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UNIVERSITY OF TECHNOLOGY

PRESS RELEASE

Source: Toyohashi University of Technology, Japan, Committee for Public Relations

Release Title: Illuminating the brain with an ultra-thin, flexible, multipoint microLED array film

Release Subtitle: Development of a new optogenetic device that enables simultaneous optical stimulation at specific/multiple regions in the brain

Overview

Researchers including Associate Professor Hiroto Sekiguchi in the Department of Electrical and Electronic Information Engineering at Toyohashi University of Technology, Associate Professor Noriaki Ohkawa in the Comprehensive Research Facilities for Advanced Medical Science at Dokkyo Medical University, and Assistant Professor Izumi Fukunaga in the Sensory and Behavioural Neuroscience Unit at Okinawa Institute of Science and Technology Graduate University, have developed a flexible, multipoint microLED array film. The film can be flexibly attached to cover the brain and can illuminate specific regions of it as microLEDs are arranged along multiple points of it.

In recent years, optogenetics[Note 1] has enabled the manipulation of neural activity by light. While this technique requires a light-emitting device, there were no optical devices that could be attached to cover entire tissues such as the brain, and with the light only influencing target neurons, or could be implanted in an organism so that the activity would be freely manipulated by light.

To implement this device, a thin, lightweight, and flexible body is required. It was thus necessary to establish a technology to arrange an LED layer a couple of micrometers thick highly precisely on an ultra-thin film that is not harmful or toxic to living tissue. The research group this time has established both (1) a technology to form a hollow structure of microLEDs with high density and in minute detail, and (2) a high-precision batch transfer technology using a thermal release sheet. With these technologies, it has also successfully developed an ultra-thin, lightweight multipoint microLED array film that maintains lighting performance even when the film is bent. The application of the developed device is expected to create a new area of neuroscience research aimed at comprehensively understanding the brain information that underpins how neural activity, behaviors, and disorders are linked.

Details

At present, attempts are being made to use light to manipulate the activity of various functional molecules inside an organism. In particular, optogenetics - a technique to activate neural activity with light by expressing photosensitive proteins that react to a specific color of light in neurons - has a high temporal resolution and has been utilized to elucidate brain function. However, to comprehensively elucidate the complex neural network created by neurons in the brain, it is necessary to employ light stimulation that will enable free manipulation of certain regions of neurons distributed across a wide range of the brain. The application of conventional optical fibers and microscopes is not sufficient to illuminate certain or multiple regions at the same time and also restricts the free movement of animals. Although this meant high hopes for the application of an implantable LED device, the size of commercial LEDs is as large as 200 µm with thickness of tens to one hundred micrometers, so that it cannot cover a wide range of the brain. As such, it was regarded as unsuitable as a device to stimulate specific neurons in the regions.

Given this, the research group sought to utilize a flexible film that is thin, lightweight, and bendable, and took the challenge of fabricating microscopic and ultra-thin microLEDs less than 100µm in size and a couple of micrometers in thickness and arranging them on multiple points. To achieve this, the group adopted the anisotropic wet etching method[Note 2] using potassium hydroxide to selectively remove the bottom LED layer, which led to the formation of a hollow structure of microLEDs that are arranged at high density. As the hollow structure separates the LED layer from the substrate, only the LED layer can be removed at one time using a thermal release sheet with no damage to either microLEDs or biocompatible Parylene films[Note 3]. By applying this technique, the group has successfully fabricated a microLED array on the film. This microLED-mounted film maintains the lighting performance even when being bent. It has also been verified that bright blue light can be obtained and used in actual optogenetic experiments with the film adhered to the surface of a mouse's brain.

Future Outlook

The multipoint microLED film developed through this study has potential broader application with the brain and will realize the control of complex brain activity freely in the spatiotemporal aspects. The brain has diverse functionalities in various regions and serves to manipulate the whole body in a complex way. By combining measuring technology in the future, the application of this technology is expected to create a new area of neuroscience research aimed at comprehensively understanding the brain information that underpins how neural activities, behaviors, and disorders are linked. Further, with the development of photosensitive functional molecules inside an organism, it is expected that it will be possible to illuminate light onto areas where medicine is targeted and make the medicine effective in any time, which will lead to the application of the phototherapy technology using devices implanted in organisms.

The results of this research will be published online at Applied Physics Express on March 18, 2022 (8am GMT). In addition, this work was supported by the Precursory Research for Embryonic Science and Technology Agency (JPMJPR1885) of the Strategic Basic Research Programs in Japan Science and Technology Agency (JST), under the project title "Innovation of invasive LED devices for biological optical stimulation" in the research area " Development of optical control technologies and elucidation of biological mechanisms."

Reference

Hiroto Sekiguchi, Hayate Matsuhira, Ryota Kanda, Shuto Tada, Taiki Kitade, Masataka Tsutsumi, Atsushi Nishikawa, Alexander Loesing, Izumi Fukunaga, Susumu Setogawa, Noriaki Ohkawa (2022). Adhesionable flexible GaN-based microLED array film to brain surface for in vivo optogenetic stimulation, Applied Physics Express.
https://doi.org/10.35848/1882-0786/ac5ba3

Glossary

Note 1: Optogenetics

Optogenetics is a technique to manipulate the activity of target neurons with light. This is achieved by gene transfer technology with which the illumination of light with specific wavelengths can express proteins that changes their activity. Channelrhodopsin-2, known as a typical protein, can introduce sodium ions into cells during neural activity when applying blue light and can artificially induce the activity of target neurons.

Note 2: Anisotropic wet etching

Anisotropic wet etching is a technique to selectively dissolve certain crystal orientations of semiconductors using chemicals. In this project, potassium hydroxide was used to selectively remove a certain crystal orientation of Si substrates.

Note 3: Parylene film

Parylene is the generic term for paraxylene-based polymers and is known as biocompatible material. The ultra-thin film can be formed by vapor deposition. It is applied as a coating material for biomedical devices such as pacemakers.

Further information

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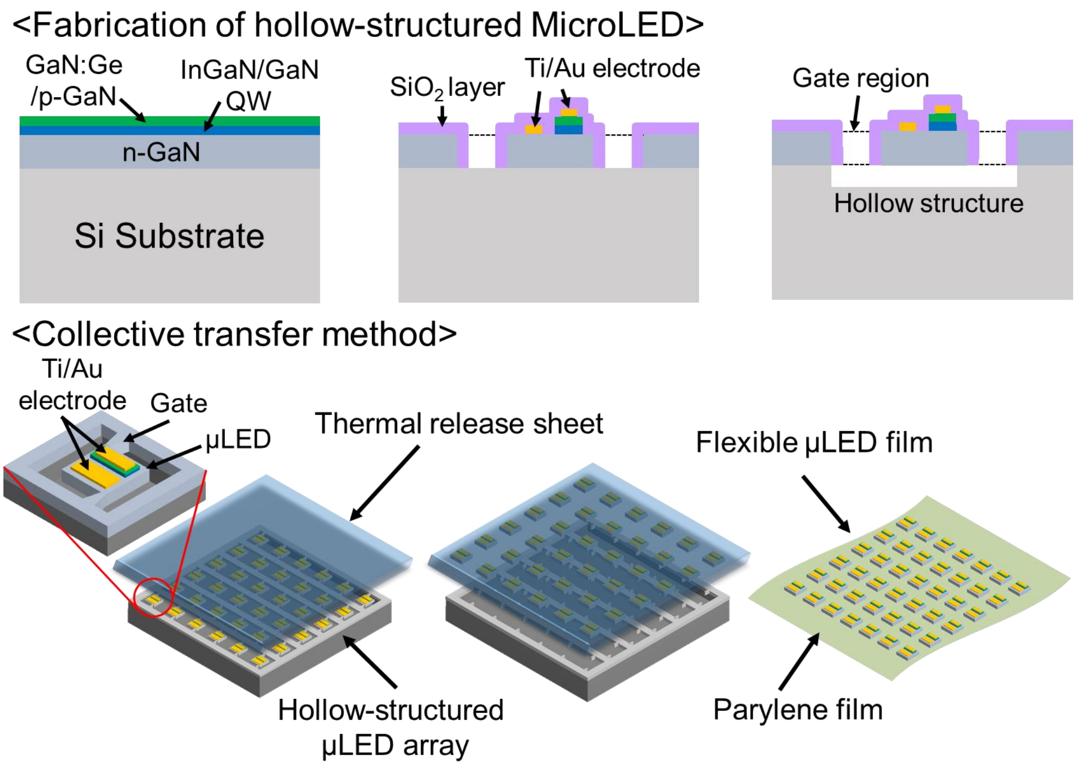
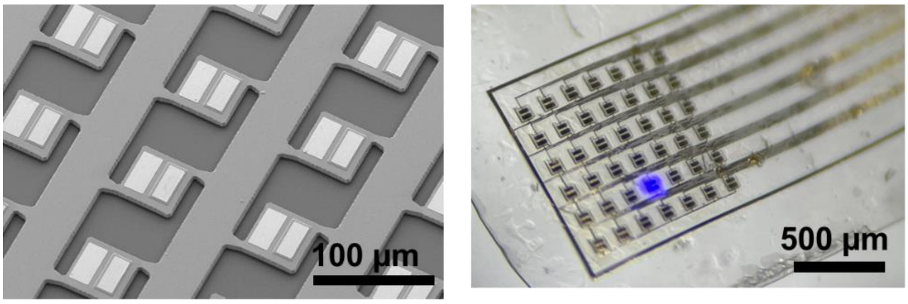
Figure1:



Title: Technology to fabricate a flexible microLED film

Caption: Technology to form a hollow structure of microLED (Upper) MicroLED array batch transfer technology (Lower)

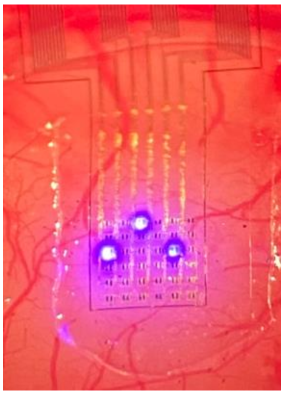
Figure2:



Title: Photo of the developed microLED array

Caption: Hollow structure of a microLED array (Left)　Lighting image of an ultra-thin microLED array film (Right)

Figure3:



Title: Ultra-thin microLED array film adhered to the mouse's brain

Caption: Lighting LEDs targeting three points

Keywords: Optogenetics, Neurons, Medical technology, Optical devices, Brain tissue