferred graphene exhibits structural integrity, high conductivity, and hydrophilicity. Neonatal Rat Ventricular Myocytes (NRVM) cultured on the graphene-integrated platform demonstrate improved cell-to-cell communication, morphology, contraction force, and mature protein expression. Moreover, these cells exhibit enhanced resistance to drugs and faster recovery. This transparent cell culture platform holds significant promise for biomedical research, drug discovery, and tissue engineering applications.

Background

The conductive cell culture substrates has been proven to enhance cell behavior, such as adhesion, proliferation, signaling, and maturation. Common approaches include mixing conductive particles into the substrate or depositing metal layers. Recently, a study published in IEEE MEMS [1] reported that conductive films containing silver nanowires (AgNWs) and PDMS can promote cell maturation. There are also conductive scaffolds composed of CNT and GelMA [2] that have also been shown to promote cell phenotype. However, substrates that incorporate nanoparticles often have low and uneven conductivity, and high concentrations of nanoparticles can be cytotoxic and not widely applicable, while deposited metal films are opaque.

Methodology

We propose a novel conductive platform using graphene transferred onto the SU-8 cantilever by TRT, as depicted in Fig. 1. The transferred graphene was characterized using Raman spectroscopy, AFM, and sheet resistance measurements. NRVMs were cultured on both the SU-8 and graphene platforms, with cell regions isolated by PDMS, and beating was analyzed using tracker software. Immunocytochemistry staining was used to characterize protein expression and drug testing was performed on NRVMs cultured on both the SU-8 and graphene cantilevers. The cell communication under different conditions is illustrated in Fig. 2.

Result and Discussion

The characterization of transferred graphene is presented in Fig. 3, which demonstrates that it remains structurally intact with high transparency, conductivity, and hydrophilicity. The isolation of NRVMs in different areas through PDMS is depicted in Fig. 4, where cell beating analysis confirms that graphene can facilitate intercellular communication by transmitting electrical signals. The effect of graphene on NRVM morphology and contractile force is shown in Fig. 5 through differences in cantilever displacement, and mature protein expression is demonstrated in Fig. 6. The influence of graphene on cell behavior is further illustrated in Fig. 7, which reveals that NRVMs cultured on graphene exhibit greater resistance to Verapamil, faster recovery, and more mature properties. The transparent cell culture platform consisting of SU-8 and graphene has demonstrated significant improvements in cell adhesion, electrical coupling, and maturation. The graphene-integrated platform has the potential to open up new avenues for studying cellular behavior and interactions in real-time, providing a valuable tool for biomedical research and drug discovery. The results of this study could pave the way for the development of more sophisticated and effective tissue engineering strategies and medical devices.

Word Count: 481

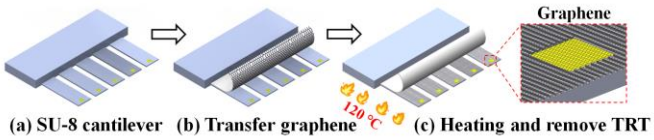

Figure 1. *Graphene transfer process using thermal release tape.*

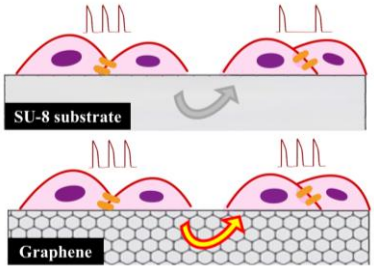

Figure 2. *Mechanism of conductive graphene substrate for cardiomyocytes communication*

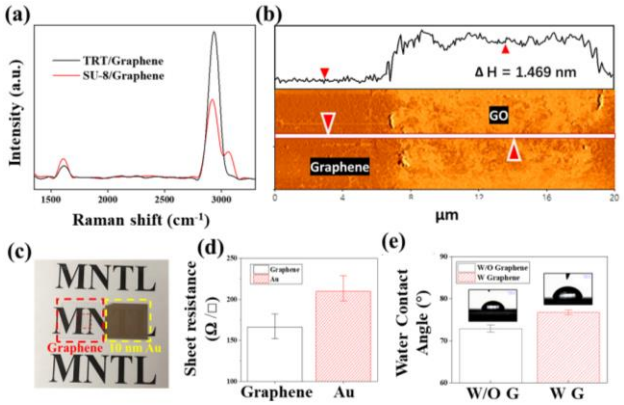

Figure 3. *Characterization of transferred graphene. (a) Raman spectra of graphene before and after transfer. (b) AFM topography of the graphene surface after laser lithography. (c) Comparison of the transparency of graphene. (d) The film resistance of the transfer graphene. (e) Water contact Angle before and after transfer.*

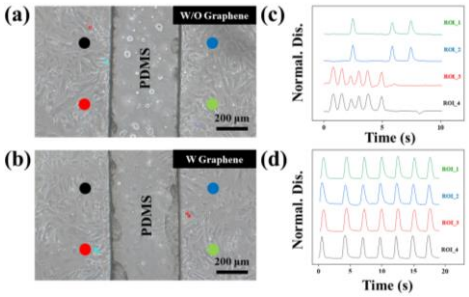

Figure 4. *Cell electrical signal propagation on culture day 12. Cell growth state without (a) and with (b) graphene. Determination of cell beating in different regions (c, d).*

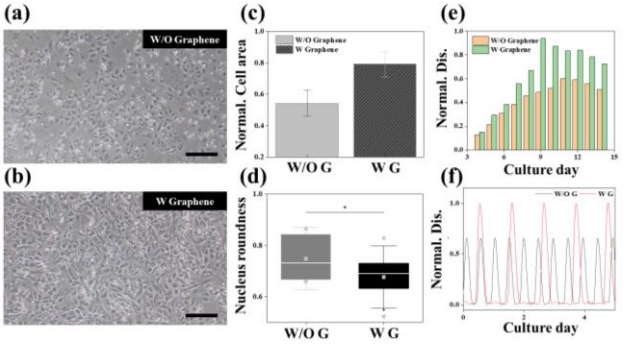

Figure 5. *Morphology of cardiomyocytes on with or without graphene. In the cell condition without (a) and with(b) graphene substrate. (c) cell area. (d) cell nucleus roundness (Circle=1). (e) displacement of the cell in the cantilever with or without graphene, and (f) comparison of the maximum displacement.*

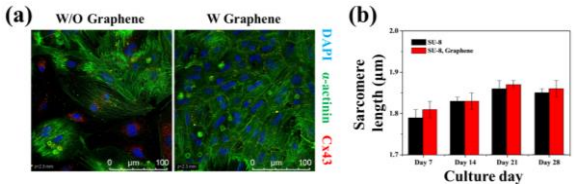

Figure 6. *Immunocytochemical (ICC) staining images with (a) or without graphene and comparison of sarcomere lengths (b) on the time axis (1 - 4 weeks).*

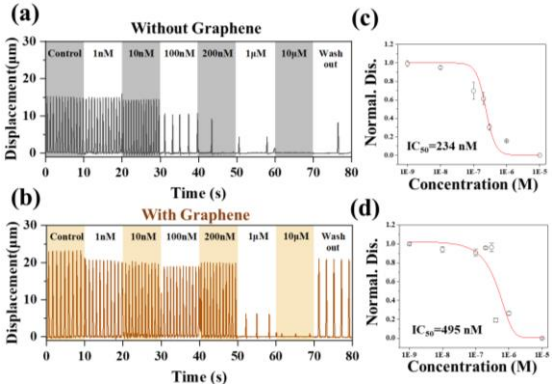

Figure 7. *Drug test by cantilever on culture day 9. Changes in the displacement in response to Verapamil with different concentration (a, b). Drug dose response curve of the cardiomyocytes cultured on the without or with graphene cantilever (c, d).*

REFERENCES

1. Liu, Yuyan, et al. "AGNW-Embedded and Nano-Patterned PDMS Thin Film for Improved Adhesion and Connection of Cardiomyocytes." *2022 IEEE 35th International Conference on MEMS Conference*. IEEE, 2022.
2. Lee, Junmin, et al. "Nanoparticle-based hybrid scaffolds for deciphering the role of multimodal cues in cardiac tissue engineering." *ACS nano* 13.11 (2019): 12525-12539.