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Research Highlight

Rolling 2D sheets into monolithic 3D neural interfaces

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As neural networks in the brain are distributed across three-dimensional (3D) space, forming complex architectures for distinct functions and regions, neural interface systems with a 3D form factor are essential for directly observing and understanding brain structure, activity, and inter-regional connectivity[2]. Importantly, neural signals do not propagate strictly within two-dimensional (2D) planes but instead spread through 3D tissue volumes with defined directionality and circuit-specific mechanisms. Understanding these spatiotemporal dynamics therefore requires volumetric access to neural signals beyond the capabilities of planar architecture. However, conventional neural electrode or probe arrays based on silicon microfabrication are typically realized through a combination of planar processes. While this facilitates 2D scalability, extending these systems into three dimensions to simultaneously monitor neural activity across multiple locations and depths remains a significant challenge[3–5].

Recently, Yi Qiang et al. reported a study in *Nature Electronics* on the implementation of monolithic 3D neural probes achieved by rolling soft electronics defined on a planar surface (Figure 1(a)). The multi-institutional research team, including Dartmouth College, demonstrated that this strategy—termed "rolling of soft electronics (ROSE)"—allows for the determination of the spatial distribution and configuration of the final 3D neural probe array by controlling planar design parameters and spacer thickness (Figures 1(b)–(d)). Using this method, the device geometry and electrode density could be freely tuned, successfully realizing various configurations of 3D probes scaling up to 256 shanks through a monolithic process. By analyzing the insertion dynamics associated with these hardware parameters, the researchers verified the conditions necessary for the successful insertion of the device into brain tissue (Figure 1(e)). Moreover, the final rolled devices utilized Au/PEDOT:PSS electrode sites to reduce impedance, and maintained excellent electrical properties (average impedance ~239 kΩ at 1 kHz, 10 × 20 μm^2) with negligible degradation from the rolling process. The core distinction of the ROSE process lies in its deterministic planar-to-volumetric transformation based on the Archimedean spiral model. From a manufacturing perspective, unlike traditional manual assembly or discrete module stacking which are prone to errors, this monolithic rolling strategy preserves the precision and scalability of 2D lithography within a 3D volumetric architecture. This approach establishes a versatile 3D manufacturing paradigm for high-density system integration, extending its utility well beyond specific neural probe applications. To validate the structural integrity of this transformation, through finite element analysis (FEA) and cyclic bending tests, the researchers confirmed that the mechanical strain

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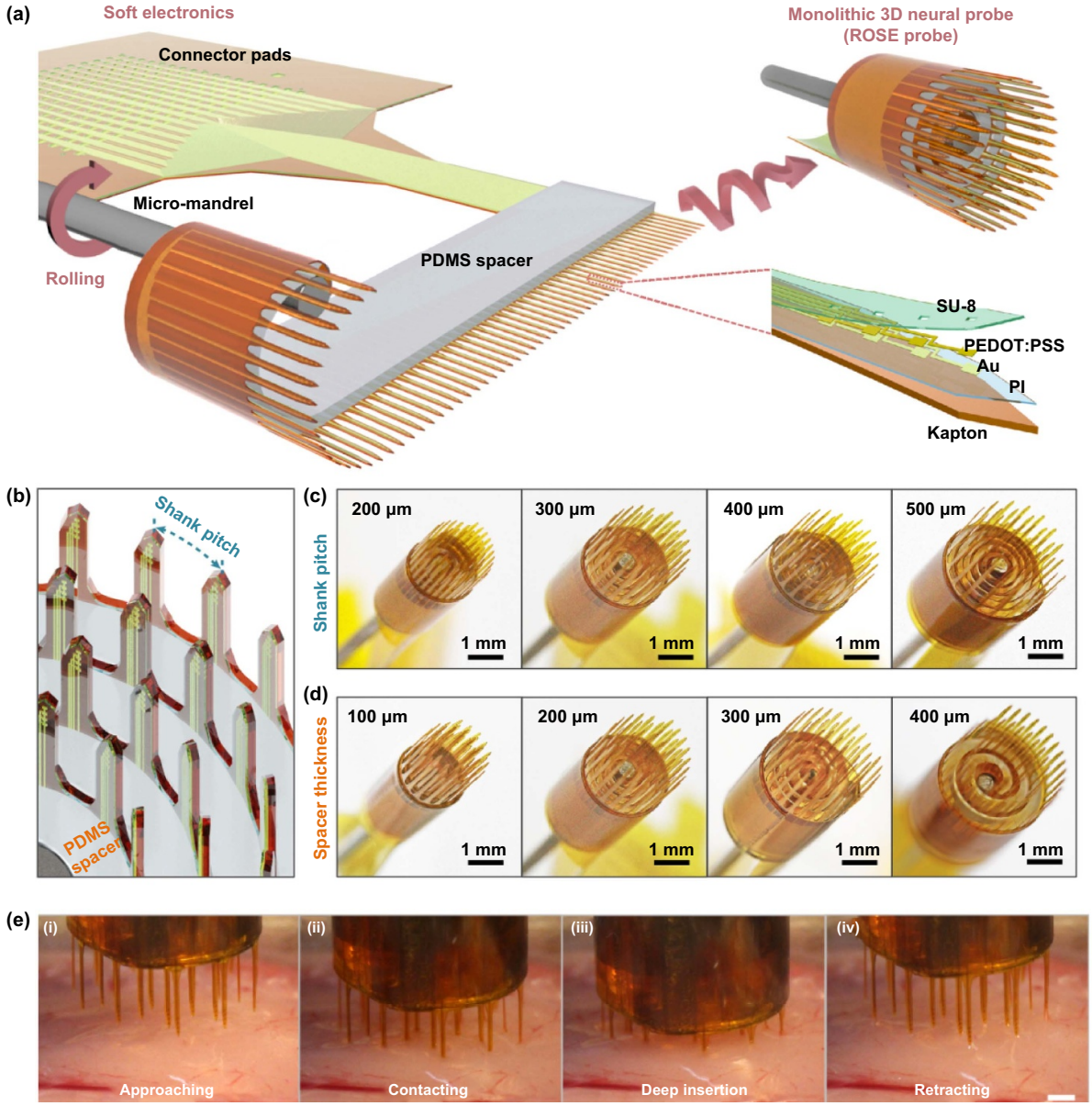

Figure 1. The ROSE (Rolling of Soft Electronics) strategy for scalable 3D neural interfaces. (a) Monolithic transformation of planar flexible electronics into a 3D cylindrical probe using a micro-mandrel and PDMS spacer. Reproduced from[1], with permission from Springer Nature. (b) Detailed view of electrode shanks precisely distributed within the spiral geometry following the deterministic rolling process. (c), (d) Independent control of electrode density and device dimensions for the 256-channel, 64-shank probe by varying the shank pitch (c) and PDMS spacer thickness (d). (e) In vivo photograph showing the 128-channel ROSE probe (32 shanks) inserted into the rat visual cortex. Scale bar represents 0.5 mm.

induced during rolling is negligibly transferred to the electrode sites. Furthermore, they established mechanical reliability by demonstrating that electrical performance was maintained even after 10 000 bending cycles.

Building on this platform validation, the team conducted in-depth in vivo experiments in rodent and non-human primate models, demonstrating the practical efficacy of the ROSE probe. Notably, despite the inherent flexibility of the device, the researchers achieved successful aid-free insertion without the need for temporary stiffening coatings. Specifically, the high-density probe array established through the rolling process induces lateral confinement and inter-layer friction; this mechanism significantly increases the effective critical buckling load, thereby preventing slipping-induced instability during penetration. The researchers formalized this mechanical interaction into a theoretical scaling law, providing a design framework to predict the critical boundary between successful insertion and slipping failures. First, in rodent experiments, a 128-channel probe consisting of 32 shanks was implanted into the visual cortex, successfully recording single-unit signals with high signal-to-noise ratios (median SNR $>$ 4) and local field potentials (LFPs). Notably, during a five-week semi-chronic recording period, stable spike yields were maintained without degradation of signal quality. Histological analysis

further verified the biocompatibility of the flexible material-based 3D structure, revealing a significantly reduced immune response (Iba-1 expression) compared to conventional silicon probes ($P < 10^{-37}$). This biological advantage is attributed to the flexible polymer substrate, which possesses a Young's modulus two orders of magnitude lower than that of silicon, thereby minimizing the mechanical mismatch with brain tissue. Furthermore, 3D orientation tuning analysis in awake mice demonstrated a dramatic reduction in visual information decoding error to an average of 6.4° when utilizing 3D volumetric data, representing a threefold improvement in precision over the >20° error limitations of single-plane (2D) data. In this process, the researchers also experimentally confirmed the "salt-and-pepper" organizational characteristic, in which the orientation selectivity of neurons within the visual cortex is randomly distributed across 3D space. Moreover, experiments with non-human primates (Rhesus macaque) confirmed the feasibility of large-scale 3D recording within the cerebral cortex, suggesting potential scalability toward clinical translational research. By implanting a large-area, 256-channel ROSE probe into the V4/inferior parietal lobule (IPL) region, the team captured not only high-yield spike signals (44% single-unit yield) but also high-resolution laminar profiles of LFPs and current source density (CSD). This implies that ROSE technology is effective for precisely mapping neural signal flows in three dimensions within the complex brain circuitry of large animal models, extending beyond rodents.

This study demonstrates that the inherent flexibility of electronics fabricated via mature silicon processes can serve as a defining design principle—not merely for biocompatibility, but as a means to architect scalable 3D neural interfaces. By leveraging the fine patterning capabilities of conventional planar semiconductor fabrication and eliminating the need for complex stacking or assembly, this approach enables the creation of customized devices tailored to the anatomical size and depth of specific brain regions. This paradigm shift in neural probe design opens new possibilities for high-density, volumetric brain mapping and advanced neuroscience applications. Crucially, this platform extends beyond neural interfaces, offering a versatile strategy for system integration in manufacturing. By maintaining compatibility with mature planar processes, the approach paves the way for incorporating active CMOS backplanes or optoelectronic components into volumetric architectures, thereby stimulating broader developments in the field of 3D microfabrication. However, realizing high-density volumetric mapping still presents certain trade-offs. Increasing the number of penetrating shanks to enhance resolution may inevitably lead to greater tissue displacement, which could pose risks of acute trauma and chronic foreign body reactions. Therefore, finding the optimal balance between the demand for large-scale, high-resolution recording and the necessity of minimizing tissue perturbation remains an important task for the future of neural interface technology.

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