Microscopy TODAY

Coming Events

Due to COVID-19, please check to see if the listed events have been postponed or cancelled.

2021

RMS Event: International Microscopy Focus Lecture Series
"A brief history of the impact of Transmission Electron Microscopy on Materials Science"
Professor Sir Peter Hirsch
October 5, 2021
Virtual
www.rms.org.uk/rms-event-calendar/2021-events/imfls-professor-sir-peter-hirsch.html

RMS Event: Imaging ONEWORLD
"Finding the needle in the haystack with 3D correlative light and electron microscopy"
Dr. Lucy Collinson
October 11, 2021
Virtual
www.rms.org.uk/rms-event-calendar/2021-events/imaging-oneworld-finding-the-needle.html

flowcytometryUK 2021 (formerly One Day flowcytometryUK)
November 17–18, 2021
Virtual
www.rms.org.uk/rms-event-calendar/2021-events/flowcytometryuk-2021.html

2021 Gordon Research Conference on Three-Dimensional Electron Microscopy
October 31–November 5, 2021
Waterville Valley, NH
www.grc.org/three-dimensional-electron-microscopy-conference/2021

Neuroscience 2021 (Hybrid)
November 8–11, 2021 (virtual)
November 13–16, 2021 (in person)
Chicago, IL and Virtual
http://www.sfn.org/meetings/neuroscience-2021

2021 MRS Fall Meeting & Exhibit (Hybrid)
November 29–December 2, 2021 (in person)
December 6–8, 2021 (virtual)
Boston, MA and Virtual
www.mrs.org/fall2021

Cell Bio Virtual 2021
December 1–10, 2021
Virtual
https://www.ascb.org/cellbio2021

2022

Microscopy & Microanalysis 2022
July 31–August 4, 2022
Portland, OR
www.microscopy.org/events/future.cfm

2023

Microscopy & Microanalysis 2023
July 24–28, 2023
Minneapolis, MN
www.microscopy.org/events/future.cfm

2024

Microscopy & Microanalysis 2024
July 28–August 1, 2024
Cleveland, OH
www.microscopy.org/events/future.cfm

Carmichael's Concise Review

Window to the Brain Allows Observation of Cellular Neural Activity

Stephen W. Carmichael
Mayo Clinic, Rochester, MN 55905

carmichael.stephen@mayo.edu

Calcium indicators that are genetically encoded, along with transgenic approaches to broadly express these indicators in the mammalian brain in a cell type-specific fashion, have enabled simultaneous imaging of multiple cortical regions. Studies have revealed how neural activity across several regions are coordinated in a variety of brain states and behaviors. For numerous technical reasons these studies have been done mostly in mice while their heads are immobilized. Clever manipulations allow the brain to be imaged during some behaviors, but these behaviors cannot be considered normal. Several head-mounted miniaturized imaging devices have been developed that allow resolution at the cellular level in freely moving animals but only from small fields of view (FOV). A head-mounted imaging device with a relatively large FOV has recently been engineered for useful imaging in rats, but there is a much larger array of genetic tools available for mice than for rats. In an elegant study, Mathew Rynes, Daniel Surinach, and others working in the laboratory of Suhasa Kodandaramaiah introduced the mini-mScope, a miniature fluorescence microscope capable of simultaneously imaging an 8×10 mm^2 FOV with resolutions ranging from about 39 to 56 µm. This imaging device could be positioned on the head of a freely moving mouse.

Rynes and Surinach, who co-led the effort, specified three criteria that constrained the design of the mini-mScope. First, to permit free behavior and mobility, the overall weight of the device needed to be less than 4 grams, which is about 15% of the body weight of a mouse. Second, the device needed to image most of the dorsal cortex of the mouse brain. Third, the imaging resolution needed to be sufficient to provide useful images of calcium activity dynamics across the FOV. Briefly, this was accomplished by first performing a large craniotomy over the dorsal cortex of an anesthetized animal, then covering the opening with a 3D-printed transparent shell that was glued in place. Magnets were placed to provide attachment of the mini-mScope before experiments were conducted. Three blue light-emitting diodes (LEDs) and one green LED with appropriate filters were mated with a biconvex lens and a complementary metal oxide semiconductor (CMOS) sensor. The device weighed 3.8 g and allowed a repertoire of behaviors, including grooming and rearing, indicating that the mice were relatively comfortable with the device in place. Since a single biconvex lens was used to image a convex surface, not all of the surface was in focus, and the optical resolution varied within the FOV.

For some experiments, the team used a transgenic mouse (Thy1-GCaMP6f), which expresses fluorescent reporters of calcium activity in excitatory neurons. Several studies demonstrated that the mini-mScope acquired calcium signals that are comparable to a conventional epifluorescence microscope. Specific stimuli (brief vibrations to a hind limb and flashes of white light in one eye [Figures 1 and 2]) evoked a robust increase in calcium activity in the

doi:10.1017/S1551929521001127

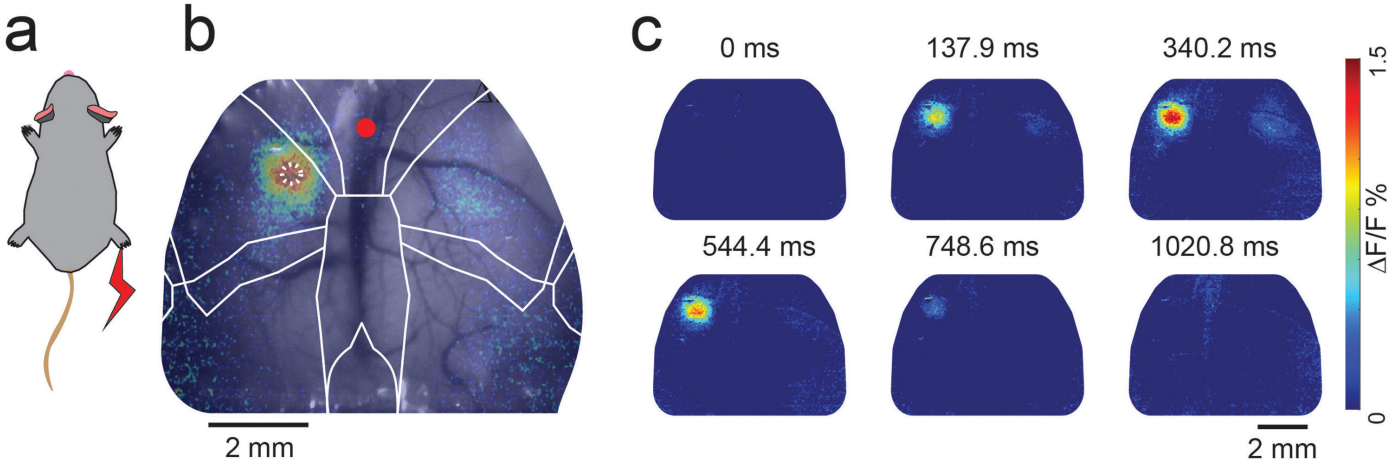


Figure 1: Hindlimb vibration stimulus: a) Schematic of a vibrational stimulus applied to the right hind limb while imaging with the mini-mScope. b) Composite of a raw grayscale image of the brain and the pseudocolor frame where the largest average $\Delta F/F$ occurred within the 1-s stimulus period. The white dashed circle indicates the region of interest with maximum response. c) Montage of average cortical calcium response to the vibration stimulus across time.

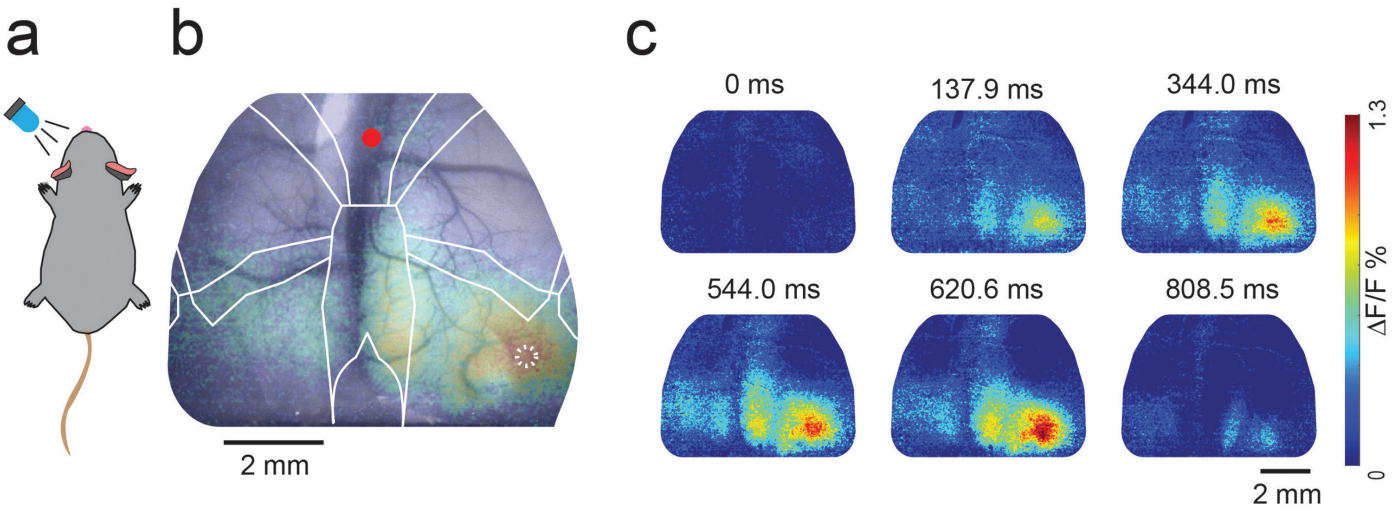


Figure 2: Left eye visual stimulus: a) Schematic of a visual stimulus applied to the left eye while imaging with the mini-mScope. b) Composite of a raw grayscale image of the brain and the pseudocolor frame where the largest average $\Delta F/F$ occurred within the 1-s stimulus period. The white dashed circle indicates the region of interest with maximum response. c) Montage of average cortical calcium response to the vibration stimulus across time.

appropriate cortical region with a physiological lag time. Some studies involved solitary mice, and other studies included a companion mouse of the same sex. Numerous results demonstrated the utility of the mini-mScope to study functional connectivity during behaviors that are unique to freely behaving mice.

These and other studies provide proof-of-concept for the use of the mini-mScope with a wide range of transgenic mice for broad expression of genetically encoded calcium indicators. Furthermore, the availability of mouse models of neurodegenerative and neuropsychiatric disorders opens the opportunity to use this unique instrument to examine a wide range of complex behaviors in healthy mice and to observe how these activities may be disrupted in disease states.

Dr. Kodandaramaiah's laboratory is currently developing sensors with increased sensitivity and imaging speed along with other improvements to the mini-mScope. They are also working to expand the FOV to examine other brain regions. These and other efforts are certain to result in a microscope that yields more important revelations of normal and abnormal mammalian brain function.

References

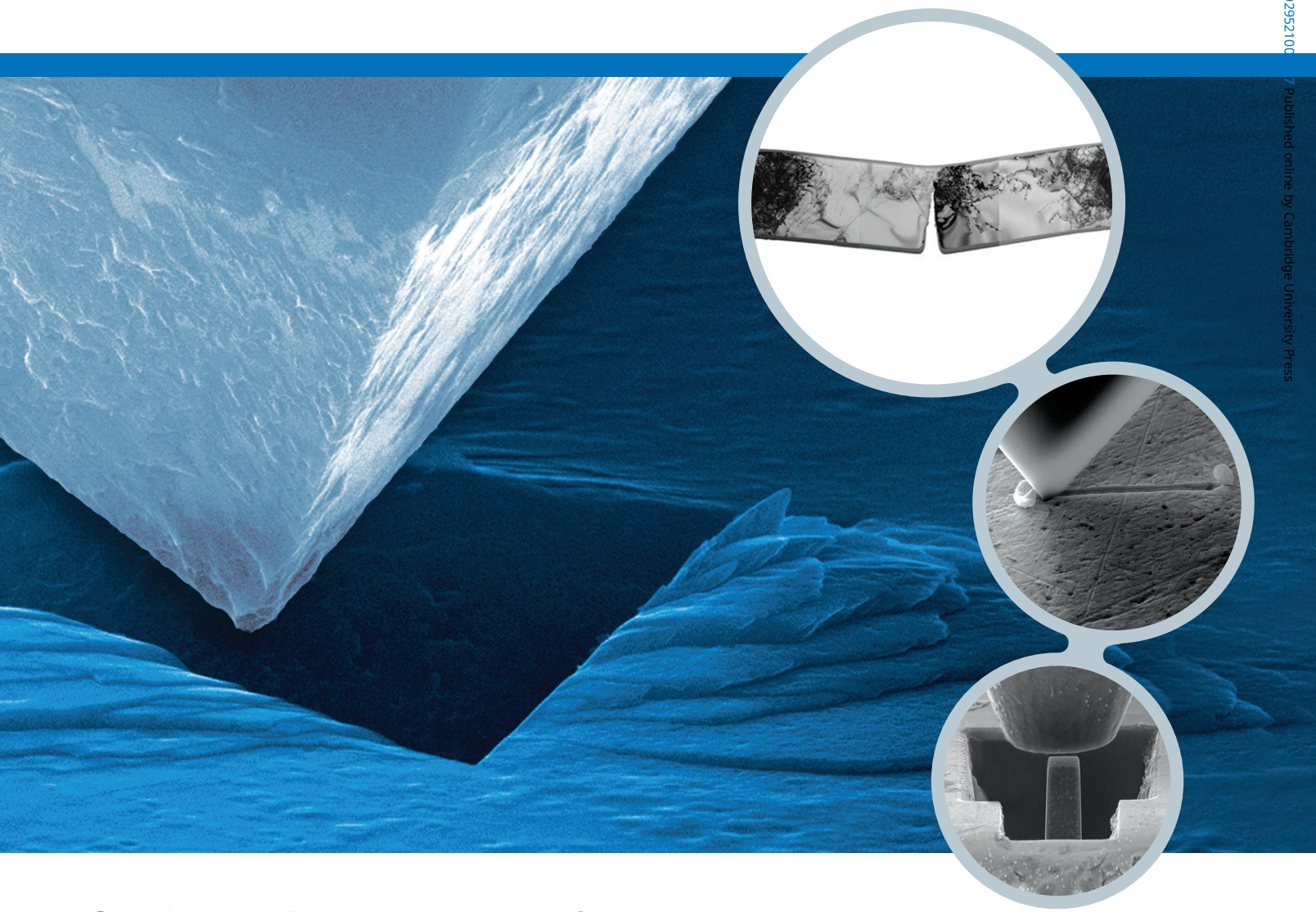
[1] Rynes et al., *Nat Methods*, 18 (2021) https://doi.org/10.1038/s41592-021-01104-8.

[2] The author gratefully acknowledges Dr. Suhasa Kodandaramaiah for reviewing this article.

MT

Transform Your Electron Microscope

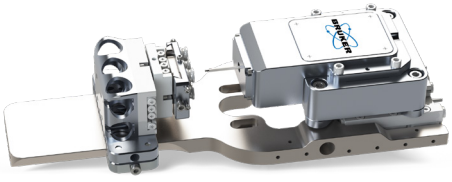
Into a Powerful, Nanoscale Mechanical Testing Chamber



Gain Insights Into Mechanical Performance at the Nanoscale

Bruker's comprehensive suite of in-situ nanomechanical instruments combines powerful electron microscopy with small-scale mechanical testing. Each system is capable of a wide variety of testing modes, enabling unprecedented insights into nanoscale material behavior across the research spectrum.

- Nanoindentation
- Microbeam Bending
- Pillar or Particle Compression
- Tensile Testing
- NanoTribology
- High Temperature
- Electrical
- Dynamic and Fatigue



Hysitron PI 89 SEM PicoIndenter

Hysitron PI 95 TEM PicoIndenter

www.bruker.com/picoindenters

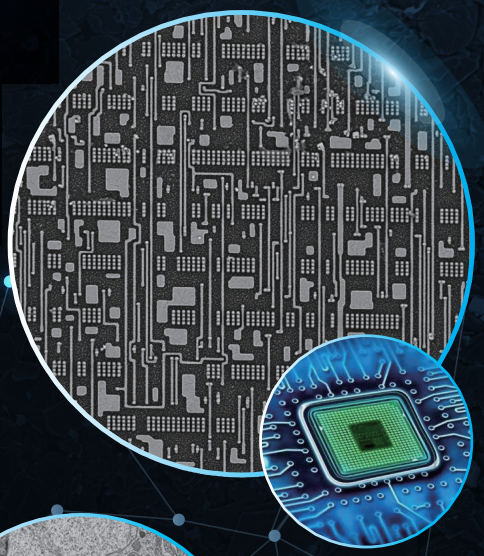
Innovation with Integrity

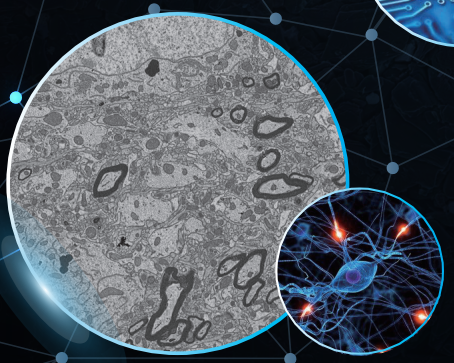
FBT

First
HIGH THROUGHPUT SEM System

Navigator-100

- 10 times faster than conventional FE SEMs
- Direct electron detection technology and Dual channel imaging (SE&BSE)
- Intelligent atlas and cross-scale material characterization
- Big data intelligent analysis and AI computing





FBT Navigator SEM X10

Conventional FE SEM

ACCSI2018 Award

BCEIA2019 Gold Award

CE

ISO 9001

CHINA
FOCUS EBEAM TECHNOLOGY(BEIJING) CO. ,LTD
Tel: +86 010 67832505 ext 813

SINGAPORE
FOCUS EBEAM TECHNOLOGY PTE.LTD
Tel: +65 6349 8868 ext 8921

www.focus-ebeam.com contact@focus-ebeam.com