IMPLANTABLE DEVICES

Omnidirectional optogenetic stimulation

A wireless, low-power optoelectronic platform, which is based on micro-LEDs, can provide multimodal programmable control over optogenetic stimulation parameters.

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Optogenetics is a powerful tool for perturbing populations of specific cell types[1,2]. Here, individual cell types of the central and peripheral nervous systems are tagged with light-sensitive opsins. Specific wavelengths of light can then be used to turn the cells off and on, allowing complex neural circuitry to be dissected. For example, blue light can be used to activate neurons and green light can be used to deactivate neurons depending on the expression of either channelrhodopsin-2 (ChR) or halorhodopsins (Halo), respectively (Fig. 1a). The technique has been important in elucidating new neural pathways in many preclinical models of disease (including those related to memory, depression, sleep, anxiety, and restoration of vision) and could lead to potential new disease targets.

Light delivery in optogenetics is usually achieved using implantable optical fibres connected to light sources such as lasers or light-emitting diodes (LEDs). However, implantable wireless micro-LEDs (or μLEDs) could offer a more elegant alternative. In particular, μLEDs have small form factors, which means they are easier than conventional optical fibres to implant in fragile areas of the body, such as around nerves or muscles. Furthermore, the wireless configuration means an animal can be studied without the use of tethers[3], allowing unrestricted movement and a more natural behavioural setup to be created. This is the ideal case in long-term implantation studies, which require stimulation of cells over weeks or months in order to understand disease and normal models.

The μLEDs require wireless power harvesting in order to operate and the delivery of power is angle dependent (Fig. 1b), which means that the components for transmitting and receiving power need to be carefully position (for example, directly above the animal's head). Moreover, controlling multiple μLEDs at once through a wireless method is difficult, as modulating abilities are required and need to be incorporated into challenging integrated circuit designs.

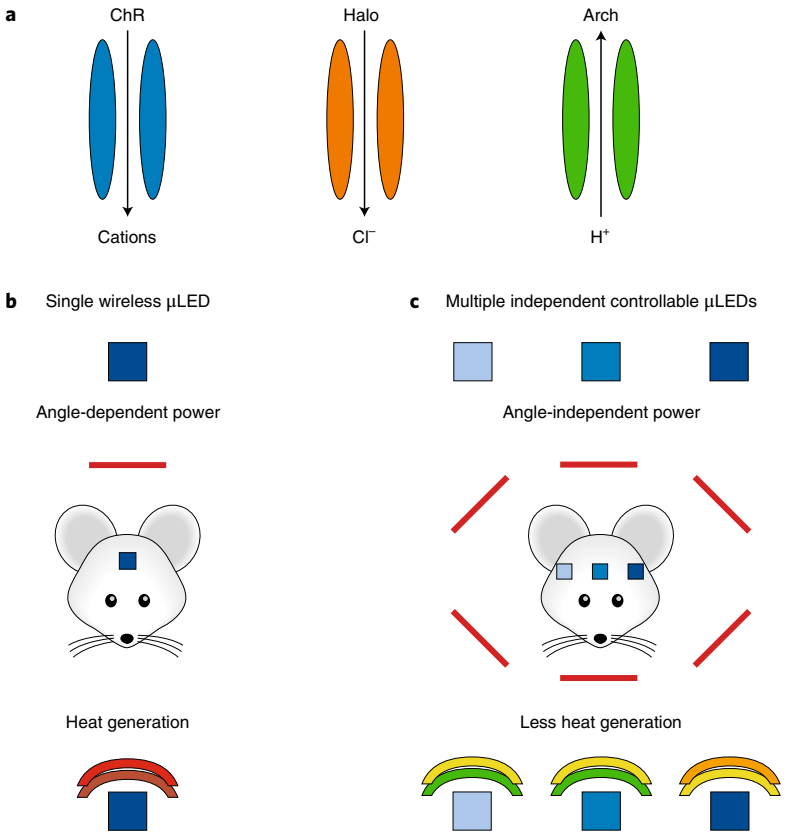

Fig. 1 | Optogenetics based on μLEDs. a, Basics of optogenetics, which uses light to control cells. Blue light causes activation of neurons expressing channelrhodopsin-2 (ChR). Yellow or green light can be used to deactivate neurons expressing either halorhodopsin (Halo) or archaerhodopsin (Arch). **b**, Classical approaches use implanted μLEDs that are typically low in number and inefficient, which causes heat build-up. Furthermore, the wireless power harvesting the devices require is angle dependent. **c**, The approach of Rogers and colleagues[4] allows multiple, efficient μLEDs to be implanted that also offer angle-independent power harvesting. This creates a more natural behavioural setup in which an animal is free to move.

Writing in *Nature Electronics*, John Rogers and colleagues now demonstrate an angle- and position-independent method of controlling μLEDs[4]. Their approach can also be used to control individual and groups of μLEDs, capabilities that could potentially be used to control multiple brain regions or areas that have expressed opsins.

When in operation, μLEDs and LEDs can cause heating that can potentially damage biological tissue, especially if they are implanted in great numbers in confined brain regions[5]. The researchers — who are based at Northwestern University, RMIT University, the University of Central Florida, the University of Illinois at Urbana-Champaign, and Southeast University in Nanjing — address this issue by employing μLEDs with high efficiencies and show, through extensive finite-element modelling

and measurements in air, that temperature rises to surrounding tissue would not cause damage (Fig. 1c). This is the case even when multiple μLEDs are powered at the same time at the irradiances required to drive optogenetic-induced neural activity.

The use of such technology in optogenetics can be a powerful approach to understanding — and manipulating — the neural circuitry related to disease. One example is bioelectronic medicine, in which disease symptoms are alleviated through peripheral nerve neuromodulation. Light delivery access to peripheral nerves is often complicated due to the physical location of the nerves, as well as other surgical factors that do not easily permit the implantation of ferrules, or end terminals, associated with optical fibres. The devices developed by Rogers and colleagues could avoid these issues. The devices could also allow the entire nervous system to be probed simultaneously and with the precise millisecond control that is available through established optogenetic techniques. This could open the door to a range of interesting experimental approaches for the neurological and biological science communities. ❐

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