Neuron-size probes promise better recordings
New electrode designs aim for seamless integration in brain tissue

By Kelly Servick

For a hair-thin probe penetrating the brain to listen in on neurons' electrical chatter, finesse is key. It's easy to rip tissue on the way in. And once in place, a probe can do further damage that muffles the signals it aims to detect. But recent reports describe a generation of finer probes that should prove less damaging. Just a few micrometers thick—comparable to neurons themselves—these tools may soon capture unprecedented long-term recordings from hard-to-reach parts of animal brains. And they may lead to more sophisticated brain-computer interfaces for people.

Improved material fabrication techniques have helped labs create the exquisitely fine probes, says neural engineer Timothy Hanson, who developed a system for inserting tiny electrodes while at the University of California, San Francisco (UCSF). And lab tests have shown that brain research using ultrasmall electrodes “can be done, and that it’s worthwhile.”

Conventional brain probes are already vanishingly tiny. Stiff electrodes known as Michigan probes, commonly used in neuroscience research, are pointed, ribbonlike shafts that can be as thin as 15 micrometers and are usually 60 micrometers wide or more. In a standard grid known as the Utah array, each spike is roughly 200 micrometers thick at its base. But in the months after either device is implanted, its connection to neurons typically weakens and its signal fades.

A key reason is that the probe provokes an immune reaction in the brain. Its initial plunge into the tissue can tear blood vessels. And even after that damage heals, the probe continues to push and pull on surrounding tissue. In response, nonneuronal cells called glia multiply and form scars that push neurons away from the electrode.

Damage also limits the number of electrodes a brain can host, says Cynthia Chestek, a neural engineer at the University of Michigan in Ann Arbor. To get valid data, “We need animals that act normally after they get these implants.” Introduce too many probes and “you’re studying traumatic brain injury.” The constraint on probe number also limits the performance of brain-machine interfaces such as the robotic limb control systems her group is developing; fine motor skills will require more recording channels, Chestek says. So her team is developing much smaller electrodes using rigid carbon fibers roughly 8 micrometers in diameter. These fibers have been shown to record from individual neurons in a rat’s brain for several months with no significant glial scarring or neuron death.

Other groups are betting on a different class of material: strong polymers that bend when extremely thin. “The surrounding tissue can resolve how the roles of individual neurons evolve in response to animals’ experiences.”

Because polymer probes are so flexible, driving them into the brain is challenging. Lieber’s team loads its neuronlike strands into a syringe and uses a rigid 400-micrometer-wide needle to deliver the electrodes to precise spots. In a March preprint, Hanson and colleagues at UCSF described a neural “sewing machine,” in which a robotic arm swiftly punctures the brain with a metal needle to push in soft probes. And neural engineer Nicholas Melosh and his team at Stanford University in Palo Alto, California, attach a stiff wire to bundles of their 7-by-1.5-micrometer polymer probes, which peel off as the wire descends into the brain.

Last month at a meeting of the Brain Research through Advancing Innovative Neurotechnologies Initiative in Washington, D.C., Melosh presented vivid evidence that smaller probes really are gentler. His group made precise recordings of the minute forces that probes ranging in diameter from 13 to 200 micrometers exerted as they penetrated a living mouse brain. At probe sizes 25 micrometers and below, microscopy showed virtually no tearing of blood vessels. Instead of puncturing capillaries, these smaller wires pushed them aside.

That finding is “really, really good news” for ultrasmall electrodes under development, Chestek says.

Neuron-scale probes still have to fully demonstrate their longevity and prove they can get good signals in larger animals. But the early signs of safety are encouraging, Chestek says. She points to videos Melosh shared of massive, spreading bleeds from the poke of an 80-micrometer probe. “We used to think 80 microns was small.”