Supramolecular Chemistry Enables Highly Conductive and Stretchable Bioelectronics

By Weilai Yu

Implantable and wearable bioelectronics constitute crucial functional components underpinning a variety of biomedical applications, such as monitoring physiological signals and modulating biological activities for diagnosis and therapeutics purposes. A major challenge confronted by this exciting technology is the mechanical mismatches between the rigid electronics and the soft biological systems, which can cause device failure as the surfaces are continuously moving. One promising solution is to establish seamless and conformal bioelectrode interfaces based on intrinsically stretchable organic materials with high mechanical robustness and electrical conductivity. These organic materials should be patternable with a facile fabrication process to produce high-density micro-electrode arrays that can effectively collect biological signals and deliver electrical stimulation when in contact with tissue.

One of the persisting hurdles is to combine high mechanical robustness with good electrical conduction, especially when patterned at small feature sizes for bioelectronic devices. Poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS) is a well-known conducting polymer with promising performances for use in soft bioelectronics. Previous efforts using ionic and molecular additives improved conductivity and stretchability of PEDOT:PSS, but their performance dropped substantially right after contact with solvent or immersion in physiological fluids because the non–cross-linked additives were washed away. To meet the complex requirements of bioelectronics, a group of scientists led by **Prof. Zhenan Bao** leveraged supramolecular chemistry to rationally construct a topological supramolecular network using multi-functional molecular building blocks, as described in a recent report in ***Science***.

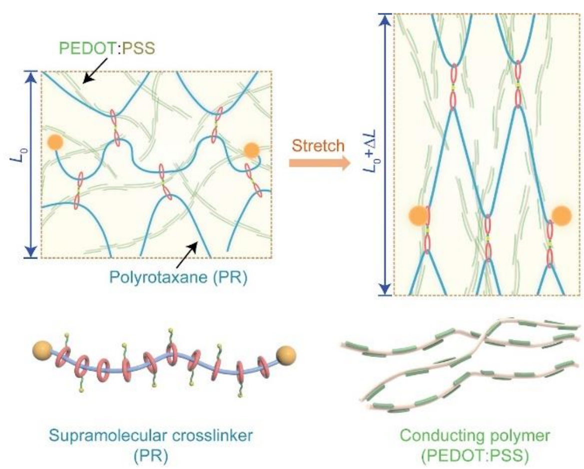

Figure 1. Schematic diagram illustrating the intrinsically stretchable topological network, composed of the conductive PEDOT:PSS and supramolecular cross-linkers. Image credit: Dr. Yuanwen Jiang, Bao Group, Stanford U.

Supramolecular design for high stretchability and conductivity

To simultaneously induce high conductivity, stretchability, and photo-patternability of PEDOT:PSS, the researchers first designed an unique cross-linker combining a polyethylene glycol (PEG) backbone with sliding cyclodextrins (CDs) functionalized with PEG methacrylate (PEGMA) side chains (**Figure 1**). Simply blending PEG into PEDOT:PSS resulted in higher conductivity by inducing the aggregation of PEDOT, but at the same time reduced the stretchability when the phase separation of PEG caused it to crystallize. To resolve this dilemma, the scientists introduced bulky CD rings into the polymer network to disrupt the PEG crystallization and improve the stretchability. However, the CDs functionalized with short PEGMA side chains alone cannot form uniform blend with PEDOT:PSS due to its poor solubility in water. Only by attaching the functionalized CDs onto the long hydrophilic PEG backbone, can both high water solubility and reduced PEG crystallization be realized. Finally, the photo-induced cross-linking between the PEGMA side chains produces a monolithic supramolecular network (TopoE) that prevents the dissolution of PEDOT:PSS in contact with water or other solvents.

Thanks to the optimized polyrotaxane (PR) structure, the resulting TopoE film showed an electrical conductivity two orders of magnitude higher than the pristine PEDOT:PSS. TopoE film treated with acid (TopoE-S) further increased electrical conductivity to ~2700 S cm^{-1}. The superior electrical performances of TopoE-S also showed in its lower electrochemical impedance in all frequency ranges, outperforming cracked gold, which is one of the best stretchable bioelectrode materials.

The high charge storage capacity as well as the high charge-injection capability of PEDOT:PSS allows effective electrical stimulation with low voltage. To customize this material for biological applications, the scientists developed a photolithography-based micro-fabrication process for making high-density stretchable electrode arrays with high uniformity. As a result of the low modulus of the entire electrode array, its conformal capability towards biological surfaces such as human skin allows reliable electrical functioning even when the devices are patterned at small sizes.

Lead author, Dr. Yuanwen Jiang (left) and team leader, Prof. Zhenan Bao (right)

Soft bioelectronics enables stable monitoring and stimulation of biological activities

The soft and elastic electrode array can remain in stable contact with skin over moving muscles, thus enabling surface electromyography (sEMG) recording with high signal fidelity and spatial resolution. Efficient collection of sEMG signals can be realized even on a soft-bodied creature like an octopus whose muscles can undergo much larger deformations than those of a human. In comparison, rigid electrodes based on polyimide substrates were unable to follow the tissue contour under continuous muscle movement, yielding low signal-to-noise ratio.

To demonstrate high-precision bioelectronic stimulation, the researchers implanted the electrode array onto the brainstem of a rat, which formed intimate contact with the floor of its fourth ventricle. Then they successfully stimulated organ-specific activities by delivering current pulses to individual electrodes. The precise stimulation was confirmed by initiating movement at the tongue, whisker, and neck regions. Further, the researchers constructed high-resolution activation maps correlating with individual nuclei that independently controlled the activities of different nerves, while showing that the strength of the evoked signal in the muscle could be modulated by the intensity of bioelectronic stimulus. Notably, the soft electrode exhibited much better biocompatibility and negligible damage of brain tissue, whereas other rigid probes made on polyimide substrates caused severe damage to the fragile brainstem.

In summary, the researchers rationally designed a topological supramolecular network for PEDOT:PSS, to simultaneously achieve both high stretchability and conductivity well suited for bioelectronic applications. The team further developed compatible micro-fabrication process to create high-density electrode arrays that can consistently monitor and precisely stimulate biological activities.

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