

New method captures neural and vascular dynamics at high spatiotemporal resolution deep in brain

August 11 2020, by Li Yuan

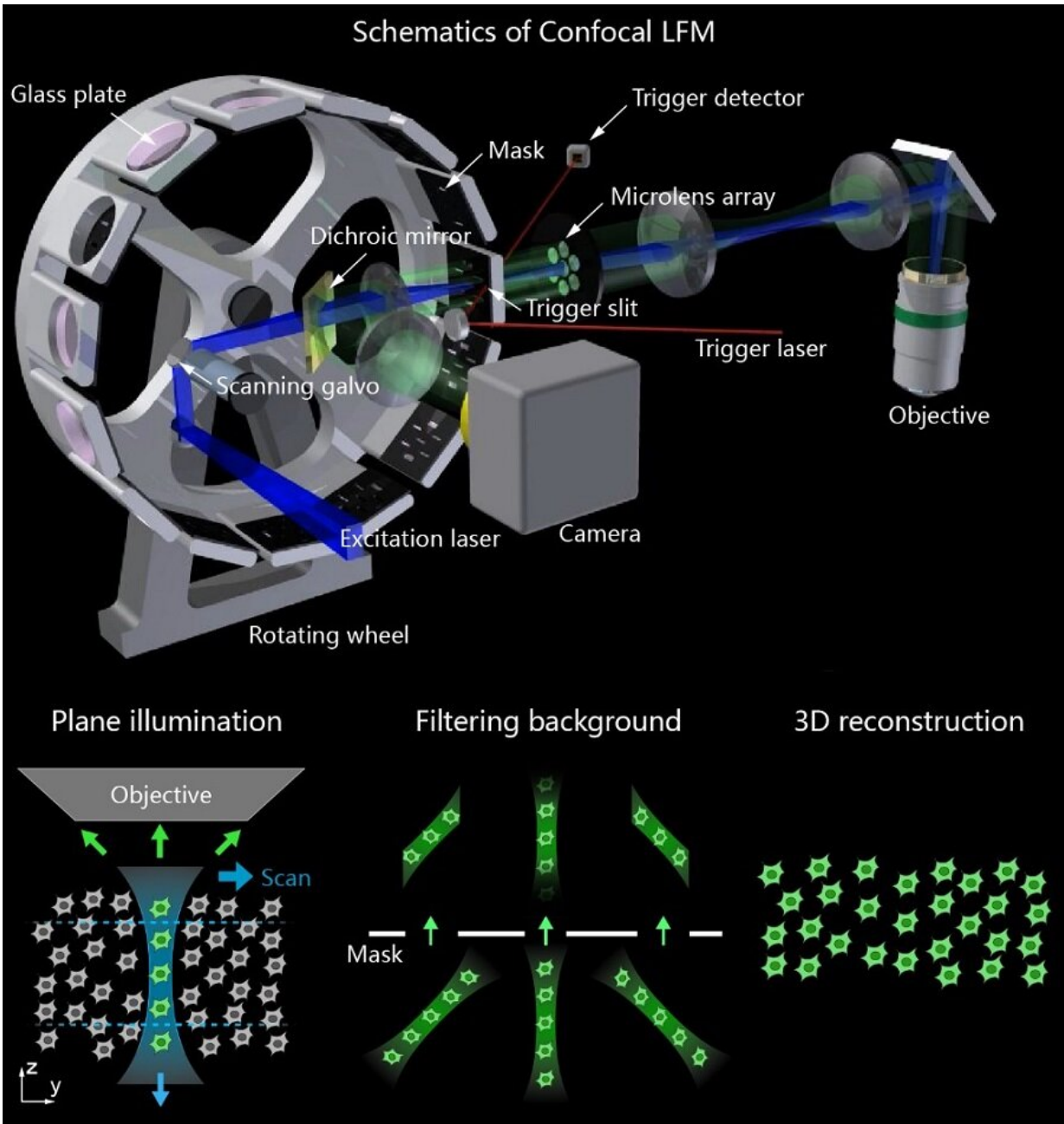


Fig. 1 Schematics of Confocal LFM. (Upper) Overview of the optical system. (Lower) Vertical light sheet scans in the sample plane and images formed by micro-lens array are spatially filtered by the mask to get in-focus volume after 3D reconstruction. Credit: CEBSIT

A joint research team led by Dr. Wang Kai and Dr. Du Jiulin from the Institute of Neuroscience, Center for Excellence in Brain Science and Intelligence Technology of the Chinese Academy of Sciences reported a novel volumetric imaging method—confocal light field microscopy (Confocal LFM)—to image fast neural and vascular dynamics at high speed, deep in the brain.

The study was published in *Nature Biotechnology* on August 10.

Traditional tools developed for in-vivo imaging in the [brain](#), such as [confocal microscopy](#) and two-photon scanning microscopy, are based on point scanning scheme and are too slow to study rapid volumetric dynamics.

Light field microscopy (LFM) has attracted attention due to its instantaneous volumetric imaging capability, which captures the information from the whole 3-D volume all together on the [image sensor](#) in a single camera exposure.

Conventional LFM has been previously introduced to image brains. However, the technology has two major problems: reconstruction artifacts and lack of optical sectioning capability, preventing them from wide application.

In 2017, Wang's group developed a new type of LFM, XLFM, to address the first problem. However, the second one remained unsolved.

Introducing optical sectioning capability in LFM is of key importance because it prevents out-of-focusing background from interfering with in-focusing signal and plays a vital role for thick tissue imaging.

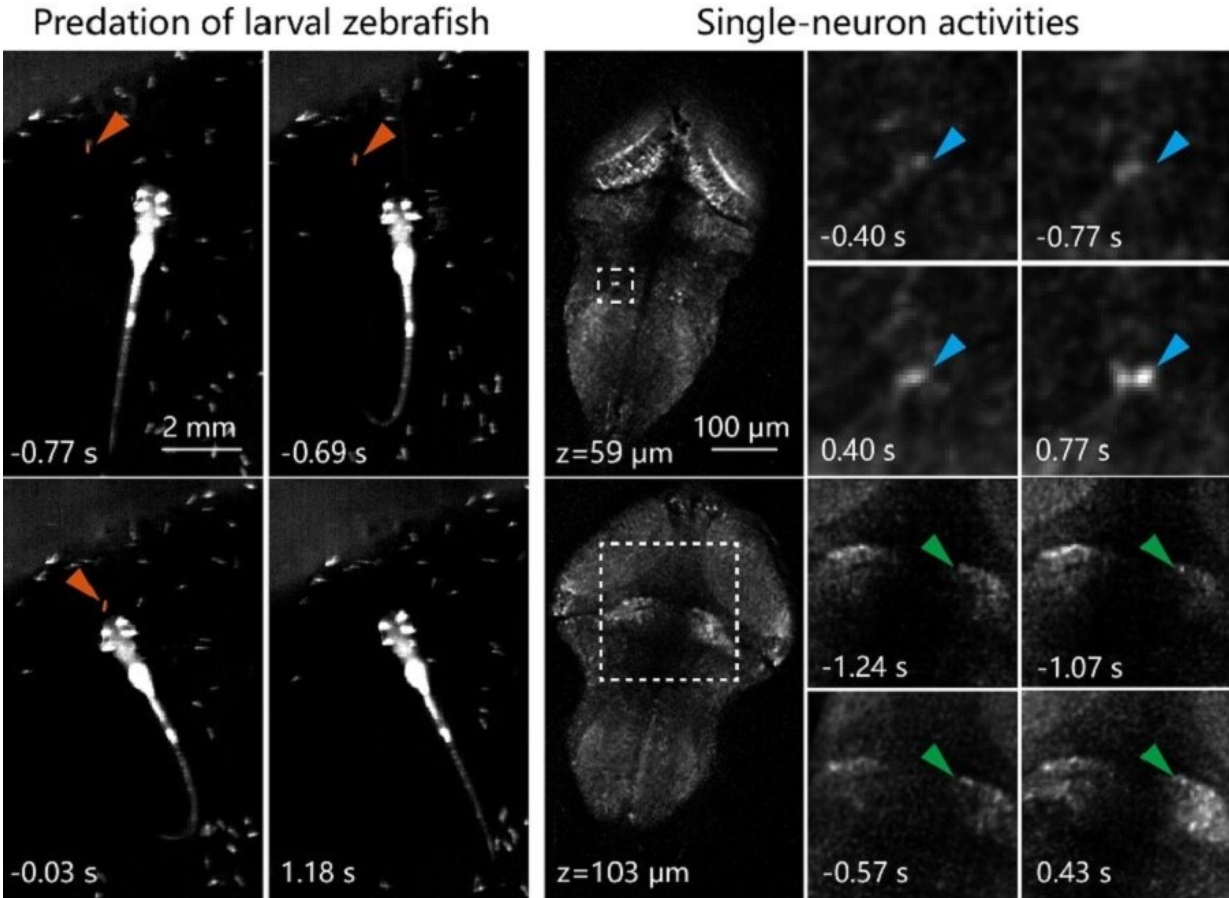


Fig. 2 (Left) An example of larval zebrafish's prey capture. Time was aligned to prey ingestion (0s). (Right) Zoomed-in views of single-neuron activities in several brain regions during prey capture in left. Credit: CEBSIT

Directly adopting the concept of confocal detection that confers 3-D imaging capability seems to be straightforward. However, it turned out to be impossible due to the very distinct instantaneous volumetric imaging manner of LFM from conventional plane-by-plane imaging scheme.

To meet this challenge, Wang's lab came up with a novel idea to generalize the concept of confocal detection and made it compatible

with LFM without compromising its imaging speed, which was called Confocal LFM.

Without interfering background noise, confocal LFM significantly improved imaging resolution and calcium signal detection sensitivity in functional imaging of neuronal activities over the whole zebrafish brain.

It was also integrated with a fast 3-D tracking system to capture correlated behavioral neural activations in freely swimming larval zebrafish. For example, single-neuron activities during larval zebrafish's prey capture could be reliably recorded.

The researchers further applied confocal LFM on imaging calcium transients and circulating [blood cells](#) in awake mouse brain. Its highly parallelized and light-efficient imaging enabled continuous recording for more than 100,000 volumes without significant photobleaching.

They also showed imaging of populations of circulating blood cells in a complicated 3-D vascular network. The results showed that it was possible to track and quantify the flow dynamics of blood cells accurately and represented more than 100 times increase in throughput compared to conventional imaging techniques.

The flexibility, increased resolution and sensitivity of confocal LFM demonstrated in this work make it promising for wide applications in capturing and studying extremely fast volumetric dynamics deep in the brain, or within other types of thick tissues in general.

More information: Zhenkun Zhang et al. Imaging volumetric dynamics at high speed in mouse and zebrafish brain with confocal light field microscopy, *Nature Biotechnology* (2020). [DOI: 10.1038/s41587-020-0628-7](https://doi.org/10.1038/s41587-020-0628-7)

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