

BIOELECTRONICS

Injection and unfolding

The delivery of flexible electronic scaffolds to precise locations in biological tissues or cavities is achieved by injecting them via a syringe needle with a diameter much smaller than the size of the scaffold.

Dae-Hyeong Kim and Youngsik Lee

Deformable electronics integrated with specific biological systems, also called soft bioelectronics, show potential as a solution to various clinical challenges. These include disease-specific bioelectronic device strategies, such as high-resolution brain mapping electronics for epilepsy¹, intracortical optogenetic stimulation devices for brain/computer interfacing², epicardial electrophysiology webs for arrhythmia³, and electronic dura mater integrated with the spinal cord⁴. Implantable bioelectronics have been improved significantly in terms of multifunctionality, biocompatibility, and mechanical matching between electronics and biological tissues. However, the effective, accurate, and patient-friendly delivery of electronics with desired shapes to diseased regions without invasive routes, via surgeries, remains challenging. Now, writing in *Nature Nanotechnology*, Charles Lieber and co-workers at Harvard University and the National Center for Nanoscience and Technology in Beijing report soft 3D electronic scaffolds that can be delivered to specific regions, such as cavities and living organs, through a syringe needle with a diameter of 100 μm , with minimal invasiveness⁵. The researchers could use these syringe-injectable electronics, which are reconfigurable into desired forms, inside small cavities to monitor physiological and electrophysiological signals *in vivo* and

overcome some of the challenges faced in the delivery of implantable bioelectronics.

Figure 1a shows the syringe injection process. A thin syringe needle loaded with free-standing, mesh-shape electronic components is inserted into the targeted internal cavity; in certain applications, the syringe needs to be implanted deep beneath bones to reach the subdural neurons. The so-called mesh electronics are then injected into the target region while the needle is simultaneously withdrawn. After injection into the cavity, the mesh electronics reshape to the originally designed layout. Input/output wirings connect the mesh electronics to the outside measurement and data storage systems. Suitable designs that consider the mechanics of the mesh electronics enable successful injection without entanglements. Ultrathin mesh electronics have an angular deviation of 45° (α in Fig. 1b) from the conventional rectangular mesh^{6,7}. This facilitates bending in the transverse direction and successful rolling-up of the mesh while suppressing buckling and/or crumpling in the needle. With further optimizations of the design parameters, mesh electronics with a width that is 33 times larger than the inner diameter of the needle have been successfully delivered without mechanical fractures and electrical malfunctions^{6,7}. In contrast, the rectangular design allows the

delivery of a mesh with a width, at most, four times larger than the inner diameter of the needle; furthermore, substantial entanglements cannot be avoided.

Lieber and co-workers consider models of various internal regions and cavities in animals to investigate the reconfiguration and mechanical deformation behaviour of the mesh electronics. Microcomputed tomography imaging shows that the mesh electronics relax to $\sim 80\%$ of the original configuration during injection, followed by the post-injection reconfiguration occurring in less than 1 hour without any failures. Individually addressable piezoresistive strain sensors are incorporated on the mesh platform. The compressive and tensile strain variations caused by the internal deformations of cavities are thus monitored. Other nanowire-based electronic devices can also be integrated for pH and chemical detection. Preliminary experiments in which mesh electronics and embryonic rat neurons were co-injected into a Matrigel neural tissue engineering scaffold have shown potential for tissue engineering applications *in vitro*.

The researchers also injected the mesh electronics into the brain of live animals to monitor the brain activity *in vivo*. Confocal microscopy was used to image rodent brain tissues in which macroporous mesh electronics had interpenetrated and

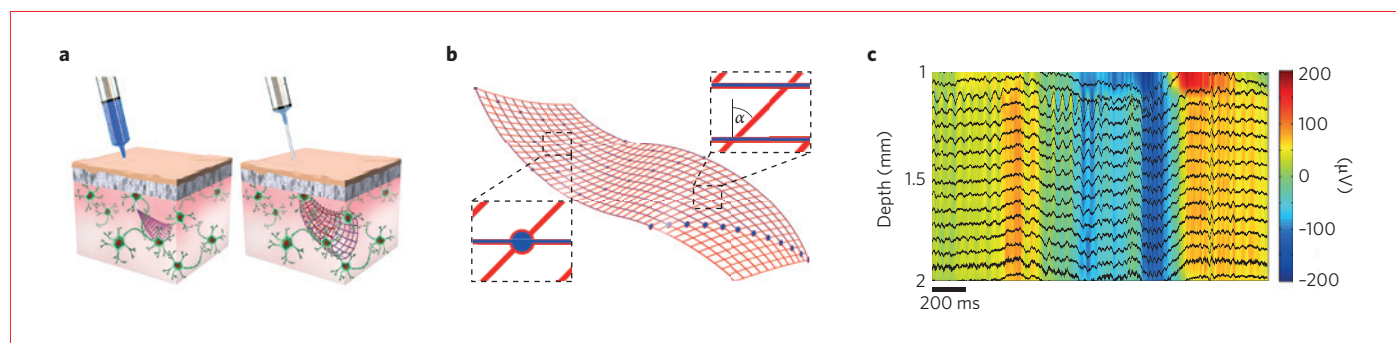



Figure 1 | Schematic illustration and representative biomonitoring results of syringe-injectable electronics. **a**, Injection process of mesh electronics loaded in a syringe into biological cavities. **b**, Design of mesh electronics and magnified views (black dashed boxes). The blue dots represent electrodes that make contact with biological tissues. α is the critical design factor of angular deviations. **c**, Sixteen-channel neural mapping *in vivo* by using mesh bioelectronics. Figure adapted from the Supplementary Information for ref. 5, Nature Publishing Group.

tightly associated with nearby neurons. The comparable glial fibrillary acidic protein expression between the experimental and the control groups indicated no chronic tissue responses to the foreign mesh electronics. Healthy neurons networked to the mesh were observed by high-intensity fluorescence signals of neuron markers. The reduced bending stiffness of the mesh (0.087 nN m) and the small size of its unit cell (comparable to that of neurons) caused minimal mechanical damage to brain tissues⁸. Well-defined neural signals were recorded through the 16-channel array of metal electrodes in the mesh electronics (Fig. 1c). The characteristic waveform (average duration, ~2 ms; peak-to-peak amplitude, ~70 μ V), the action potential of a single neuron⁸, was reliably identified in the recorded data. The strong neurophilic

interactions of the macroporous mesh and its long-term stability and compatibility enable the electrophysiological monitoring of neural networks *in vivo* over long periods.

The syringe injection of mesh electronics represents a novel strategy for the minimally invasive delivery of soft bioelectronics to deep cavities of biological systems. The description and optimization of the mechanical design parameters related to injection and reconfiguration reported by Lieber and colleagues are helpful for the design of future devices as well as for clinically relevant applications *in vivo* and tissue engineering applications *in vitro*. Further integration of the injectable electronics with other functional units and/or wireless components is expected to lead to promising pathways for innovations

in implantable bioelectronics and continuous biomonitoring. 

Dae-Hyeong Kim and Youngsik Lee are at the Center for Nanoparticle Research of Institute for Basic Science (IBS), School of Chemical and Biological Engineering, Seoul National University, Seoul 151-742, Republic of Korea.
e-mail: dkim98@snu.ac.kr

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