# Wearable microscopes advance spinal cord imaging in mice

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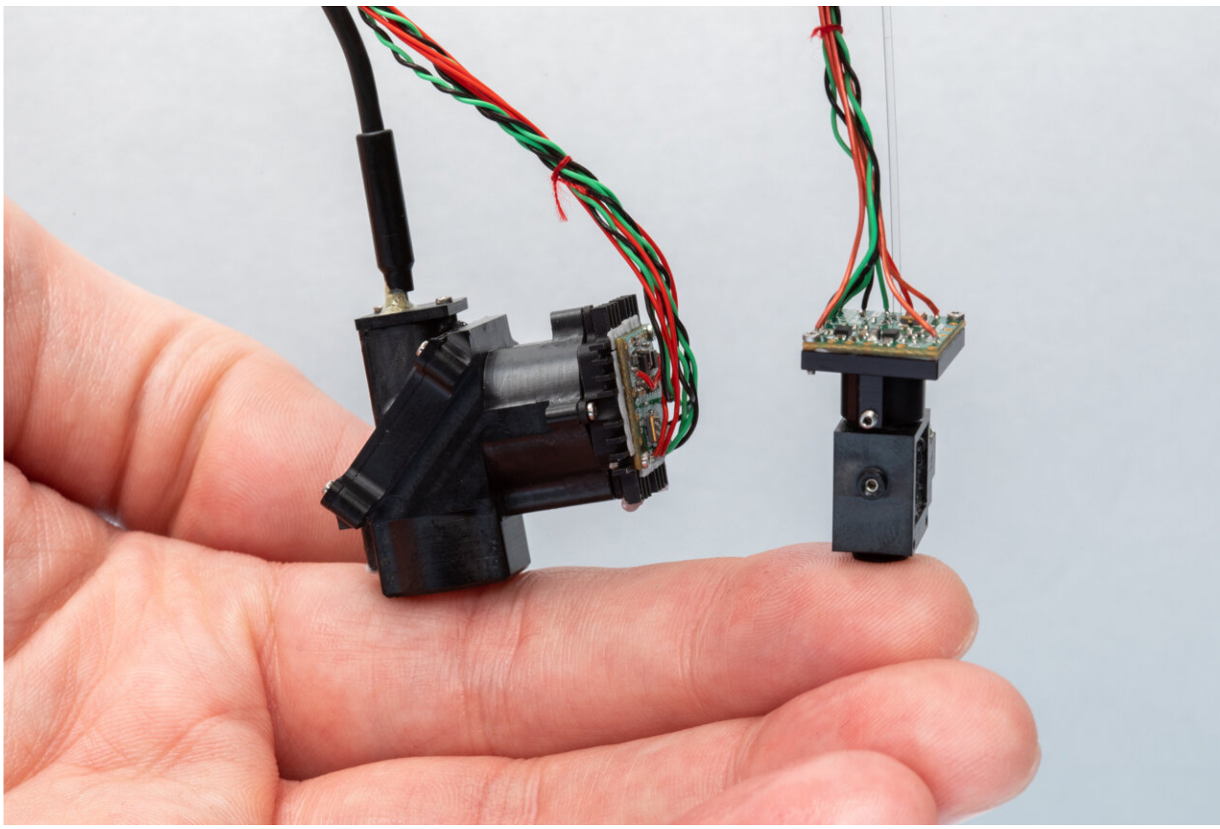


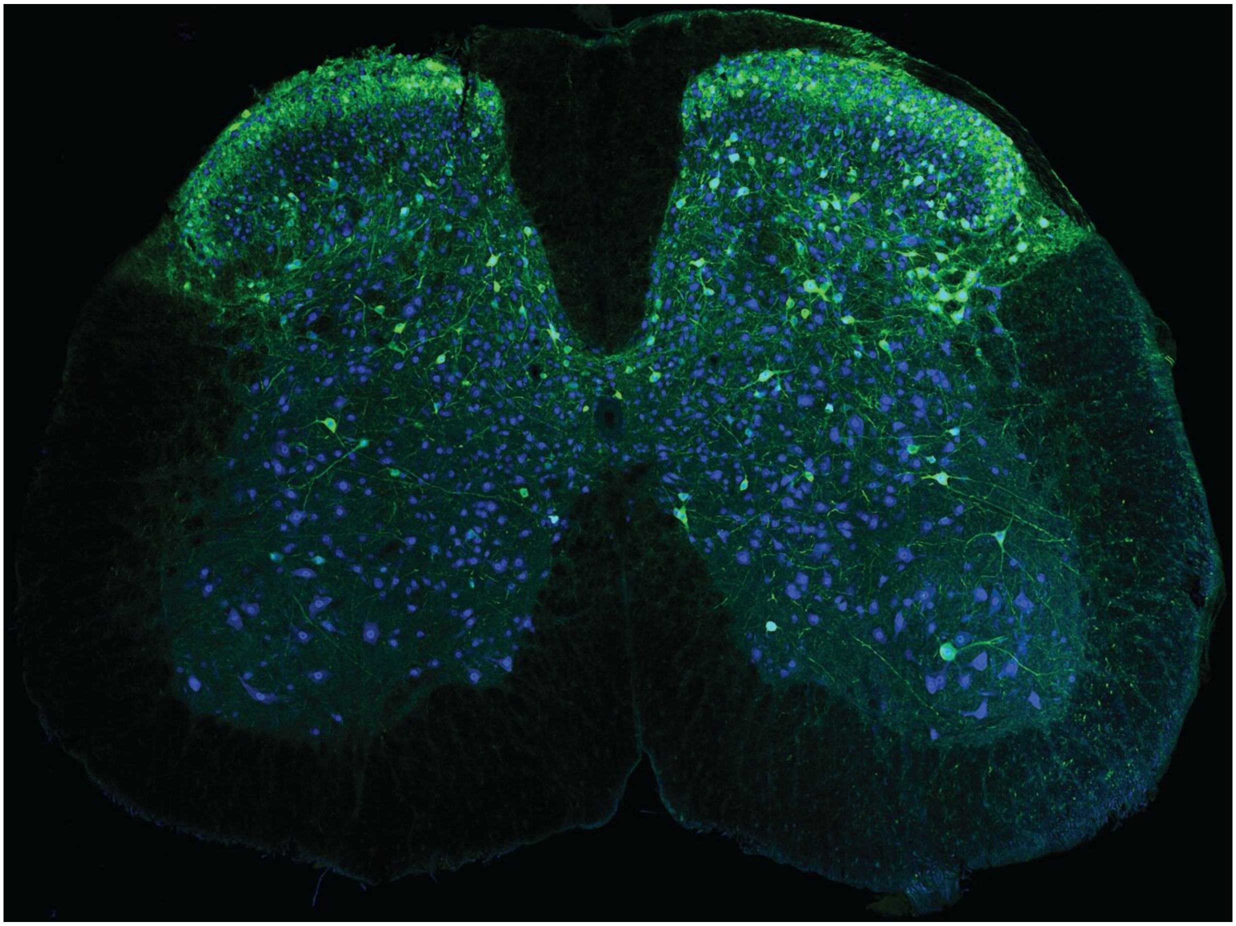
Salk researchers developed two wearable microscopes to image cellular activity in previously inaccessible regions of the spinal cord of moving mice in real-time. Credit: Salk Institute

The spinal cord acts as a messenger, carrying signals between the brain and body to regulate everything from breathing to movement. While the spinal cord is known to play an essential role in relaying pain signals, technology has limited scientists' understanding of how this process occurs on a cellular level. Now, Salk scientists have created wearable microscopes to enable unprecedented insight into the signaling patterns that occur within the spinal cords of mice.

This technological advancement, detailed in two papers published in *Nature Communications* on March 21, 2023, and *Nature Biotechnology* on March 6, 2023, will help researchers better understand the neural basis of sensations and movement in healthy and disease contexts, such as chronic pain, itch, amyotrophic lateral sclerosis (ALS), or multiple sclerosis (MS).

"These new wearable microscopes allow us to see nerve activity related to sensations and movement in regions and at speeds inaccessible by other high-resolution technology," says senior author Axel Nimmerjahn, associate professor and director of the Waitt Advanced Biophotonics Center. "Our wearable microscopes fundamentally change what is possible when studying the central nervous system."

The wearable microscopes are approximately seven- and fourteen-millimeters wide (about the width of a little finger or the human spinal cord) and offer high-resolution, high-contrast, and multicolor imaging in real-time across previously inaccessible regions of the spinal cord. The new technology can be combined with a microprism implant, which is a small reflective glass element placed near the tissue regions of interest.



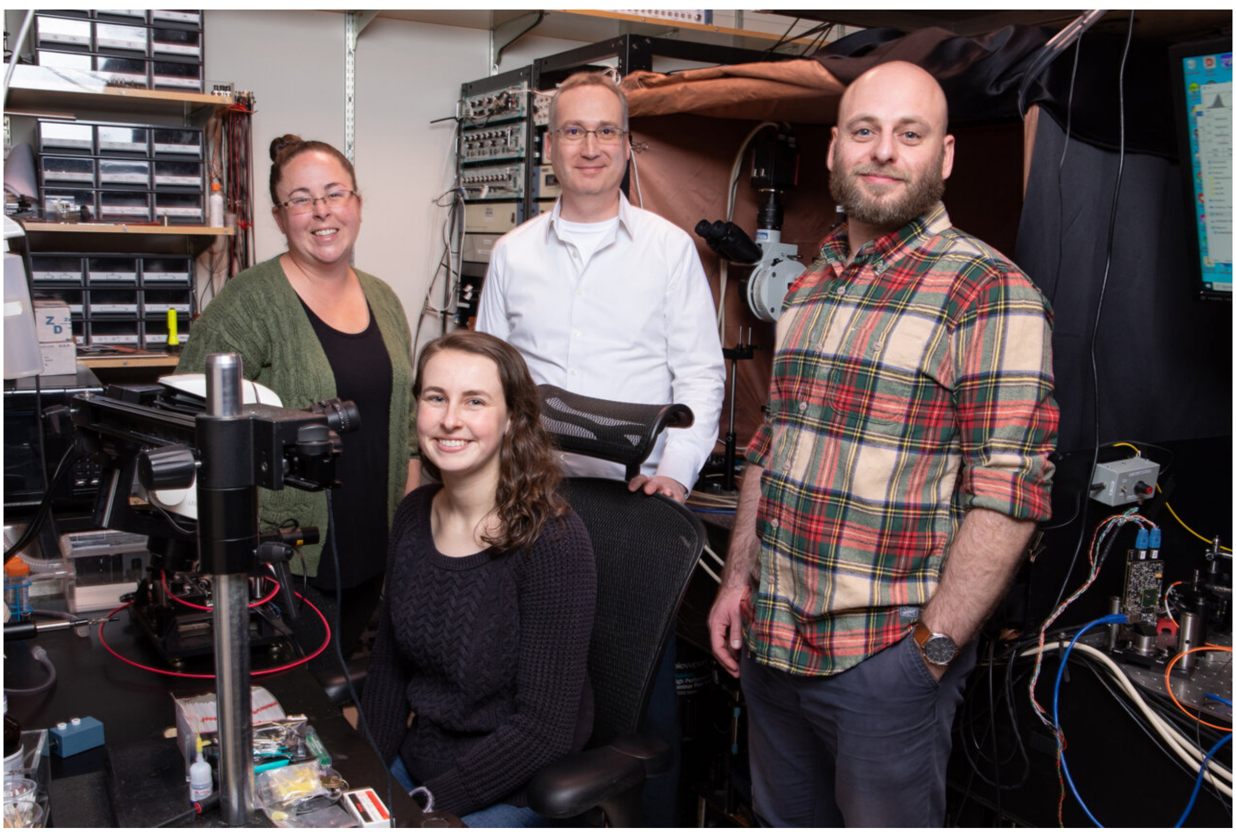
Neurons in the spinal cord (blue), including those that send signals about pain (green), captured using one of the new wearable microscopes. Credit: Salk Institute

"The microprism increases the depth of imaging, so previously unreachable cells can be viewed for the first time. It also allows cells at various depths to be imaged simultaneously and with minimal tissue disturbance," says Erin Carey, co-first author of one of the studies and researcher in Nimmerjahn's lab.

Pavel Shekhtmeyster, a former postdoctoral fellow in Nimmerjahn's lab and co-first author on both studies, agrees, "We've overcome field-ofview and depth barriers in the context of spinal cord research. Our wearable microscopes are light enough to be carried by mice and allow measurements previously thought impossible."

With the novel microscopes, Nimmerjahn's team began applying the technology to gather new information about the central nervous system. In particular, they wanted to image astrocytes, star-shaped non-neuronal glial cells, in the spinal cord because the team's earlier work suggested the cells' unexpected involvement in pain processing.

The team found that squeezing the tails of mice activated the astrocytes, sending coordinated signals across spinal cord segments. Prior to the invention of the new microscopes, it was impossible to know what astrocyte activity looked like—or what *any* cellular activity looked like across those spinal cord regions of moving animals.



From left: Daniela Duarte, Erin Carey, Axel Nimmerjahn, and Pavel Shekhtmeyster. Credit: Salk Institute

"Being able to visualize when and where pain signals occur and what cells participate in this process allows us to test and design therapeutic interventions," says Daniela Duarte, co-first author of one of the studies and researcher in Nimmerjahn's lab. "These new microscopes could revolutionize the study of pain."

Nimmerjahn's team has already begun investigating how neuronal and non-neuronal activity in the spinal cord is altered in different pain conditions and how various treatments control abnormal cell activity.

Other authors include Alexander Ngo, Grace Gao, Nicholas A. Nelson, Jack A. Olmstead, and Charles L. Clark of Salk.

**More information:** Multiplex translaminar imaging in the spinal cord of behaving mice, *Nature Communications* (2023). DOI: 10.1038/s41467-023-36959-2

Pavel Shekhtmeyster et al, Trans-segmental imaging in the spinal cord of behaving mice, *Nature Biotechnology* (2023). DOI: 10.1038/s41587-023-01700-3

Provided by Salk Institute