A flexible mesh to record the brain

Implantable electronics that can sense and potentially alter neuronal activity are powerful research and therapeutic tools. But one of the hurdles to their use has been implanting the devices in specific sites without damaging the tissue or generating scar tissue that would prevent long-term recordings. The recent findings of Charles Lieber, Ying Fang and colleagues[1] from Harvard University and The National Center for Nanoscience and Technology in Beijing make a big step forward by delivering flexible electronic sensory networks to spaces in the brain using a syringe and a small needle.

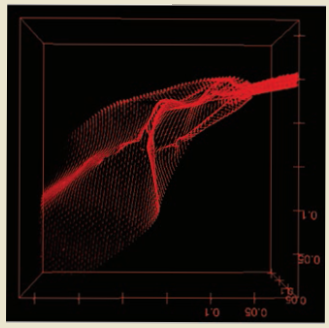
One of the big remaining challenges in neurotechnology is the development of the biophysical sensor—its functionality, biocompatibility and long-lasting potential. Most of the electrodes being tested today are based on rigid materials. "Current technology doesn't work for more than a few years because of scar tissue formation, material degradation, inflammation caused by the micromotion of the brain and infection," says Jose Carmena of the University of California at Berkeley. "After a while, you end up recording noise."

Lieber and his group[2] previously developed macroporous nanowire electronics, flexible three-dimensional scaffolds that can support neuronal and cardiac cell growth. But they noticed that when the substrate on which these electronics are made is dissolved, the devices "are floating in solution, much like a polymer," says Lieber. "This made us think that we could take them up with a syringe and inject them into other materials."

The researchers recognized that for the device to be taken up with a needle that has a much smaller diameter than itself, the device would need to be rolled up like a scroll. The other possibility, crumpling it, would damage the electronics or clog the needle. To roll up the mesh electrode and prevent it from crumpling as it encounters the tissue during injection, Lieber and colleagues[1] increased the angle at which the mesh bends in the transversal direction. As the mesh electronics are taken up with the needle from one end, they are forced to roll up "taking on the contour of the inside diameter of the needle, because it is the lowest energy deformation," explains Lieber.

The mesh electrode is tethered by a wire to input/output pads, sensors that enable reading and recording of the electrical signals, and that are glued to the outside of the animal's skull. Injecting the electronics into a lateral brain ventricle and the hippocampus of anesthetized mice, Lieber and colleagues[1] found evidence that they work. In the hippocampus, a denser tissue than the ventricle, the mesh electronics unfold only to a minimal extent, but can record brain activity nonetheless. Lieber explains that the mesh electrodes were designed to be soft and flexible and thus do not unfold—if they were more rigid, they might cut through the tissue. Analyses of the brain 5 weeks after injection show that the extent of gliosis and astrocyte proliferation around the site is limited and that neurons surround the mesh, suggesting the electronics are biocompatible.

These mesh electrodes are much more flexible and smaller than any other electrodes that have been implanted in the brain before, says Carmena, who was not involved in the



study. This is important because "you want to minimize the footprint of whatever you are injecting into the brain, and you want to minimize the rigidity, especially if that rigid structure is anchored to another part of the device."

Although promising, at this point the findings provide only a proof of principle. "But," says Carmena, "if this technology can be accurately deployed to specific areas of the brain and is shown to record brain function in freely moving animals for long periods of time, it would be a big advance for the field." The authors suggest that using biochemically functionalized probes and co-injecting the electronics with other injectable reagents would allow a high degree of versatility to probe, enabling more sophisticated studies of brain activity and disease.

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2. Tian, B. *et al. Nat. Mater.* **11**, 986–994 (2012).