Optogenetic Manipulation of Neurons Using Organic Light-Emitting Diodes

Kukjoo Kim, Congqi Yang**, Yong Hee Kim***, Dae Hyun Ahn*, Sukyung Choi*, Jin-Wook Shin*, Jong-Heon Yang*, Chun-Won Byun*, Sang-Don Jung***, and Seongjun Park***

*** Reality Display Research Section, Electronics and Telecommunications Research Institute, Daejeon, Republic of Korea**

**** School of Transdisciplinary Innovations, Seoul National University, Seoul, Republic of Korea**

***** CybreBrain Research Section, Electronics and Telecommunications Research Institute, Daejeon, Republic of Korea**

Abstract

We developed tandem-structured blue and yellow OLEDs optimized for optogenetics, achieving peak optical power densities of ~3.1 mW/mm² and ~3.8 mW/mm², respectively. The emission spectra were matched to the activation spectra of opsins like ChR2 and Arch, enabling effective neuronal activation and inhibition. With a custom-made 64-channel MEA, we demonstrated precise temporal correlations between OLED stimulation and neuronal responses. These results establish OLEDs as promising light sources for optogenetic applications.

Author Keywords

Organic light-emitting diodes; OLEDs; optogenetics; neuroscience; MEAs

1. Introduction

Optogenetics has revolutionized the field of neuroscience by enabling precise temporal and spatial control of neural activity using light. The technique relies on light-sensitive opsins, which respond to specific wavelengths to either excite or inhibit neuronal activity [1–3]. Traditional light sources for optogenetics, such as lasers, provide high optical power density (OPD) and wavelength specificity but come with limitations, such as bulky experimental setup. Organic light-emitting diodes (OLEDs) present a promising alternative due to their compact form factor, customizable emission spectra, and potential for integration with conventional recording electrode arrays, such as microelectrode arrays (MEAs). In this study, we developed tandem-structured blue and yellow OLEDs with tailored emission spectra and high OPD. This study evaluates the performance of these OLEDs in activating and inhibiting neuronal activity, demonstrating their potential as practical light sources for optogenetics.

2. Experimental

Blue and yellow tandem OLEDs were fabricated on glass/ITO substrates. Detailed evaluation of the materials and structures of the OLEDs were previously reported [4,5]. The OLED spectra were measured by CS-2000 spectroradiometer (Konica Minolta) and the OPD was measured by LE-5400 (Otsuka Electronics). 64-channel MEAs were fabricated based on AuPt electrodes and Al_2O_3 passivation [6]. The primary hippocampal neuronal cells were cultured on the MEA and were transfected with either AAV2-CaMKIIα-hChR2-mCherry or AAV2-CaMKIIa-eArchT3.0-eYFP. Either blue or yellow OLED was then fixed under the MEA and mounted in a custom-made stim-recording setup. We used the Intan RHS system and headstages for in-vitro recording. The spike monitoring and raster plot were performed by Intan RHX software.

3. Results and discussion

We aimed to develop and evaluate OLED-based light sources for optogenetic applications, focusing on their ability to effectively activate and inhibit neural activity through precise control of optical parameters. By leveraging the customizable emission spectra of OLEDs, we designed blue and yellow light-emitting OLEDs tailored to match the activation spectra of specific opsins.

Figure 1(a) illustrates the excitation spectra of several opsins alongside the emission spectra of blue and yellow OLEDs. Opsins are light-sensitive proteins that function as light-gated ion channels or pumps when stimulated by specific wavelengths of light. For instance, channelrhodopsin-2 (ChR2) is activated by blue light, which opens cation channels and depolarizes the neural membrane, thereby generating action potentials. Archaerhodopsin

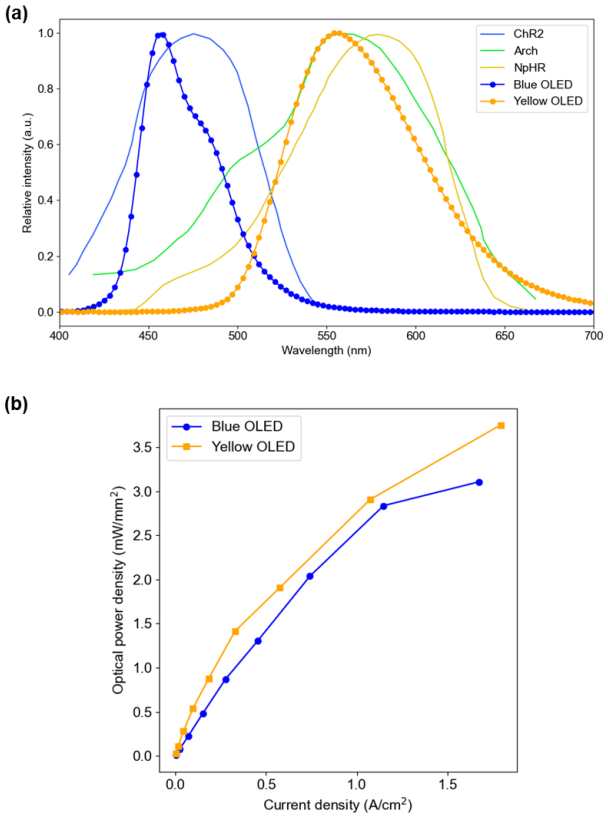

Figure 1. (a) Spectra for opsin activation and OLED emission. (b) Optical power density of blue and yellow OLEDs.

ISSN 0097-996X/25/5601-0580-$1.00 © 2025

(Arch), responsive to green-yellow light, acts as a proton pump, transferring protons from inside the neural membrane to the outside. This induces membrane hyperpolarization, suppressing the generation of action potentials. Similarly, halorhodopsin (NpHR) inhibits neuronal activity by functioning as an inward chloride pump when exposed to yellow light.

Different types of opsins respond to specific wavelengths of light, necessitating distinct light sources tailored to each opsin. To address this, we designed and fabricated blue and yellow OLEDs, with their emission spectra presented in Figure 1(a). The blue OLED exhibits a peak emission wavelength at around 460 nm, aligning well with the activation spectrum of ChR2. Similarly, the yellow OLED has a peak emission wavelength at around 560 nm, effectively overlapping with the activation spectra of Arch and NpHR. In this study, the blue OLED was used for ChR2 activation, while the yellow OLED was employed for Arch activation.

Another critical factor for the efficient activation of opsins is the OPD of the light source. While the required OPD vary across studies, it is generally considered to be above 1 mW/mm^2 for ChR2 activation and above 5 mW/mm^2 for Arch activation [7,8]. Unlike lasers, which are commonly used as light sources in optogenetics, achieving such levels of OPD with OLEDs is challenging. To achieve the highest possible OPD, we developed bottom-emitting tandem blue and yellow OLEDs. The OPD of each OLED is shown in Figure 1(b). The maximum OPD for blue and yellow OLEDs are ~3.1 mW/mm^2 and ~3.8 mW/mm^2, respectively.

The fabricated OLEDs were fixed beneath an in-house-developed 64-channel MEA and mounted onto a custom-made stimulation-recording setup, as shown in Figure 2(a). Two 32-channel stim/recording headstages (Intan Technologies) were used to record neural activities upon OLED stimulation. The inset in Figure 2(a) shows a fluorescent microscopic image of ChR2-expressing neurons cultured on the MEA. For this specific sample, 23 electrodes (marked in yellow) successfully obtained action potentials when the blue OLED stimulated the neurons. Figure 2(b) shows 20 overlaid evoked action potentials recorded by one channel demonstrating a typical shape of a spike with a very low noise level.

To verify the temporal correlation between the OLED stimulation and the measured spikes, raster plots were generated as shown in Figures 2(c) and (d). The blue OLED stimulation consisted of pulses with a width of 5 ms at a frequency of 5 Hz, delivering a total of 5 pulses per 1-second trial. The OPD of the blue OLED, in this specific case, was about 0.5 mW/mm^2. As shown in Figure 2(c), spikes occurred immediately after the OLED stimulation with a delay of approximately 3-5 ms, confirming that neurons can be effectively excited using OLEDs. The yellow OLED stimulation was conducted over a longer duration. In this case, short pulses were insufficient to observe inhibition effects, so the experiment was designed with trials where the OLED remained on for 5 s followed by 5 s off. The OPD of the yellow OLED was approximately 1.8 mW/mm^2. As shown in Figure 2(d), neuronal activity was suppressed while the OLED was on, and neurons became active again once the OLED was turned off. Some spikes were still observed during the OLED-on-state, but it is anticipated that increasing the OPD would further reduce this activity.

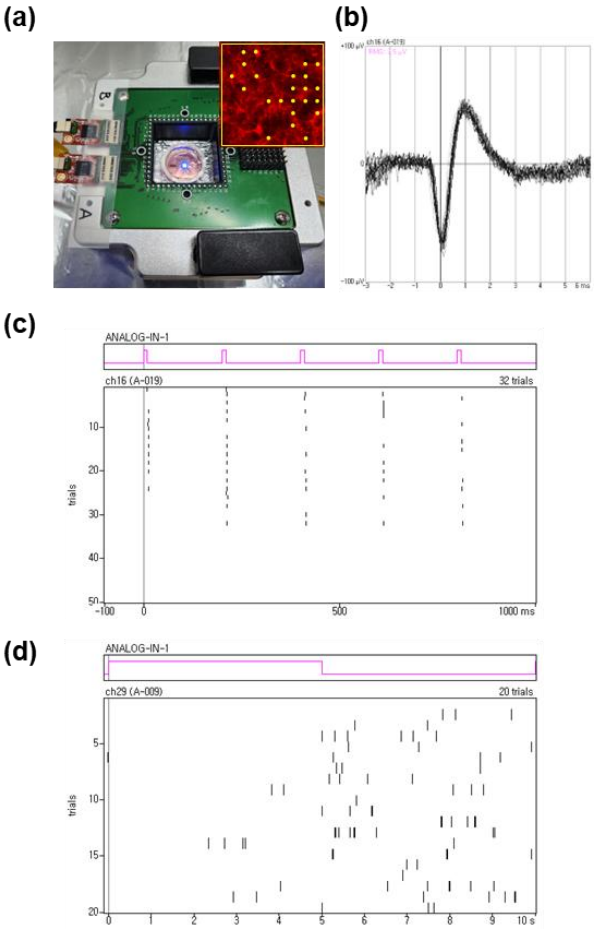

Figure 2. (a) Custom-made OLED-MEA stim-recording setup. (Inset: Fluorescent microscopic image of cultured neurons on the MEA. Yellow dots indicate electrodes that recorded action potentials.) (b) Optogenetic-evoked potentials. Twenty potentials overlapped. (c) Raster plot of ChR2-expressing neurons with the blue OLED stimulation. (d) Raster plot of Arch-expressing neurons with the yellow OLED stimulation.

4. Conclusion

We successfully developed blue and yellow tandem OLEDs tailored for optogenetic applications. The emission spectra of the OLEDs were designed to overlap with the activation spectra of specific opsins, such as ChR2 and Arch. With high OPDs for the blue and yellow OLEDs, our devices achieved sufficient intensity to activate or inhibit neural activity in vitro. Experiments with an in-house-developed 64-channel MEA confirmed the effective stimulation and inhibition of neurons using these OLEDs. The results demonstrate that OLEDs can provide an efficient and compact alternative to traditional light sources in optogenetics, paving the way for their integration into advanced neuroscience research tools and implantable devices.

5. Acknowledgements

This work was supported by Electronics and Telecommunications Research Institute (ETRI) grants funded by the Korean government [25ZC1300 and 25ZB1330].

6. References

1. Deisseroth K. Optogenetics. Nat Methods. 2011;8(1):26–9.
2. Han X. In Vivo Application of Optogenetics for Neural Circuit Analysis. ACS Chem Neurosci. 2012;3(8):577–84.
3. Rein ML, Deussing JM. The optogenetic (r)evolution. Mol Genet Genomics. 2012;287(2):95–109.
4. Park J, Lee JH, Lee J, Cho H. Effect of a P-doped hole transport and charge generation layer on single and two-tandem blue top-emitting organic light-emitting diodes. J Inf Disp. 2021;22(2):107–13.
5. Cho H, Joo CW, Choi S, Kang CM, Kim GH, Shin JW, et al. Design of white tandem organic light-emitting diodes for full-color microdisplay with high current efficiency and high color gamut. ETRI J. 2021;43(6):1093–102.
6. Kim YH, Lee J, Lim JW, Kim K, Ahn DH, Yang C, et al. In vitro recording and stimulation performance of multi-electrode arrays passivated with plasma-enhanced atomic layer-deposited metal oxides. Nanoscale. 2025, Advance Article. DOI: 10.1039/d4nr05179c.
7. Kale RP, Kouzani AZ, Walder K, Berk M, Tye SJ. Evolution of optogenetic microdevices. Neurophotonics. 2015; 2(3):031206.
8. Mattis J, Tye KM, Ferenczi EA, Ramakrishnan C, O'Shea DJ, Prakash R, et al. Principles for applying optogenetic tools derived from direct comparative analysis of microbial opsins. Nat Methods. 2012;9(2):159–72.