

Mechanically invariant molecular bioelectronics

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The past decade has witnessed a paradigm shift in bioelectronics from rigid devices toward soft, tissue-like systems capable of intimate integration with the human body. Advances in stretchable conductors, flexible substrates, and mechanically adaptive material systems have enabled wearable and implantable platforms that conform to dynamic biological tissues while continuously monitoring physiological signals.¹ Such developments have transformed electrophysiological sensing, allowing long-term acquisition of electrical signals including electrocardiograms, electromyograms, and neural activity. Yet despite these remarkable achievements, the realization of continuous molecular monitoring remains considerably more challenging.

Chemical biomarkers often provide more direct and clinically actionable information than physical signals alone. Dynamic changes in metabolites, ions, inflammatory mediators, and oxidative stress markers can reveal disease progression, therapeutic response, and physiological adaptation before macroscopic symptoms emerge. Consequently, electrochemical biosensors have attracted substantial interest as a route toward precision

medicine and closed-loop healthcare.² However, unlike electrical sensing, electrochemical signal transduction depends on a delicate interplay among electron transport, ion diffusion, interfacial charge-transfer kinetics, and molecular recognition processes.³ These coupled mechanisms are highly susceptible to mechanical deformation. Stretching can alter electrode morphology, disrupt conductive pathways, modify electrochemically active surface area, and induce cracking or delamination of functional coatings, ultimately leading to signal drift and loss of analytical fidelity.

In a recent study published in *Science*, Xu and colleagues address this longstanding challenge through the development of a strain-resilient intrinsically stretchable interface for electrochemical sensing (SIRES) (Figure 1A).⁴ Rather than treating mechanical robustness and electrochemical performance as separate objectives, the authors establish a unified materials-and-circuit framework that preserves electrochemical fidelity under extreme deformation. The central insight is that strain-induced sensing degradation results from the coupled evolution of electrical and electrochemical proper-

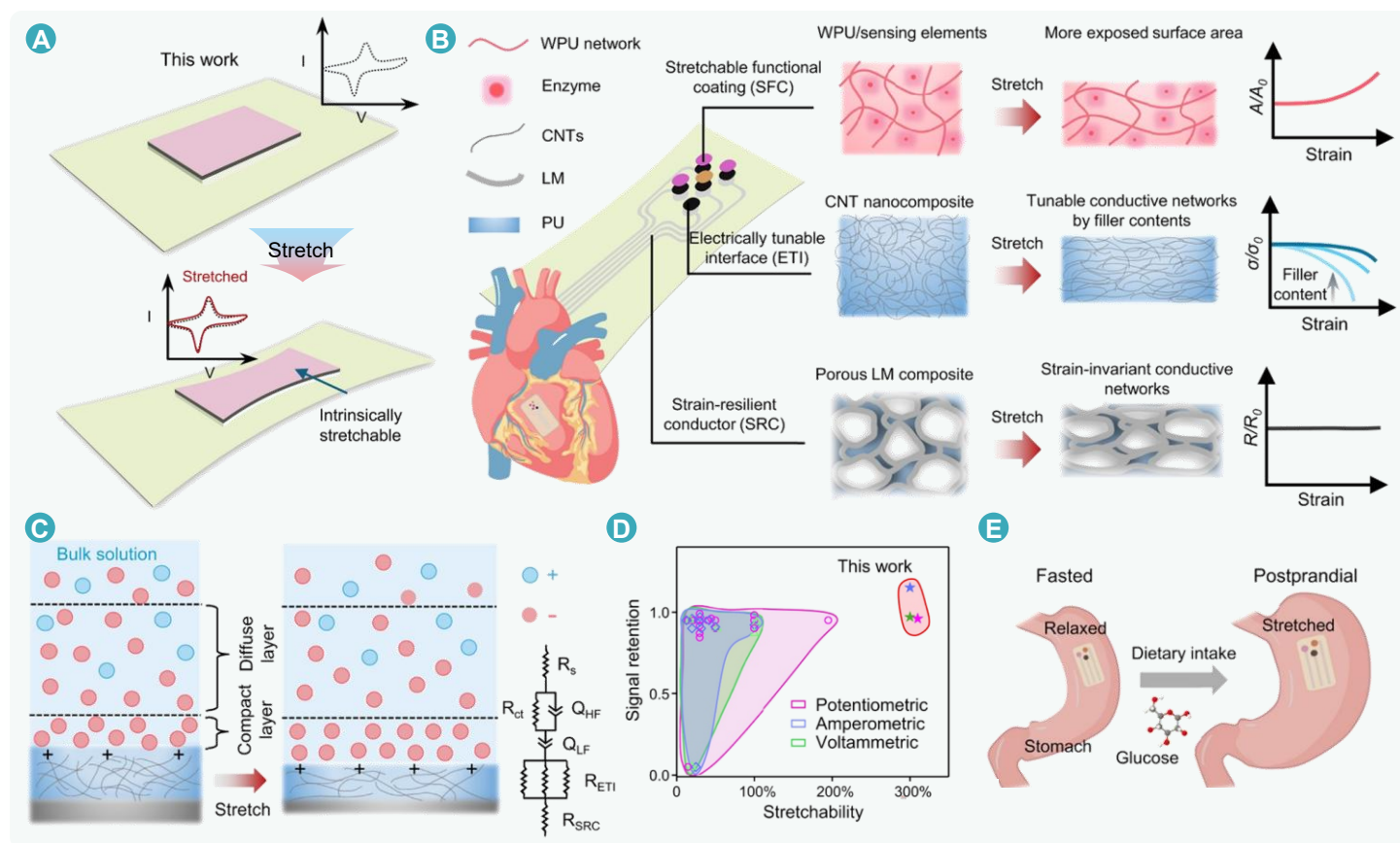


Figure 1. Mechanically invariant electrochemical biointerfaces for molecular sensing (A) Conceptual illustration of the strain-resilient intrinsically stretchable interface for electrochemical sensing (SIRES). (B) Trilayer architecture consisting of a strain-resilient conductor (SRC), an electrically tunable interface (ETI), and a stretchable functional coating (SFC). (C) Working mechanism based on balancing strain-induced changes in interconnect resistance and electrochemically active surface area to maintain stable electrochemical responses. (D) Quantitative comparison between SIRES and previously reported stretchable electrochemical sensors. (E) Example implantable application in which SIRES conforms to the stomach and enables molecular sensing under dynamic organ deformation. (Reproduced with permission.⁴ Copyright 2026, the American Association for the Advancement of Science)

ties rather than from a single failure mechanism. Conventional approaches have largely focused on improving the stretchability of conductors through serpentine geometries, nanomaterial composites, or liquid-metal interconnects. Although these strategies can preserve electrical conductivity, they do not necessarily stabilize electrochemical performance because deformation simultaneously changes resistance, active surface area, and interfacial kinetics.

Xu et al. address this challenge through a trilayer architecture consisting of a strain-resilient conductor (SRC), an electrically tunable interface (ETI), and a stretchable functional coating (SFC) (Figure 1B). The SRC employs a phase-separated liquid-metal/polyurethane composite that maintains efficient charge transport under large tensile strains. A carbon nanotube–polyurethane ETI functions as an electromechanical regulator by balancing strain-induced resistance increases with changes in electrochemically active surface area. The outer SFC layer stabilizes bioactive sensing chemistries and prevents fracture of functional coatings during repeated deformation. Importantly, the significance of this design extends beyond materials selection. Through a modified Randles equivalent circuit framework (Figure 1C), the authors show that electrochemical stability can be achieved by maintaining an approximately constant total resistance during stretching, transforming deformation from a detrimental factor into an engineered parameter.

The resulting performance demonstrates the effectiveness of this design strategy. SIREs maintains stable voltammetric, amperometric, and potentiometric responses under strains of up to 300%, representing a level of deformation tolerance that exceeds the requirements of many physiological environments (Figure 1D). Compared with conventional stretchable electrochemical interfaces, which often experience signal distortion as deformation alters electrical resistance and electrochemical properties, SIREs highlights the importance of simultaneously engineering mechanical and electrochemical stability. The platform retains performance after 1000 of deformation cycles while resisting interfacial delamination and crack propagation. The use of a common polyurethane matrix across functional layers further improves interface integration. In addition, SIREs supports multiple sensing modalities, including voltammetric detection of uric acid, amperometric sensing of glucose, lactate, and hydrogen peroxide, and potentiometric pH monitoring. The incorporation of intrinsically stretchable reference and counter electrodes enables fully integrated electrochemical measurements, suggesting broad applicability beyond a single sensing target.

Beyond its materials innovation, an important aspect of the study is its demonstration of SIREs across both wearable and implantable bioelectronic scenarios, which present distinct engineering requirements. For wearable applications, the primary requirements are mechanical conformity, user comfort, and stable sensing during body motion and skin deformation. SIREs-based sweat-monitoring systems address these demands by maintaining conformal contact while continuously tracking glucose, lactate, and pH during exercise. In contrast, implantable applications require long-term compatibility with dynamic internal environments, where tissues undergo complex deformation and interact continuously with biological fluids (Figure 1E). By maintaining stable molecular readouts on dynamically moving organs, SIREs expands the possibility of electrochemical sensing beyond conventional epidermal platforms toward deeper physiological monitoring.

Despite its considerable strengths, several challenges remain before clinical translation becomes feasible.⁵ Long-term stability over months or years, rather than days or weeks, remains to be established. Biofouling, immune responses, and degradation of sensing chemistries continue to pose signifi-

cant barriers for chronic implantation. Beyond mechanical invariance, achieving truly continuous molecular bioelectronics will require reversible sensing operation over extended periods. Although SIREs effectively stabilizes electrochemical responses against mechanical deformation, long-term monitoring demands reversibility at multiple levels: mechanical recovery after repeated deformation, electrical reversibility of strain-dependent resistance changes, electrochemical reversibility of interfacial charge-transfer processes, and molecular reversibility of analyte recognition events. Failures in these processes may manifest as baseline drift, hysteresis, receptor or enzyme saturation, irreversible fouling, and progressive sensitivity loss. Future mechanically invariant biointerfaces will therefore need to integrate reversible sensing chemistries with antifouling coatings, regenerable recognition elements, dynamic hydrogel interfaces, self-calibrating circuits, electrochemical surface renewal strategies, or ratiometric measurement schemes. Addressing these challenges will be essential for translating mechanically robust molecular sensors into reliable long-term monitoring platforms.

Furthermore, physiological environments impose mechanical and biochemical challenges that extend beyond simple tensile deformation. Implantable interfaces may experience combined compression, shear, torsion, cyclic loading, and tissue sliding during normal organ function. Meanwhile, the surrounding biological environment contains proteins, enzymes, mucus, inflammatory mediators, and fluctuating chemical conditions that can alter electrode interfaces and sensing performance. Although SIREs establishes an important strategy for preserving electrochemical fidelity under large tensile strain, future studies will need to evaluate whether similar principles can maintain performance under these coupled mechanical and biochemical stresses. Addressing these complex conditions will be critical for advancing strain-resilient biointerfaces toward chronic implantation and clinical applications.

Despite these challenges, SIREs provides a valuable framework for advancing soft bioelectronic systems. The ability to engineer mechanically invariant electrochemical interfaces creates opportunities for integrating affinity-based biosensors, wireless communication, machine-learning-assisted analytics, and therapeutic actuators toward closed-loop bioelectronic medicine. More broadly, this work reflects a transition from monitoring physical signals to decoding biochemical information directly at the tissue interface. By establishing a strategy for strain-resilient molecular sensing while highlighting the remaining challenges of reversible and long-term operation, Xu and colleagues advance the development of adaptive biointerfaces capable of functioning within complex physiological environments.

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DECLARATION OF INTERESTS

The authors declare no competing interests.