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Tiny microscope peers into mice brains

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- Celeste Biever

A microscope the size of a matchbox is allowing US biologists to peer inside the brains of live animals.

Weighing a mere 3.9 grams, the microscope has been used to image blood vessels lying a few millimetres below the surface of the brains of anaesthetised mice, with a resolution of 1 micrometre (one-thousandth of a mm).

The researchers believe they may one day be able to view brain cells in the same way. In future the tiny microscope could be strapped to the head of a conscious, moving animal and beam back a movie of the neurons while the animal engages in a variety of activities, say its creators, led by Mark Schnitzer of Stanford University, US.

“It’s a microscope that fits in the palm of your hand,” says co-creator Ben Flusberg. It could also be a quick, easy way to image diseased or tumour-laden brains, which currently require an MRI scan or large machinery, he says. Or it could pave the way for a mobile, pocket-sized diagnostic tool.

But it is not clear whether the device would ever be used in humans because of its invasive nature. “It’s an ingenious device, but whether it’s transferable from mouse to man is not mentioned,” says Britton Chance, a biophysicist at the University of Pennsylvania, US, who focuses on non-invasive imaging.

Hole punch

A pin-like probe, 1 mm in diameter, protrudes from the bottom of the device and is inserted into a tiny hole punched in the head of the anaesthetised mouse. The probe, called a microendoscope, sits on top of the region of the brain being imaged, for example, the hippocampus. There it images blood vessels directly below it, which are inside the brain, by illuminating tiny sections of the hippocampus one at a time with near infra-red light.

The projected light causes the animal’s blood – previously injected with a fluorescent marker called fluorescein – to emit light of a particular frequency. The probe, which is packed with optical fibres, detects the light and transmits it back to the matchbox-sized device where it is recorded. The image can then be displayed on a connected computer screen. Watch a movie of the researchers demonstrating the technique, here (.ram format).

Although blood vessels that lie below the surface of the brain had been imaged before by the group using a microendoscope, the probe had to be connected to a large piece of machinery, which illuminated the brain areas and detected the fluorescent vessels. This meant that the device could not have been used on moving animals or be developed as a portable system for humans. “It was too big,” admits Flusberg.

Strappingly small

Schnitzer’s group is the first to cram all this functionality into a device the size of a matchbox, he says. Their secret has been to harness a tiny piezoelectric motor contained within the device to focus laser light on the sections of the brain being examined.

They say only now is the device small enough to be strapped to a live animal. “We want to understand what the cells in the brain are doing during animal behaviour,” Flusberg explains.

But Chance points out that there is currently no way to work out exactly where inside the brain the probe is. “This gives you an image of a single blood vessel in an unknown place,” she says.

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