

# MICROSCOPY

## Tech Pulse



March 2019

Microscopy Tech Pulse is a special edition newsletter from Photonics Media and Mad City Labs Inc. covering key developments in microscopy technology. Manage your Photonics Media membership at [Photonics.com/subscribe](http://Photonics.com/subscribe).

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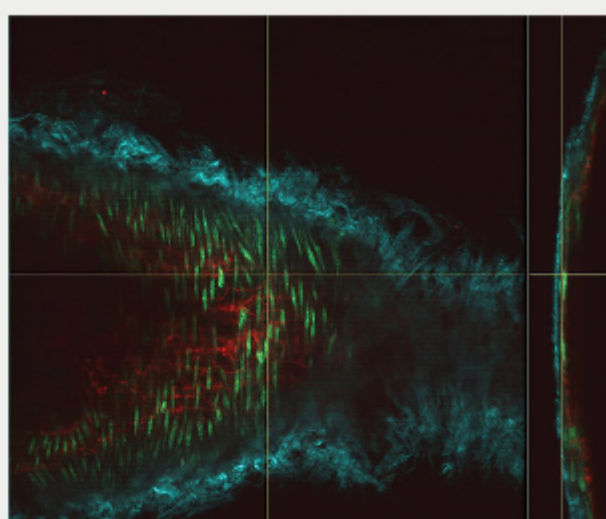


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### Lasers: A Unique Microscopy Source


Although filtered lamps and LEDs have their uses as simple light sources in wide-field microscopy, the laser is at the heart of most of the advanced techniques and experiments involving fluorescence excitation. The latest developments in lasers for microscopy are delivering a powerful combination of improved functionality and operational simplicity.




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### Mad City Labs Inc. Fluorescence Microscopy Technique Provides New Views of Biological Processes

Introduction to the technique of MicroMirror TIRF (total internal reflection fluorescence) microscopy. The MicroMirror TIRF microscopy technique offers significant signal-to-noise ratio improvements compared to dichroic based TIRF microscopy when using multiple wavelength light sources. Short overview of the types of biological processes that can be studied via this method. Mad City Labs is the only commercial provider of a MicroMirror TIRF microscope.



### Fluorescence Microscopy Technique Provides New Views Of Biological Processes



**MicroMirror TIRF Microscopy: Technique and Application**

Fluorescence microscopy has long been a powerful tool in biological research. A team known as total internal reflection fluorescence (TIRF) microscopy has more recently been used to watch biological processes unfold in real time. By taking advantage of the ability to label individual molecules with different colors of fluorescent tags, TIRF microscopy now allows scientists a view into the complex molecular assemblies that govern cellular processes. But TIRF microscopy can be limited by its signal-to-noise ratio. As scientists seek to understand ever more complex processes, they have to label more components with more colors, and this signal-to-noise problem worsens. Fortunately, a newer version of TIRF microscopy that relies on micro-mirrors allows researchers to view their samples with unprecedented clarity, opening up new vistas in biological research.

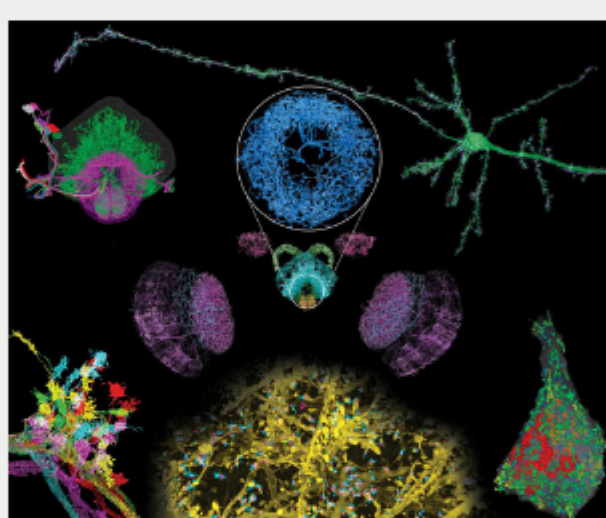
**Viewing Molecular Assembly**  
 Almost all biological processes — DNA replication, RNA splicing, the opening and closing of ion channels that conduct neuronal signaling — are governed by so-called molecular machines. These machines are transient assemblies of molecular complexes often made up of many components, which come together, perform a task, and then break apart. How are these assemblies and disassemblies ordered and regulated? What happens when these processes go awry? Since these questions are central to an understanding of both normal and pathological cellular processes, scientists are hard at work seeking answers to them.

One way they do this is through a method known as total internal reflection fluorescence microscopy (TIRF-MFM). Imagine a particular molecular machine made up of four molecules — A, B, C, and D — and each can be labeled with a uniquely colored fluorescent tag. Researchers can anchor molecule A to a microscope slide and wait for the other molecules to join up with it — to assemble. In other words, there are many ways the molecular machine could assemble. For instance, perhaps C and D have to bind together before they can bind to A, and only after all three are together does B join in. By watching the order in which the various components come together and seeing

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### Two Microscopy Techniques Combine for Nanoscale Brain-Wide Optical Imaging

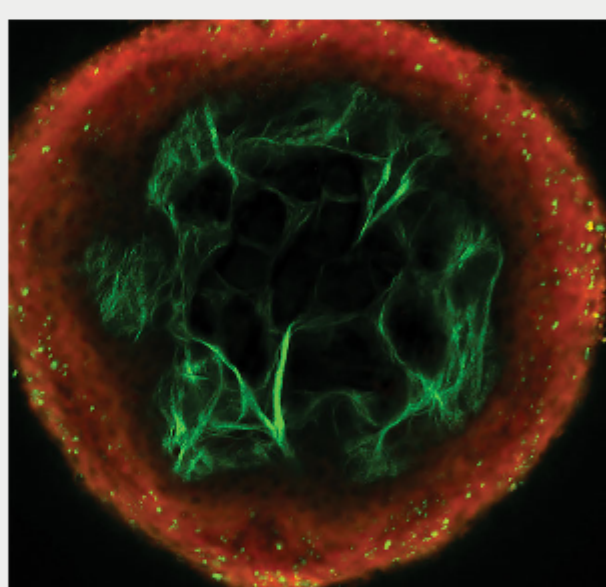
Scientists from the Eric Betzig lab at Howard Hughes Medical Institute's Janelia Campus and the Ed Boyden Lab at MIT collaborated to develop an imaging technique that combines expansion microscopy with lattice light-sheet microscopy for nanoscale imaging of fly and mouse neuronal circuits at the molecular level.



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### SHG Microscopy Brings Live Cells into 3D Focus

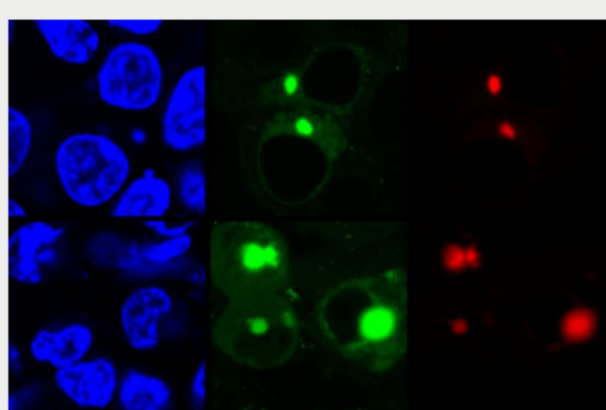
Second-harmonic generation (SHG) microscopy highlights biomolecules that follow a specific structural organization within biological tissues, and complements two-photon excited fluorescence (TPEF) microscopy, as both imaging modalities can operate simultaneously on the same laser scanning microscope.



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### New Fluorogenic Method Can Simultaneously Detect Aggregation of Two Proteins in Live Cells

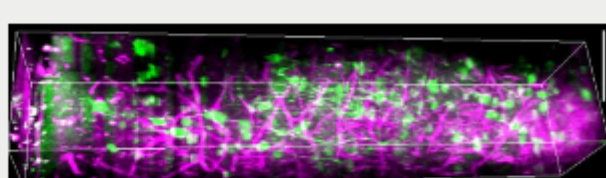
Researchers re-engineered a fluorescent compound and developed a method by which two different proteins can fluoresce at the same time as they misfold and aggregate inside a living cell, highlighting forms that could play a role in several neurodegenerative diseases.



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### Three-Photon Microscope Reveals All Cortical Layers of Awake Mouse Brain

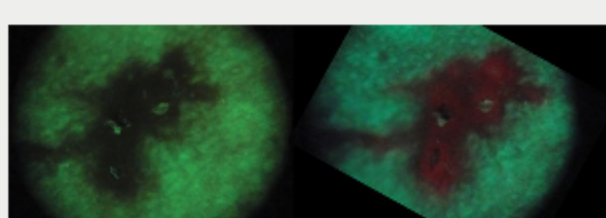
A new three-photon microscope can deliver rapid, short, low-power light pulses capable of reaching deep targets within the brain without causing functional disturbance or physical damage. It can then detect the resulting fluorescence emitted by cells with high efficiency and produce images with sharp resolution and a fast frame rate.



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### PDT, Customized Protocols Team Up for Enhanced Clinical Translation

Photodynamic therapy (PDT) is a robust treatment procedure that can be designated to treat some types of cancer, as well as infectious diseases and other tissue disorders. It involves the use of a photosensitizer — a chemical compound that is activated by light — which results in the production of reactive species (mainly singlet oxygen) and further induction of cell death.



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