

"High-Density µLED Optoelectrodes for Local Circuit Mapping" – Webinar Q&A

1. How many LEDs can we have on a shank?

a. Current version we are disseminating has 12 LEDs, 3 on each shank. For the next version we are planning to make a decision among several configurations, but definitely more than 32 microLEDs per probe. We have not determined the final number yet. We should be able to accommodate 128 individually controlled microLEDs.

2. Is it possible to be implanted in the spinal cord? In rats or mice.

a. Some users are using a flexible probe for spinal implantation but remember the microLED probes are silicon probes. Some users, that I have talked to, use silicon probes for accessing and implanting the spinal cord. In this case, simply they can replace those probes with our microLED probe. They may be in almost identical configuration or probably in the same shank dimensions, but with LEDs allowing for optical stimulation.

3. What is the approximate volume of tissue illuminated by a single LED?

a. The LED has a diverging Lambertian profile with an angle, and we have succeeded in optical stimulation of neurons within tens and hundreds of microns from a single LED. However, this probe is not meant to illuminate a large portion of the brain; it is for local stimulation, possibly modulating at single neuron resolution.

4. Do you plan on other wavelengths than blue, for example yellow?

a. Our next research goal is making color LEDs/stimulation. We are currently providing blue only. It is unlikely to provide other wavelengths, such as yellow/red in the next year, but it is coming.

5. Are there plans to use these probes in humans?

a. Not really, because of longevity. In humans you need a really long longevity. We have some interest from non-human primate scientists, but not targeting humans yet.

6. What is the headstage configuration/hardware requirements to test the uLED probes?

a. Current headstage is using two Omnetics connectors: 32 recording sites accessed through the 36 channel Omnetics connector and 12 LEDs accessed through the 18 channel Omnetics connector. For recording you can use any recording systems, including Intan, Plexon, TDT, etc., which are compatible. For stimulation you can use your own stimulation instrument, even a simple function generator. Be careful not to damage the LED. Also, the MINT hub provides the microLED controller as an open source available at Github. Either, you can make it for yourself, or get it from the MINT hub at manufacturing cost.

Additional Information

Plexon has its own stimulating headstages, which is compatible with the uLED probes. Also, Plexon will soon have available its own uLED Probe Control Box, which will allow for precise control of the uLED probes. This system, which includes hardware and software, will have digital input and output functionality, a GUI for creating patterns of stimulation, and allow for precise control of the LEDs.



7. Will the LED power decrease during recording?

a. We have a longevity testing of the LEDs; the power reduced a little bit but not significantly. Probably fine for in vivo study, as there are a lot of biological variables that would impact stimulation more than the probe technical side. The reduction of the optical power is about less than 10%, pretty minor.

8. Why did you select a 60 um interelectrode distance between the LEDs? And how did you choose the LED power?

a. This came from Eran Stark and Buszaki when we initially developed the microLED probe. The opsin resolution in neuroscience studies was also a deciding factor. We can make it smaller, but this is a reasonable size for our current probe configuration. Let us know if you need anything smaller than that, but I believe the opsin spatial resolution is not there yet.

9. What is the power range of the LED light? Can they adjust independently?

a. Power range can be independently adjusted by either voltage or current applied to each LED. We recommend current control as it can safely and precisely control the optical power. You can adjust the current from 0-100 micro-Amps, and the LED power is dependent on this.

Additional Information

Plexon encourages the validation of optogenetic stimulation as it exits the system prior to entering the tissue. Plexon offers the <u>PlexBright Light Measurement Kit</u> which includes a power meter and an integrating sphere photodetector.

10. How do you verify that the neuronal activity is due to optical stimulation and not due to the current flowing through the probe?

a. We had wild animal experiments. We had an animal that was expressing channelrhosdopsin (the target of the experiment) and the other a wild animal, no opsins expressed. We didn't see any current-induced or heat-induced stimulation from the wild animal. Only the animal expressing the opsins is responding to optical stimulation. This indicates that the electrical signal is not inducing neural activities. We also made sure that the increase in temperature of the brain is less than one degree.

11. Can the probe be cleaned and reused?

a. Yes, but it is depending on your skillset. Even chronic probes can be explanted and reimplanted and works, not always, not 100%. But it is doable depending on implant area, surgery, how you fix the probe after surgery, and how you explant them. It is doable but no promises or guarantees. For acute probes, you can definitely reuse multiple times, more than a few.

12. What is the stability like for acute recording?

a. We have pretty good recording stability. During surgery we record, and it is not much different from other silicone probes in terms of recording capability. It depends on surgery skills and the region of the brain that you are targeting.

13. What is the size of the artifact free probe and is it thicker than the standard probe?

a. Not really, it is a little thicker but not more than a couple of microns. I do not think the thickness increase is phenomenal, you can assume it is the same.



14. Are the specifications for these probes customizable? Can I get shanks of a certain length?

a. Yes and no. It requires a lot of development and engineering work to customize the probes. We are currently getting feedback from users to find out which configurations are mostly needed and what are the demands. If you really want to have a specific configuration, you can talk to us and we will try to accommodate it.

Additional Information

Two commonly requested probe configurations are available today from Plexon.

- 15. Is it technologically more challenging to design the microLEDs in another color? If yes, why? I thought that blue LEDs were the most difficult to design.
 - a. Yes, there are technical challenges. Blue is currently more favorable than other colors, with the current technology we can access. We are integrating a quantum well for the microLED on top of the silicone, so that we can machine the silicone to make the shank structure. However, if you are moving onto a different color, you have to integrate a different quantum well, and the quantum efficiency is compromised in longer wavelengths. We are still looking into options of integrating different colors at high efficiency. Theoretically doable but practically it is challenging.

16. Is there currently a method for measuring the power output from each LED?

a. Yes, we have a setup to accurately collect all the light and measure the optical power accurately.

17. Is there an off the shelf solution for precise control of the LEDs on the probes?

a. Yes, you can use a function generator or some other manufacturer's stimulation systems. Intan stimulator works, and also some others, maybe Plexon.

Additional Information

Plexon will soon have available its own uLED Probe Control Box, which will allow for precise control of the uLED probes. This system, which includes hardware and software, will have digital input and output functionality, a GUI for creating patterns of stimulation, and allow for precise control of the LEDs.

18. Where can I buy these probes?

 a. Currently the microLED probes are being disseminated by the NSF NeuroNex Michigan hub (MINT); but they are also translated for commercial availability. You can buy from Plexon currently.