

RESEARCH ARTICLE

Kinetic-Locked Fiber Networks Enable Anti-Fouling, Mechanically Robust Zwitterionic Hydrogels

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ABSTRACT

Zwitterionic hydrogels possess exceptional antifouling characteristics and biocompatibility, but their weak mechanical strength limits implantable applications. Existing enhancement strategies either introduce non-zwitterionic phases that compromise antifouling performance or employ zwitterionic fillers that still fall short of achieving high mechanical robustness. Here, we present a kinetic-locking strategy to fabricate strong, antifouling zwitterionic composite fibers for hydrogel reinforcement. Co-dissolving hydrophilic zwitterionic and hydrophobic polymers followed by electrospinning kinetically traps molecular entanglement via ultrafast solvent evaporation, suppressing thermodynamic phase separation. The kinetically preserved molecular entanglement maintains the antifouling properties of the zwitterionic component while enabling the hydrophobic polymer to contribute substantial mechanical strength. In addition, the entanglement and electrostatic interaction between the fibers and the zwitterionic matrix form a robust interface for efficient load transfer. This approach is broadly applicable across polymer systems, producing hydrogels that integrate high tensile strength (2.48 MPa), extreme stretchability (1040%), and remarkable fracture toughness (27.76 kJ m⁻²—a three-order-of-magnitude improvement over pure zwitterionic hydrogels) without sacrificing antifouling properties. These advances support reliable long-term in vivo electromyography recording and effective sciatic nerve stimulation. The work establishes kinetic locking as a general design paradigm to overcome the strength–antifouling trade-off in zwitterionic hydrogels, advancing durable, long-term implantable bioelectronics.

1 | Introduction

Implantable devices face a critical challenge of biofouling—a process initiated by the non-specific adsorption of cells, proteins, and microorganisms, which leads to infection, immune

responses, signal interference, and impaired tissue regeneration, with treatment costs exceeding \$3 billion annually in the United States alone [1, 2]. Zwitterionic hydrogels have emerged as leading antifouling candidates due to their balanced density of oppositely charged groups, which form a tightly bound hydration

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layer that blocks non-specific adhesion [3, 4]. However, this same hydration layer also suppresses interchain interactions, making these hydrogels intrinsically weak and brittle [5]. Under physiological conditions, the anti-polyelectrolyte effect further disrupts interchain ionic associations, exacerbating mechanical degradation and causing severe swelling [6, 7]. These limitations significantly hinder their application in dynamic, load-bearing implants [8], such as electromyography (EMG) electrodes and sciatic nerve guidance conduits (NGCs), which require mechanical properties comparable to those of muscle (tensile stress: 10 kPa–1 MPa; elongation at break: 100%–200%) [9, 10] or nerve tissue (tensile stress: 1 MPa–7 MPa; elongation at break: 20%–80%) [11, 12]. For long-term in vivo performance, zwitterionic hydrogels should ideally achieve a tensile strength >1 MPa, elongation at break >200%, and fracture toughness >5 kJ m⁻² (comparable to that of human tissues: 0.5–5 kJ m⁻²), while retaining their antifouling and anti-swelling characteristics [13, 14].

To enhance mechanical properties, substantial efforts have focused on increasing crosslinking density through copolymerization with additional crosslinking domains [15, 16] or incorporating high-strength fillers [17, 18]. However, because proteins and cells preferentially adhere to non-antifouling hydrophobic regions, introducing these non-zwitterionic phases inevitably triggers adhesion cascades and degrades overall antifouling performance [19]. Alternatively, strategies that rely exclusively on zwitterionic components—such as constructing secondary or tertiary zwitterionic networks or reinforcing with pure zwitterionic particles or fibers [20, 21] offer excellent biocompatibility but deliver only modest mechanical gains due to the intrinsic mechanical weakness of zwitterionic polymers. As a result, these systems typically exhibit fracture strengths below 1 MPa, limited stretchability (<200%), and low fracture toughness (<5 kJ m⁻²) [22]. These limitations point to a fundamental materials challenge: how to introduce mechanically robust components into zwitterionic hydrogels while preventing the formation of hydrophobic domains that compromise their antifouling properties.

Here, we address this challenge by exploiting the electrospinning-induced kinetic locking effect to regulate phase separation in zwitterionic/hydrophobic composite fibers. By selecting an appropriate solvent system, zwitterionic polymers and high-strength hydrophobic polymers can be co-dissolved into a homogeneous solution with entangled chain conformations [23]. Although these thermodynamically incompatible components would normally evolve toward a phase-separated equilibrium state, kinetic effects are equally important [24]. During electrospinning, the submicron jet possesses an extremely high surface-area-to-volume ratio, causing rapid solvent evaporation and a consequent sharp increase in viscosity [25]. This sudden rise in viscosity significantly reduces the diffusion coefficient of polymer chains, effectively freezing the segmental motion and molecular chain configuration at the nanoscale, thereby locking the two polymers into a relatively uniform, entangled chain network [26]. This kinetically preserved molecular entanglement suppresses the formation of large hydrophobic domains—thereby minimizing bioadhesion—while simultaneously retaining the mechanical reinforcement imparted by the hydrophobic chains. The resulting fibers, which subsequently serve as reinforcing scaffolds, are infiltrated with a zwitterionic monomer solution and

polymerized in situ. During this step, zwitterionic chains within the fibers and the surrounding matrix further interpenetrate, yielding strong interfacial adhesion essential for efficient load transfer (Figure 1a). Using this approach, we achieve hydrogels that combine antifouling properties with exceptional mechanical performance—including a tensile strength of 2.48 MPa, an elongation at break of 1040%, and a fracture toughness of 27.76 kJ m⁻²—far exceeding the performance of existing zwitterionic hydrogels. The resulting materials exhibit minimal swelling, strong antifouling behavior, and robust long-term stability, enabling reliable long-term in vivo operation, such as high-fidelity EMG signal acquisition and sciatic nerve stimulation (Figure 1b–d).

2 | Results and Discussion

2.1 | Fabrication and Characterization of Fibers and Composite Hydrogels

Zwitterionic fiber-reinforced hydrogels were synthesized through a four-step process using hydrophilic poly(sulfobetaine) (PSB) and hydrophobic polycaprolactone (PCL) as representative building blocks. PSB, synthesized via free-radical polymerization without any chemical crosslinkers, was co-dissolved with PCL in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) to form a 2 wt% homogeneous solution (Figures 2a–I and S1), followed by electrospinning to yield PSB/PCL composite fibers (Figure 2a–II). HFIP, as a mutual good solvent for both polymers, enables intimate molecular mixing. During electrospinning, the ultra-fast evaporation of the solvent kinetically suppressed phase separation between PSB and PCL, resulting in a disordered PSB/PCL fiber membrane with a highly entangled molecular chain network within the fibers. Subsequently, a zwitterionic monomer solution of [2-(methacryloyloxy) ethyl]dimethyl-(3-sulfopropyl) ammonium hydroxide (SBMA) was drop-cast onto the fiber membrane. Rapid absorption, driven by the fibers' large surface area and their hydrophilicity, enabled deep monomer infiltration (Figure 2a–III). Upon polymerization, the newly formed PSB chains became entangled and crosslinked with those inside the fibers, establishing a robust fiber-matrix interfacial bonding. Collectively, kinetic-locking within the fibers and interfacial entanglement at the fiber-matrix interface yielded a mechanically integrated fiber-reinforced zwitterionic hydrogel. (Figure 2a–IV).

The intra-fiber molecular chain entanglement is essential for both morphological stability and hydrophilicity of the fibers. As shown in Figure 2b, pure PSB fibers, owing to their superhydrophilicity and lack of cross-linking, rapidly absorbed water and completely lost their fibrous structure, whereas pure PCL fibers retained their structure but remained hydrophobic. In contrast, PSB/PCL composite fibers exhibited a unique combination of rapid wettability and structural stability. At an optimized PSB/PCL mass ratio of 1:1, the fibers wetted fully within 2 s and maintained their morphology after 3 h of immersion (Figures 2b,c and S2). Scanning electron microscopy (SEM) elemental mapping further revealed stable nitrogen signals on the fiber surface before and after immersion (Figure 2d). Even after soaking the PSB/PCL fiber membrane in phosphate-buffered saline (PBS) for 1 month, the elemental nitrogen and sulfur contents remained

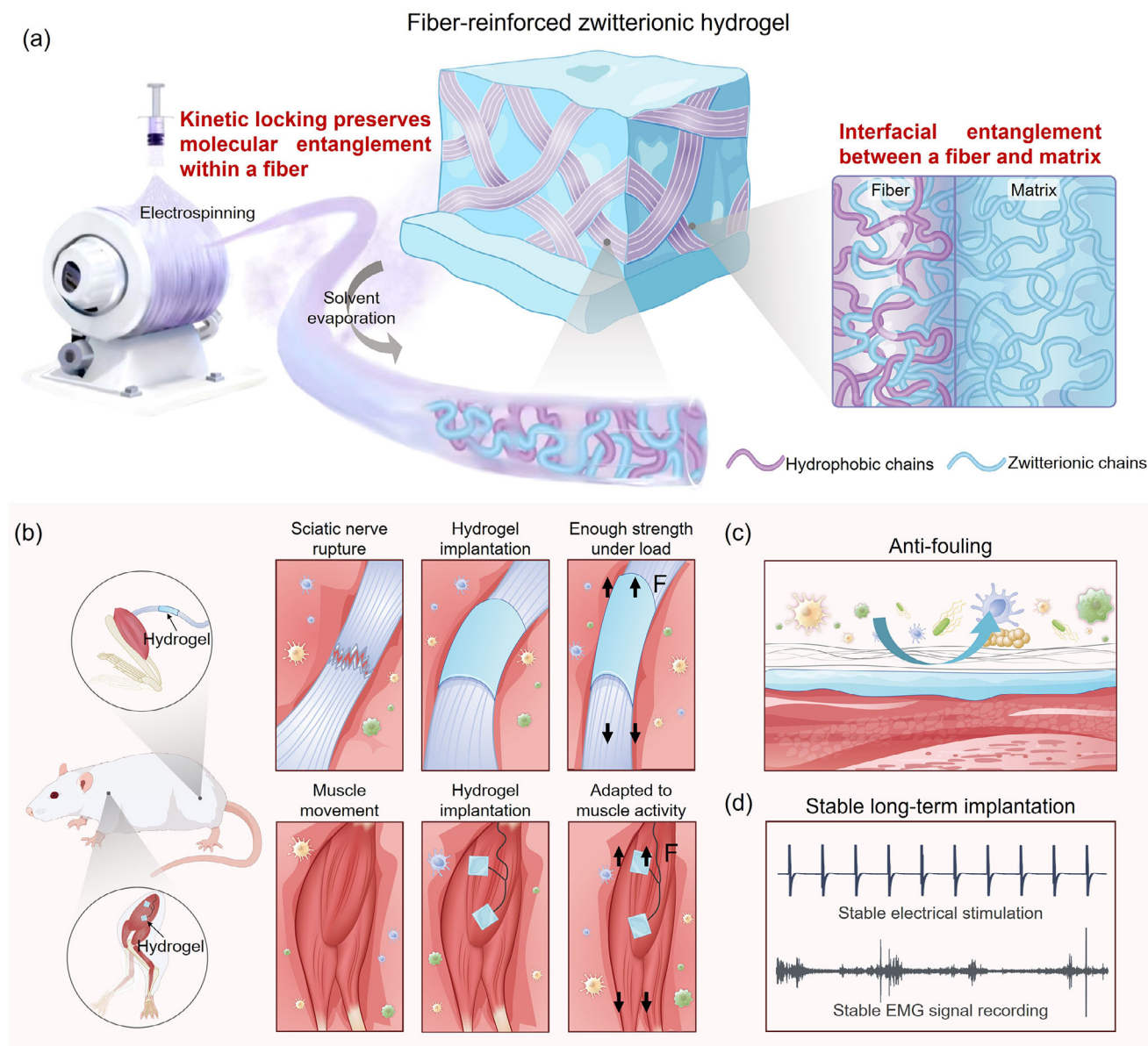


FIGURE 1 | Schematic illustration of the molecular structure and functional advantages of zwitterionic fiber-reinforced hydrogels. (a) The rapid solvent evaporation kinetically locks zwitterionic and hydrophobic chains into a uniform, interpenetrating network within the fiber, while interfacial locking via chain entanglement with the matrix enables efficient load transfer. (b) The hydrogel is designed for EMG recording and sciatic nerve electrical stimulation, offering suitable mechanical strength to withstand tissue deformation. (c) The implanted hydrogel effectively prevents the adhesion of proteins, cells, and biological factors. (d) These optimal mechanical and antifouling properties enabled reliable long-term electrical signal transmission.

stable without significant decrease, and no distinct characteristic peaks of PSB were observed in the attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy (Figures S3 and S4). Furthermore, the change in tensile strength before and after soaking was less than 6%, all of which confirms that chain entanglement effectively suppressed PSB dissolution (Figure S5). After SBMA polymerization, the fibrous microstructure was preserved within the hydrogel matrix, thereby resulting in an opaque appearance due to light scattering at fiber–matrix interfaces (Figures 2e and S6). Increasing the PSB content induced swelling or dissolution, while reducing it diminished antifouling properties; thus, the PSB/PCL (1:1) ratio was selected for subsequent studies.

The degree of intra-fiber chain entanglement also critically governs mechanical performance. Composite fibers incorporating PSB with low, medium, and high molecular weights (labeled PSB(L)/PCL, PSB(M)/PCL, and PSB(H)/PCL, respectively; Table S1) were prepared to systematically evaluate this effect. Longer PSB chains are expected to exhibit more entanglement, thereby imparting higher mechanical reinforcement [27]. Indeed, PSB(H)/PCL exhibited 2.6-, 2.3-, and 5.4-fold increases in tensile strength, elongation at break, and strain energy, respectively, compared to PSB(L)/PCL (Figure 2f,g). Unlike neat PCL fiber membranes, which fractured at low strain due to chain rigidity and limited mobility, the incorporation of flexible PSB chains markedly enhanced stretchability (from 121% to

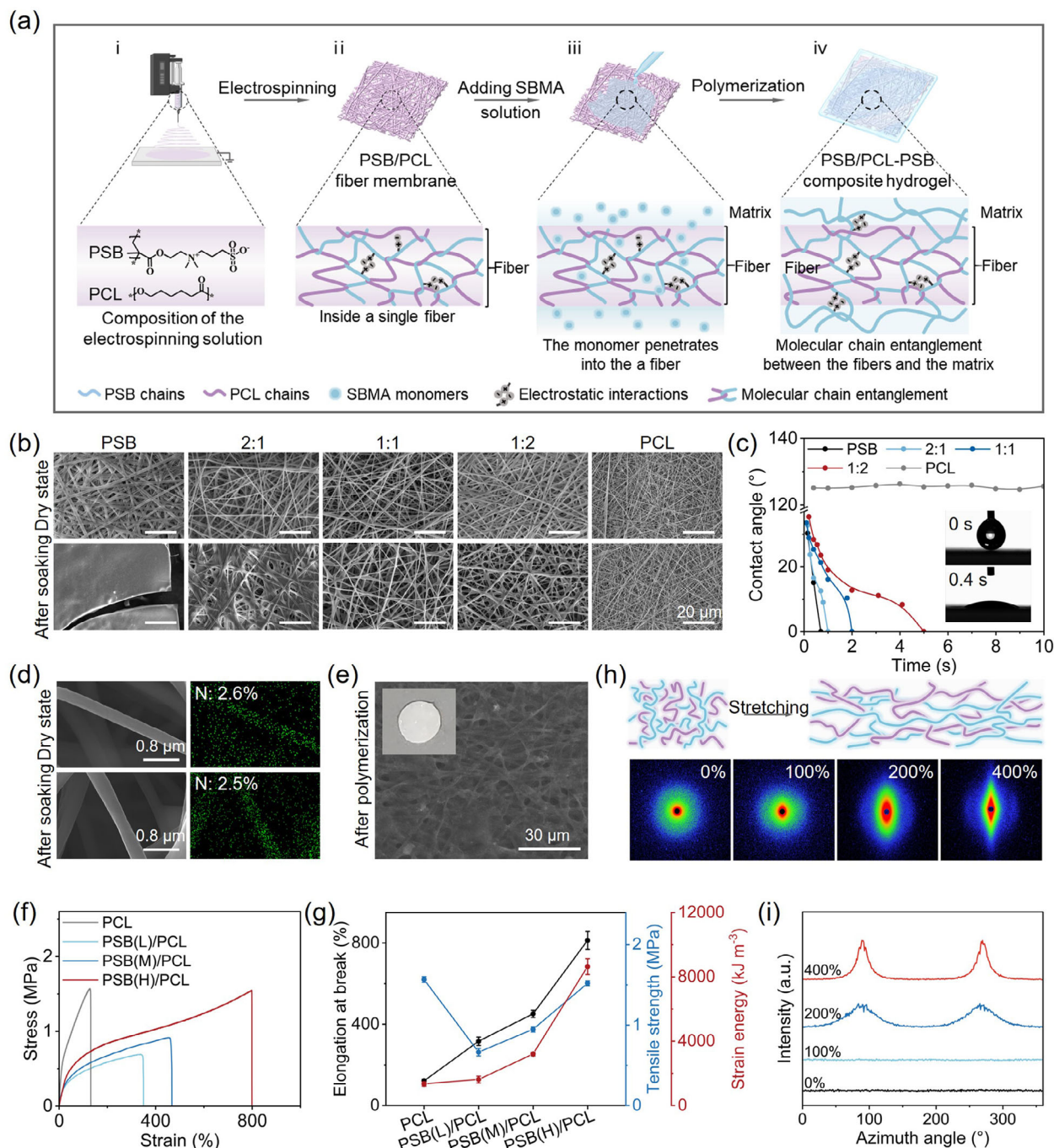


FIGURE 2 | Fabrication of the hydrogel and molecular entanglement within the composite fibers. (a) Schematic illustration of the fabrication process for the fiber-reinforced composite hydrogel. (b) SEM images of PSB, PCL, and PSB/PCL fiber membranes (mass ratios of 2:1, 1:1, and 1:2) in the dry state and after soaking in water for 3 h. (c) Time-dependent water contact angles of different fiber membranes. The inset images show the contact angle of PSB/PCL (1:1) fibers. (d) SEM images and corresponding elemental maps of PSB/PCL fibers before and after soaking. (e) Environmental SEM (ESEM) image of the composite hydrogel after polymerization. The inset shows the macroscopic appearance of the hydrogel. (f) Tensile stress–strain curves of PSB/PCL fibers with varying degrees of entanglement. (g) Tensile strength, elongation at break, and strain energy of different fiber membranes. (h) 2D SAXS patterns and (i) corresponding azimuthally integrated intensity distribution curves of PSB/PCL fibers under stretching.

813%) without compromising tensile strength at higher levels of entanglement. The entanglement nodes act as “sliding physical cross-linking points,” which not only distribute stress to enhance strength but also allow chain segments to slip and rearrange to improve ductility. In situ uniaxial tensile two-dimensional small-angle x-ray scattering (2D SAXS) further

revealed cooperative chain orientation via chain entanglement during deformation. Under stretching, PSB and PCL chains underwent synchronized alignment, transforming the initially isotropic scattering pattern into spindle-shaped features with sharp orientation peaks (Figure 2h,i). Considering the excessive viscosity encountered during electrospinning at even higher

PSB molecular weight, PSB(H)/PCL was used for hydrogel fabrication.

Hydrophilic zwitterionic chains and hydrophobic polymer chains typically undergo spontaneous phase separation driven by chemical incompatibility and entropy reduction [28]. However, rapid quenching can kinetically trap the system in a homogeneously mixed state [24]. Electrospinning represents an extreme quenching process, in which submicron jets experience ultrafast solvent evaporation due to their enormous specific surface area, leading to a sharp rise in viscosity. According to the Stokes–Einstein relation ($D \propto 1/\eta$) [29], the drastic viscosity (η) increase strongly suppresses polymer chain diffusion (D), thereby freezing the entangled molecular state at the nanoscale. This kinetically trapped entanglement further restricts chain mobility during subsequent immersion in monomer solution and matrix polymerization, effectively suppressing phase separation. The resulting structurally homogeneous fibers prevent the formation of hydrophobic domains that would otherwise disrupt surface hydration and trigger biofouling [30, 31].

To quantitatively elucidate the role of polymer mobility in phase separation dynamics, we employed a phase-field model based on the Cahn–Hilliard equation to simulate interface evolution under different kinetic conditions (Note S1). Two distinct polymer migration rates were introduced to mimic slow and fast solvent evaporation. A global phase index was defined to quantify the degree of phase separation. Under slow evaporation, the phase difference increased rapidly, driving fast growth of thermodynamically incompatible domains that ultimately coalesced into large, island-like equilibrium structures (Figure 3a,b, Movie S1). In contrast, rapid evaporation markedly retarded phase separation, confirming that solvent evaporation rate is a dominant factor governing polymer mobility and phase separation kinetics (Movie S2).

These predictions were experimentally validated by comparing spin-coated films prepared at different spinning speeds with electrospun fibers. Increasing spinning speed produced thinner films with faster solvent evaporation, leading to progressively reduced phase-separated domain sizes as revealed by SAXS (Figure 3c). In contrast, electrospun PSB/PCL fiber membranes exhibited no detectable phase separation either in the dry state or after prolonged soaking in water, indicating nanoscale mixing of PSB and PCL chains (Figure 3d). Transmission electron microscopy (TEM) elemental mapping further confirmed a homogeneous sulfur distribution across individual fiber cross-sections (Figure 3e–f). Consistent with the structural homogeneity, protein adsorption decreased monotonically with suppressed phase separation. As shown in Figure 3f, all PSB/PCL samples exhibited reduced protein adhesion compared with the non-fouling PCL membranes (control group), while the antifouling performance became more pronounced with increasing structural homogeneity. The electrospun fibers with the most homogeneous structure displayed the lowest levels of protein adhesion. Specifically, relative to pure PCL membranes, the bovine serum albumin (BSA) and lysozyme (Ly) adsorption on electrospun PSB/PCL nanofiber membranes decreased to 19.6% and 23.8% of those on pure PCL membranes, respectively (Figure 3f). A similar trend was observed in antibacterial adhesion assays, in which bacterial attachment diminished as the domain size of hydrophobic regions

decreased, further demonstrating the excellent antifouling efficacy of the PSB/PCL fibers (Figure S7). Therefore, by eliminating hydrophobic domains that typically serve as strong adsorption sites, the uniform nanoscale entanglements establish a continuous hydration barrier, which is critical for achieving potent antifouling performance.

Finally, the fibers and matrix are mechanically coupled through interfacial molecular chain entanglement and electrostatic interactions, enabling efficient load transfer in the fiber-reinforced hydrogel (PSB/PCL-PSB). TEM elemental mapping revealed a substantial increase in sulfur content inside the fibers after hydrogel formation, from 5.0% to 13.0%, confirming deep infiltration of SBMA monomers (Figure 3e and Table S2). Fiber pull-out tests were further conducted to quantify interfacial strength (Figures 3g and S8). A composite hydrogel prepared with pure PCL fibers served as the control. During fiber extraction, the stress initially increased, reached a maximum and then decreased upon interfacial debonding. Due to the hydrophobic nature of PCL fibers, SBMA infiltration was limited, resulting in poor interfacial locking and a low peak strength of 0.44 MPa. In contrast, PSB/PCL fibers exhibited a pronounced locking effect, yielding a peak pull-out strength of 2.22 MPa. These results demonstrate that the composite hydrogel achieves robust mechanical integration through a dual-locking mechanism operating both within the fibers and at the fiber–matrix interface.

2.2 | Mechanical Properties

The incorporation of PSB/PCL fibers significantly enhanced the mechanical properties of the PSB hydrogels. This remarkable improvement originated from the intrinsic strength of the PSB/PCL fibers (Figure 4a) coupled with efficient fiber–matrix interfacial locking (Figure 4b), which enabled effective load transfer and alleviated stress concentration. Compared to the pure PSB hydrogel, the strength of the PSB/PCL-PSB composite hydrogel fabricated by combining the strongest fiber and interfacial locking increased from 0.03 to 2.48 MPa, representing an 83-fold improvement. Notably, unlike previously reported composite hydrogels—where elongation at break typically decreased significantly with increasing filler content—the PSB/PCL-PSB composite hydrogels maintained a high elongation at break (1040%). This unusual combination arises from the physically entangled PSB and PCL chains within the fibers and at the fiber–matrix interface, allowing relative chain sliding and preventing premature fracture. The robustness was visually exemplified by a thin hydrogel strip (cross section: $400 \times 400 \mu\text{m}^2$) effortlessly lifting a 2 kg kettlebell (over 1000 times the sample's mass) without damage (Figure 4c). Benchmarking against state-of-the-art zwitterionic hydrogels highlights that, while previous strategies—such as enhancing interchain interactions [15, 32–36], introducing double/multiple networks [21, 37–41], or adding rigid fillers [42–47]—often strengthen hydrogels at the cost of stretchability, the kinetic-locking strategy uniquely bypasses this trade-off (Figure 4d). Moreover, the tensile strength of the present zwitterionic hydrogel nearly doubles the maximum value reported in previous studies.

Fracture toughness was equally remarkable. Pure PSB hydrogel fractured rapidly under pure shear loading (crack initiation at

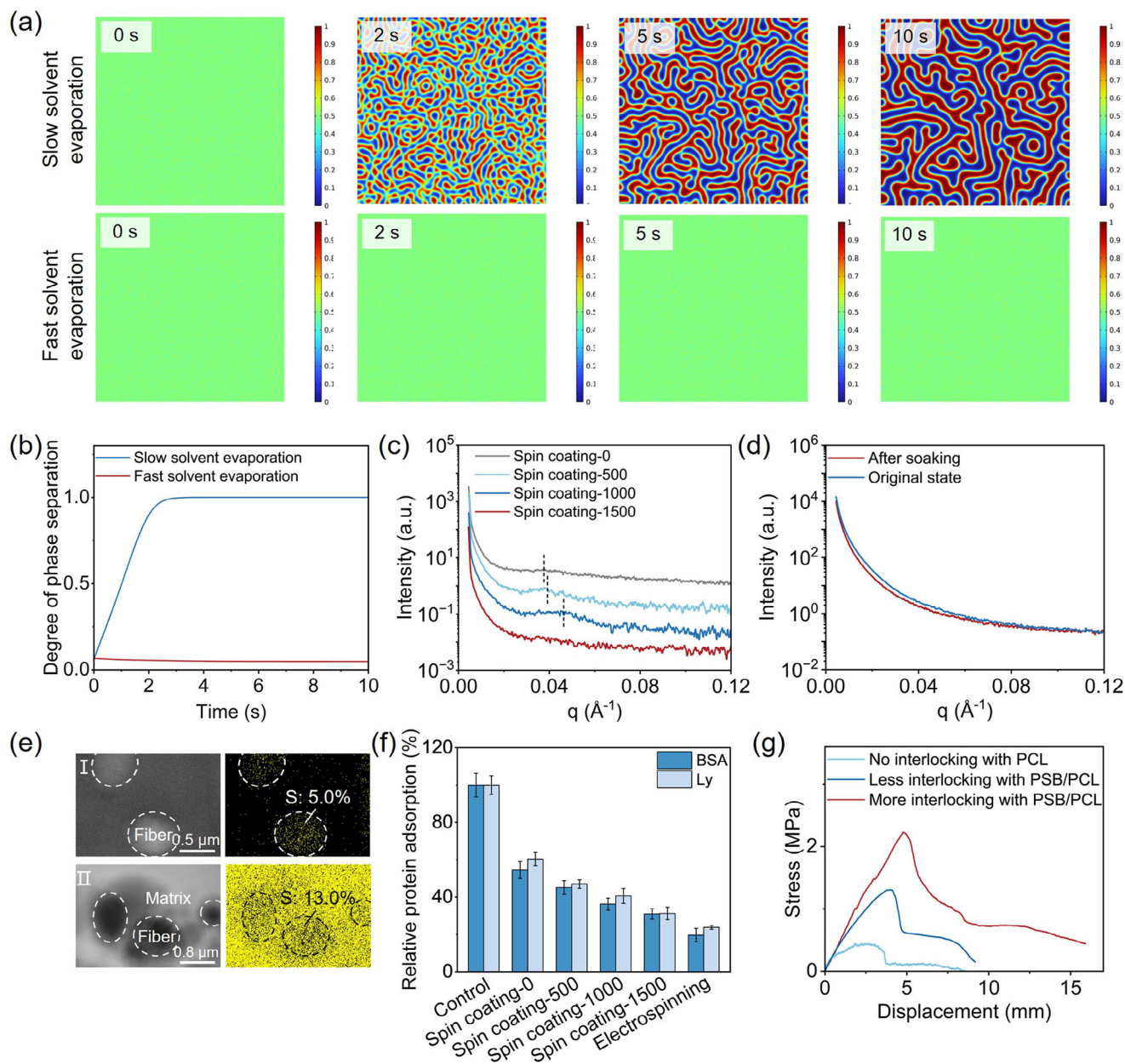


FIGURE 3 | Kinetic-locking and phase separation suppression in PSB/PCL fibers. (a) Phase-field simulation showing the time evolution of phase separation in a two-phase system under different kinetic conditions. (b) Simulated time-dependent variation of the difference between the maximum and minimum values of the global phase index. (c) 1D intensity profile obtained from the radial integration of the 2D SAXS patterns of spin-coated PSB/PCL membranes prepared at different rotational speeds. (d) 1D intensity profile obtained from the radial integration of the 2D SAXS patterns of PSB/PCL fiber membranes in the dry state and after soaking in water. (e) Cross-sectional TEM images and corresponding elemental mapping of (I) PSB/PCL fiber membranes and (II) the PSB/PCL-PSB composite hydrogel. (f) Relative protein (BSA and Ly) adsorption on PSB/PCL films prepared by spin coating at different rotational speeds and by electrospinning. (g) Fiber pull-out tests quantifying the strength of fiber-matrix interfacial locking.

67% strain, fracture at 78%, fracture toughness: 0.036 kJ m^{-2}), whereas PSB/PCL-PSB composites blunted crack tips via fiber reinforcement and interfacial adhesion (Figure 4e,f). The crack initiated up to 180% strain, extended longitudinally with minimal lateral spread, and fractured at 800% strain, yielding a fracture toughness of 27.76 kJ m^{-2} —nearly 800-fold higher than pure PSB (Figure S9, Supporting Information). This value not only surpasses zwitterionic hydrogels reported to date but also exhibits advantages over other types of toughened hydrogels (Figure 4g). The fatigue crack propagation resistance of the PSB/PCL-PSB

composite hydrogel was evaluated under cyclic tensile loading. As shown in Figure 4h, the hydrogel demonstrated exceptional resistance to crack growth, with only minimal propagation observed even at 160% strain. At a higher strain of 220%, the crack extended to 5 mm during the initial 100 cycles. Thereafter, crack progression slowed significantly, and the sample endured 2000 cycles without rupture. These results indicate that the PSB/PCL-PSB composite hydrogel possesses outstanding fatigue crack resistance. The high toughness and fatigue resistance can be explained by the generalized Lake-Thomas model proposed

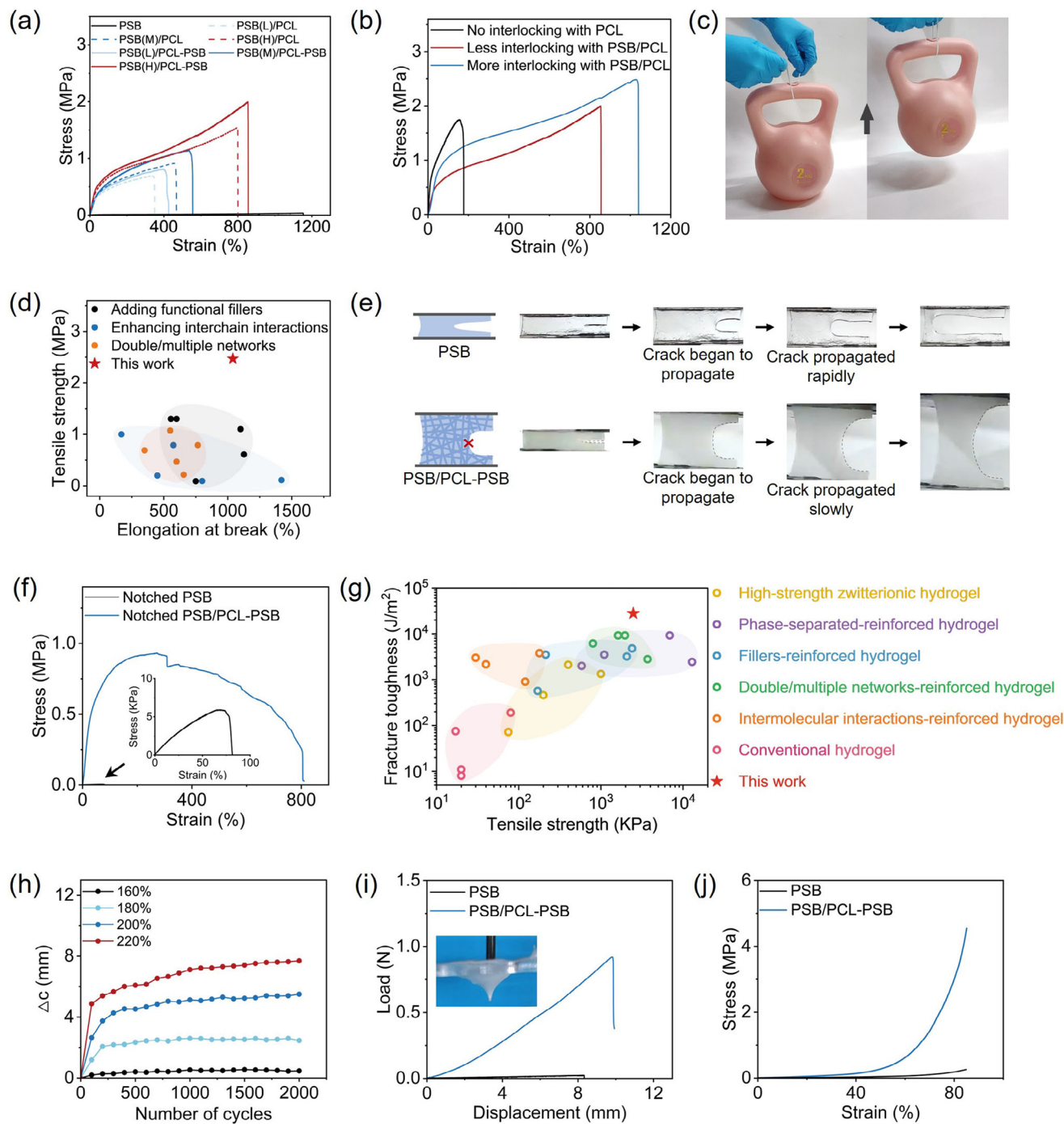


FIGURE 4 | Mechanical properties of the PSB/PCL-PSB composite hydrogels. (a) Tensile stress-strain curves for PSB/PCL fibers with varying degrees of entanglement, their corresponding composite hydrogels, and pure PSB hydrogels. (b) Tensile stress-strain curves of composite hydrogels reinforced with PCL fibers versus PSB/PCL fibers, showing premature failure due to weak interfacial locking and enhanced strength/ductility from strong interfacial locking, respectively. (c) Photographs demonstrating the mechanical robustness of a composite hydrogel strip lifting a 2 kg kettlebell. (d) Comparative analysis of tensile strength and elongation at break against previously reported high-strength zwitterionic hydrogels. (e) Crack propagation in notched hydrogel samples during tensile testing, with corresponding schematic illustrations. (f) Tensile stress-strain response of notched samples. (g) Comparison of fracture toughness with other toughened hydrogel systems, including high-strength zwitterionic hydrogels [5, 15, 50], phase-separated reinforced hydrogels [23, 51–53], filler-reinforced hydrogels [54–57], double/multiple network hydrogels [58–60], intermolecular interaction-enhanced hydrogels [61–64], and conventional hydrogels. (h) Fatigue crack growth (notch length vs. number of cycles) of the composite hydrogel under cyclic loading. (i) Puncture resistance demonstrated by force-displacement curves, with an inset showing puncture test visualization. (j) Compression stress-strain curve of PSB and PSB/PCL-PSB composite hydrogel.

recently [48, 49]. For a composite hydrogel with a strong fiber-matrix interface, the energy needed to advance the crack per unit area equals the covalent energy of a layer of fibers per unit area, which is proportional to the fiber length, the number of fibers per unit volume, and the energy required to fracture a single fiber. As the PCL/PSB fibers are continuous with centimeter-level length and possess high strain energy, a dense PCL/PSB fiber network contributes to the outstanding toughness and fatigue resistance.

The fiber-reinforced design also enhanced the puncture and compressive performance. The puncture resistance increased from 0.02 N (pure PSB) to 0.91 N, while the compressive strength improved from 0.25 to 4.6 MPa (Figures 4i,j, and S10, Supporting Information). These results establish the PSB/PCL-PSB hydrogel as a new class of zwitterionic composite that simultaneously achieves high strength, large stretchability, and exceptional toughness through a scalable kinetic-locking fiber-reinforcement strategy.

This kinetic-locking strategy and fiber-matrix interface locking can be widely applied to various fiber-matrix systems. For example, thermoplastic polyurethane (TPU) was employed to replace PCL, yielding PSB/TPU fiber-reinforced PSB hydrogels (PSB/TPU-PSB). Similarly, 2-methacryloyloxyethyl phosphorylcholine (PMPC) polymer was used to replace PSB, producing PMPC/PCL-PMPC hydrogels (Figure S11). Both systems displayed mechanical enhancements similar to those of the PSB/PCL-PSB hydrogels, including high strength (Figure S12), high fracture toughness (Figure S13), and high puncture resistance (Figure S14). These results underscore the generality of the kinetic-locking fiber strategy for constructing mechanically robust zwitterionic hydrogels.

2.3 | Anti-Swelling, Antifouling, and Biocompatible Properties

We next evaluated the long-term stability and biocompatibility of the composite hydrogels under physiological conditions, using the PSB/PCL-PSB system as an example. Conventional zwitterionic hydrogels often suffer from pronounced swelling in physiological media due to the anti-polyelectrolyte effect. In contrast, the kinetic locking of fibers and the fiber-matrix molecular chain entanglement locking design effectively restricted chain separation, providing exceptional anti-swelling properties. As expected, pure PSB hydrogels exhibited drastic volume expansion in PBS solution, with an equilibrium swelling ratio (ESR) of 595%. By comparison, the ESR of the PSB/PCL-PSB composite hydrogel was less than 8%, highlighting its remarkable swelling resistance (Figure 5a,b). Consequently, the composite hydrogel maintained its mechanical integrity in physiological environments: while the tensile strength of the pure PSB hydrogel dropped from 0.03 to 0.01 MPa after swelling, the PSB/PCL-PSB composite hydrogel exhibited a reduction in tensile strength of less than 3% (Figure 5c).

Long-term implantation further requires excellent resistance to biofouling. The PSB/PCL-PSB hydrogel, consisting of zwitterionic-based composite fibers and a zwitterionic matrix, demonstrated outstanding antifouling performance. Here, a

widely used biocompatible hydrogel polyacrylamide (PAAm) incorporating PCL fibers (PCL-PAAm) without antifouling capacity was prepared as a control. Protein adsorption tests revealed reductions of 86.1% (BSA) and 81.8% (lysozyme) relative to the control, values comparable to those of pure PSB hydrogel (Figure 5d). A cell adhesion assay further confirmed this advantage: after 24 h of contact with L929 cells, dense cell attachment was observed on the PCL-PAAm surface, whereas only sparse adhesion occurred on the PSB and PSB/PCL-PSB hydrogels (Figure 5e). Importantly, the antifouling capacity extended to bacterial resistance. Following 4 h of incubation in suspensions of *Escherichia coli* or *Staphylococcus aureus*, the PSB/PCL-PSB composite hydrogel displayed minimal bacterial adhesion, with quantitative adhesion rates of only 1.2% and 6.0%, respectively (Figure 5f,g). Such strong antifouling behavior is expected to significantly reduce post-implantation infection risks.

Beyond antifouling, biocompatibility is critical for clinical translation. The group without any added hydrogels served as the control. Live-dead staining and methylthiazolyldiphenyl-tetrazolium bromide (MTT) assays confirmed that all hydrogels supported cell viability and proliferation, showing no cytotoxicity (Figures 5h and S15). Hemolysis assays further revealed a hemolysis rate below 1% for PSB/PCL-PSB, demonstrating excellent blood compatibility (Figure S16). To further evaluate in vivo biocompatibility, the hydrogels were subcutaneously implanted into Sprague–Dawley (SD) rats for 4 weeks. It was found that the PSB/PCL-PSB composite hydrogel caused minimal inflammatory response at the implantation site, and there were no significant changes in hematological parameters compared to normal rats (Figures 5i and S17). Furthermore, histological examination of major organs (heart, kidneys, lungs, spleen, and liver) revealed no evidence of inflammatory response or pathological abnormalities (Figure 5j). Collectively, these results underscore that the PSB/PCL-PSB composite hydrogel combines exceptional anti-swelling, antifouling, and biocompatibility, making it a promising candidate for long-term in vivo applications.

2.4 | In Vivo Electrical Signal Recording and Neural Stimulation

In terms of electrical properties, the anionic and cationic groups in zwitterionic hydrogels act as natural ionic anchoring centers, promoting electrolyte dissociation and thereby increasing the concentration of free ions. Under the influence of an electric field, ions can conduct electricity through mechanisms such as hopping migration. Therefore, zwitterionic hydrogels show broad research prospects in fields such as nerve repair and regeneration, implantable bioelectronic devices, and wearable sensors [65]. For instance, in amyotrophic lateral sclerosis (ALS), implanted EMG electrodes enable continuous and accurate monitoring of muscle activity and disease progression over extended periods [66]. Similarly, implanted NGCs must maintain long-term stability to facilitate nerve regeneration and prevent muscle atrophy through sustained electrical stimulation [67]. However, conventional implantable electrodes often experience signal degradation over time due to fibrotic encapsulation triggered by non-specific protein and cell adhesion, leading to elevated interfacial impedance and unstable signal transmission. The PSB/PCL-PSB

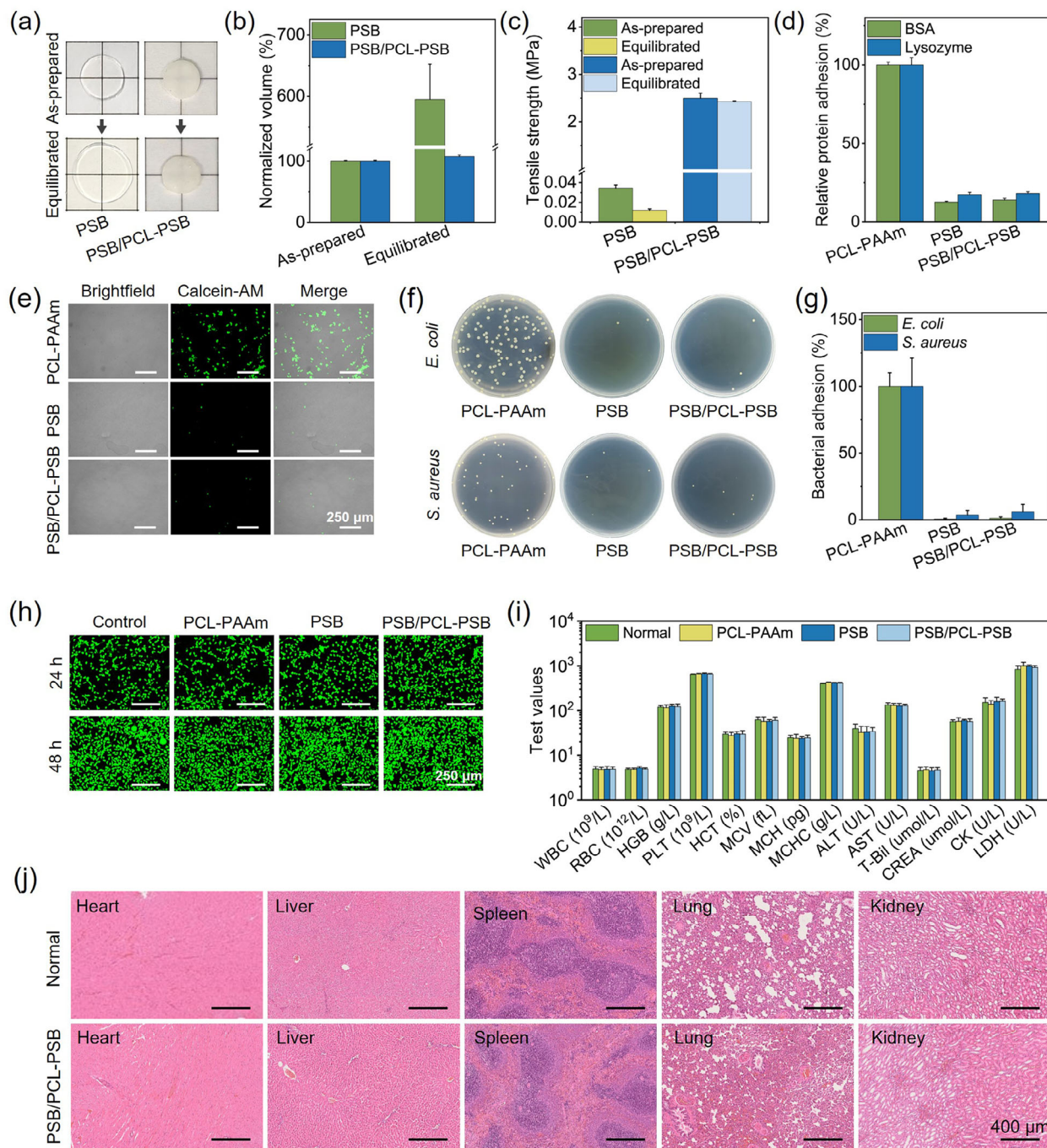


FIGURE 5 | Anti-swelling, antifouling, and biocompatible properties of PSB/PCL-PSB composite hydrogels. (a) Optical photographs of pure PSB hydrogel and PSB/PCL-PSB composite hydrogel in the as-prepared state and after equilibration in 0.01 M PBS. (b) Comparison of the ESR of hydrogels before and after reaching equilibrium in 0.01 M PBS. (c) Tensile strength of hydrogels before and after reaching equilibrium in 0.01 M PBS. (d) Relative adhesion amounts of hydrogels to BSA and lysozyme. (e) The adhesion of L929 cells on hydrogel surfaces (scale bar = 250 μm). (f) *E. coli* and *S. aureus* adhesion on different samples. (g) Statistics on bacterial adhesion rates of different samples. (h) Live/dead staining of L929 cells co-cultured with hydrogels for 24 and 48 h (green, calcein-AM for live cells; red, propidium iodide for dead cells; scale bar, 250 μm). (i) Blood routine and blood biochemistry analysis after 4 weeks of in vivo implantation of different samples. (j) H&E staining images of the heart, liver, spleen, lungs, and kidneys after 4 weeks of in vivo implantation of PSB/PCL-PSB composite hydrogel (scale bar = 400 μm).

composite hydrogels overcome these challenges by combining mechanical robustness, intrinsic conductivity, and exceptional antifouling properties, thereby ensuring stable long-term signal transmission. Four-probe conductivity measurements confirmed its effective conductivity (0.14 S m^{-1}) (Figure S18). The relative resistance changes $\Delta R/R_0$ increased by less than 0.37 under 50%

strain, while it remained stable after 500 stretching cycles at the same strain (Figure S19). The material also withstood various complex deformations, including repeated bending (Figure S20), twisting, and knotting (Figure S21), demonstrating its potential for reliable long-term performance in dynamic physiological environments.

To validate the in vivo electrophysiological recording capability, the composite hydrogel electrodes were implanted in rat neck muscles for long-term EMG monitoring (Figure 6a). The EMG setup consisted of two hydrogel electrodes (with internal circular wires), ground electrodes, and a head connector (Figure S22). Postoperative CT imaging confirmed the proper placement of the electrodes and stable connection to the head connector (Figure 6b), enabling reliable recording of movement-generated electrical signals during activities such as walking and grasping. PCL-PAAm hydrogel and PSB hydrogel were used as control electrodes (Figure S23). While all three electrode types successfully recorded EMG signals at week 0, the PSB hydrogel electrodes failed within 1 week due to mechanical fracture (Figure 6c,d-I), while PCL-PAAm electrodes ceased functioning after week 3 as a result of fibrotic encapsulation and adhesion to surrounding tissue (Figure 6d-II). In contrast, the PSB/PCL-PSB electrodes maintained robust signal acquisition for 4 weeks with consistent noise levels, mechanical integrity, and minimal fouling (Figures 6d-III and S24), underscoring their durability for long-term monitoring.

Beyond EMG recording, the PSB/PCL-PSB hydrogel was engineered into an NGC to bridge a 5 mm sciatic nerve defect (Figure 6e,f). Following transection, the leg's motor function was lost, but was restored through neural reconnection using the PSB/PCL-PSB composite hydrogel (Figure 6g). The rat's leg began to move at a voltage of 1 V, and when the voltage was increased to 2 V, the bending angle increased from 3° to 21° (Figure 6h). Long-term signal transmission was evaluated over 4 weeks by applying 1 V stimulation (50 ms duration rectangular pulses) at the upper end of the hydrogel and recording responses via a distal cuff electrode (Figure S25). The intact sciatic nerve produced a ~10 mV signal, which disappeared upon transection. Reconnection with the hydrogel restored signal amplitude and response time to normal levels (Figure 6i). In a 4-week implantation experiment, the long-term signal conduction efficiency of the hydrogel was verified by comparing the amplitude of electrical signals. Due to inadequate mechanical strength, the PSB hydrogel could not be securely fixed to the sciatic nerve and was excluded from further evaluation (Figure S26). At 1 week post-implantation, the PCL-PAAm group exhibited a 16% reduction in signal amplitude versus only 4% for PSB/PCL-PSB. From week 2 to 4, PCL-PAAm signals dropped by ~50% (to 5.1 mV), whereas the PSB/PCL-PSB hydrogel retained 94% of its initial signal fidelity (Figure 6k,l). This difference reflected acute inflammatory responses triggered by surgical nerve/tissue trauma, where cellular infiltration increased interfacial impedance and tissue adhesion.

We further evaluated the long-term inflammatory response and fibrotic deposition following implantation of the material in vivo. Over time, the PCL-PAAm composite hydrogel was gradually embedded by inflammatory cells and adhered to the surrounding tissue, with a fibrotic deposition layer approximately 293.5 ± 50.7 μm thick formed between the material and the nerve (Figures 6j, S27, and S28). In contrast, due to its excellent antifouling properties, the PSB/PCL-PSB hydrogel exhibited the least signs of adhesion within 4 weeks and did not form a noticeable fibrotic deposition (23.1 ± 4.5 μm), with a reduction in fibrosis of nearly 92% (Figures 6j, S28, and S29). This is attributed to the synergistic antifouling properties of the PSB/PCL fibrous membrane and the PSB matrix. Immunofluorescence

staining further demonstrated that the PSB/PCL-PSB composite hydrogel exhibited the lowest inflammatory response and fibrotic deposition 1 month after in vivo implantation, confirming its potential as a long-term, stable in vivo implantable electrode for signal transmission (Figure S30).

3 | Conclusion

In summary, this work presents a fiber-reinforced composite hydrogel enabled by a kinetic-locking strategy, in which electrospinning resolves the intrinsic incompatibility between hydrophilic zwitterionic chains and hydrophobic reinforcing polymers within the fibers. In the PSB/PCL-PSB system, rapid solvent evaporation kinetically traps PSB and PCL chains in a uniformly entangled state, endowing the fibers with the rare combination of high mechanical strength and robust antifouling functionality. Concurrently, molecular interfacial locking between the PSB matrix and PSB/PCL fibers ensures efficient stress transfer and homogeneous load dissipation throughout the composite. As a result, the composite hydrogel exhibits an exceptional mechanical profile, including high tensile strength (2.48 MPa), large elongation at break (1040%), high fracture toughness (27.76 kJ m⁻²), and outstanding puncture resistance. Notably, this combination of kinetic-locking strategy and interfacial locking is broadly adaptable; substituting either the zwitterionic or hydrophobic polymer components in the fibers and matrix preserves the reinforcement effect, making it promising for customization according to different application requirements. Beyond mechanical robustness, the dual-locking architecture suppresses excessive swelling and maintains long-term mechanical stability under physiological conditions. Moreover, the excellent antifouling properties of the zwitterionic components in the hydrogel significantly inhibit the adhesion of proteins, cells, and other biomolecules. Together, these attributes establish kinetically locked fiber-reinforced zwitterionic hydrogels as a versatile materials platform for long-term biointegrated electronics and soft implants, including chronic in vivo electromyogram recording and electrical stimulation for peripheral nerve repair.

4 | Experimental Section

4.1 | Materials

PCL (Mn = 80000), acrylamide (AAm, 99.8%), HFIP (99.5%), ammonium persulfate (APS, 98%), *N,N'*-methylenebisacrylamide (MBA, 99%), and *N,N,N',N'*-tetramethylethylenediamine (TEMED, 99%) were purchased from Aladdin (Shanghai, China). SBMA (95%) and MPC (97%) were obtained from Sigma-Aldrich (USA). TPU (1180A) was received from BASF (Germany). All the chemicals were used as purchased without further purification.

4.2 | Preparation of PSB/PCL Membrane

Zwitterionic PSB was synthesized through the free-radical polymerization of SBMA. Different fiber membranes—including PSB, PSB/PCL blends at ratios of 2:1, 1:1, and 1:2, along with pure PCL—were prepared via electrospinning. Initially, PSB and PCL were dissolved separately in HFIP and stirred for 12 h to obtain

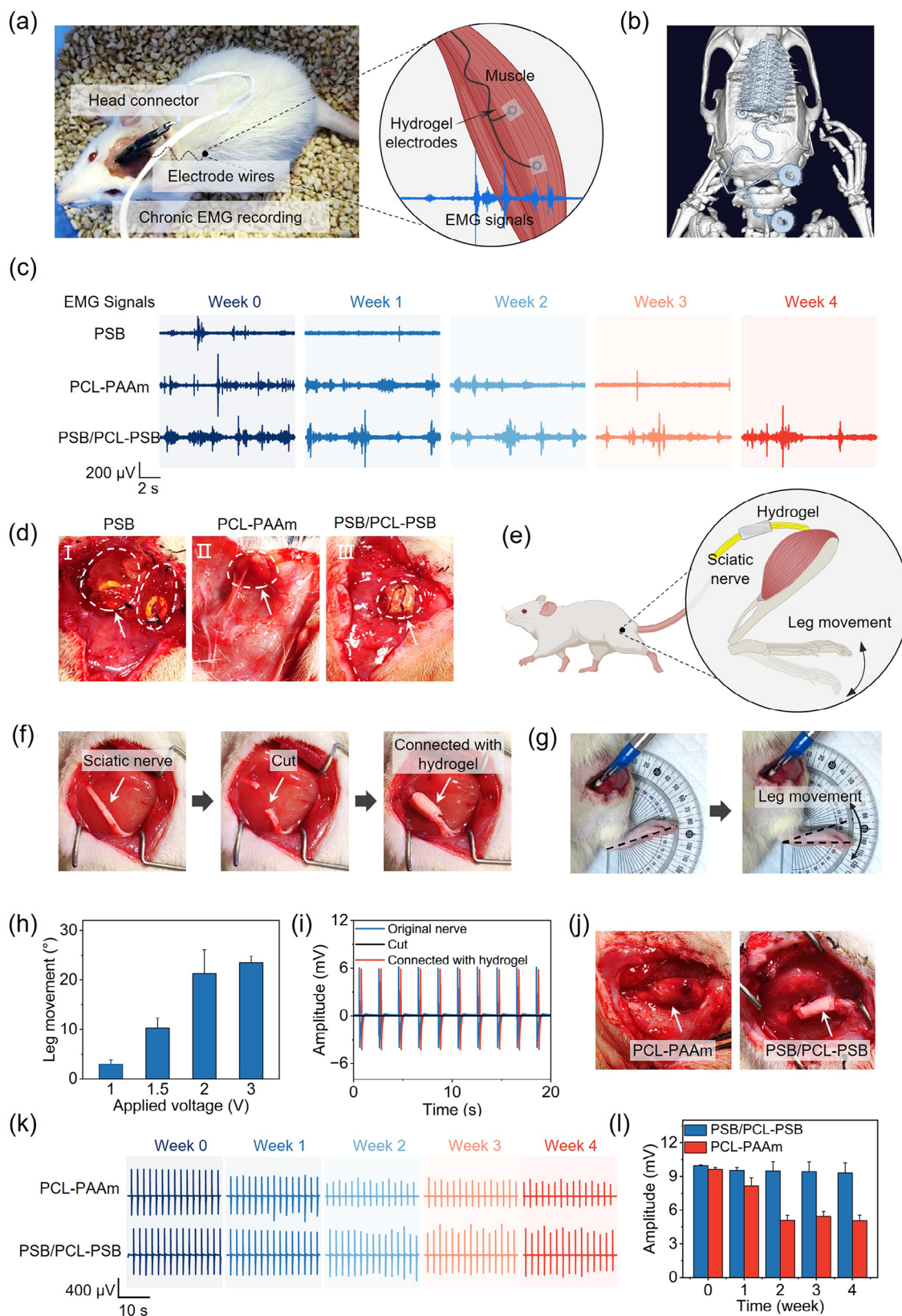


FIGURE 6 | Long-term in vivo evaluation of PSB/PCL-PSB composite hydrogel electrodes for electrophysiological signal recording and stimulation. (a) Photograph of rat models and schematic illustration of the hydrogel electrode setup for long-term EMG recording. (b) CT image confirming proper in vivo placement of the implanted EMG device. (c) EMG signals recorded by different hydrogel electrodes within 4 weeks of implantation. (d) Representative images showing: (I) mechanical failure and detachment of PSB hydrogel electrode after 1 week of implantation; (II) tissue encapsulation and adhesion of PCL-PAAm composite hydrogel after 3 weeks of implantation; (III) sustained integrity and non-adhesiveness of PSB/PCL-PSB composite hydrogel over 4 weeks of implantation. (e) The schematic illustration of electrical stimulation on a rat using the hydrogel electrode.

transparent solutions with a concentration of 2 wt%. The spinning solution was then loaded into a syringe equipped with a 22-G blunt-tip metal needle. Electrospinning was carried out at a temperature of $25 \pm 5^\circ\text{C}$ and a relative humidity of $50 \pm 5\%$, with an applied voltage of 8 kV, a flow rate of 2 mL h^{-1} , a working distance of 10 cm, and a drum collector speed of 140 rpm. For pure PSB, a solution concentration of 2 wt% and a voltage of 8 kV were used, whereas for pure PCL, the concentration was increased to 10 wt% with a voltage of 15 kV. All other spinning parameters remained consistent with those described above. Finally, the as-spun membranes with different blend ratios were dried in an oven at 40°C for 2 h to remove any residual solvent.

Subsequently, PSB fibers with varying degrees of entanglement with PCL were fabricated using PSB polymers of different molecular weights. These molecular weights were controlled by varying the amount of APS initiator used during polymerization—specifically, 0.2, 1, and 2 mol% relative to the SBMA monomer. This yielded fibers with low, medium, and high entanglement levels, designated as PSB(L)/PCL, PSB(M)/PCL, and PSB(H)/PCL fibers, respectively. The spinning solution was prepared by co-dissolving the synthesized PSB and PCL in HFIP, and electrospinning was performed under the same conditions as previously described.

4.3 | Preparation of the PSB/PCL-PSB Composite Hydrogel

The SBMA pre-gel solution was prepared by uniformly mixing 2 mL of H_2O , 2.3 g of SBMA, 90 μL of APS (20 mg mL^{-1}), 120 μL of MBA (10 mg mL^{-1}), and 25 μL of TEMED (10% v/v). A PSB/PCL fiber membrane ($10 \times 10\text{ cm}^2$) was placed in a mold and layered to a thickness of 0.5 mm, while the SBMA pre-gel solution was continuously added during the process. Polymerization was conducted at 25°C for 4 h to obtain the PSB/PCL-PSB composite hydrogel. A pure PSB hydrogel without fiber membranes served as the control.

To evaluate fiber-matrix locking strength, PSB(H)/PCL fibers were embedded into PSB matrices of varying molecular weights to form composite hydrogels with distinct interfacial strengths. For comparison, a control group was prepared using PCL fibers instead of PSB(H)/PCL fibers to obtain composite hydrogels lacking interfacial locking with the matrix.

To demonstrate the versatility of the method, hydrophobic TPU and hydrophilic PMPC were used to replace PCL and PSB, respectively. The hydrophilic and hydrophobic polymers were co-dissolved in HFIP at a 1:1 mass ratio to form a homogeneous 2 wt% solution, which was then electrospun into PSB/TPU and PMPC/PCL fiber membranes. These membranes were immersed in monomer solutions corresponding to their

respective hydrophilic components (PSB or PMPC) and polymerized to obtain PSB/TPU-PSB and PMPC/PCL-PMPC composite hydrogels.

4.4 | Characterizations

The micromorphology and elemental composition of fibrous membranes and hydrogels were examined by SEM (Zeiss Ultra 55), ESEM (Quanta 200), and energy-dispersive x-ray spectroscopy (EDS; Oxford Xplore). Cross-sectional morphology and elemental distributions of an individual fiber were analyzed by TEM (JEOL JEM-F200) and EDS. For TEM analysis, fiber membranes were resin-embedded, cured at room temperature, sectioned, and mounted on copper grids; as the resin contained nitrogen, sulfur mapping was employed. ATR-FTIR spectra were recorded on a Vertex70 Spectrometer (Bruker Germany). Optical transmittance in the 400–800 nm range was recorded using a UV-vis spectrophotometer (Lambda 950). Surface wettability was evaluated by static water contact angle measurements (OCA 15). Small-angle x-ray scattering (SAXS) was conducted on a Xeuss 2.0 system (x-ray wavelength: 0.154 nm; detector: Pilatus 3R 300K). 2D-SAXS patterns and azimuthally integrated intensity profiles of fiber membranes were collected under uniaxial tensile strains from 0% to 400%. The molecular weight of PSB was determined by gel permeation chromatography (GPC; Agilent 1260).

4.5 | Mechanical Tests

The mechanical properties of the hydrogel were evaluated using an electronic universal testing machine (CMT4304-QY). For the tensile test, hydrogel samples were molded into standard dumbbell shapes (35 mm total length, 12 mm gauge length, and 2 mm width) and stretched at a constant speed of 40 mm min^{-1} . Strain energy was calculated as the area under the stress–strain curve up to the fracture point.

For the compression test, cylindrical hydrogel samples (9 mm diameter, 5 mm height) were compressed at a rate of 1 mm min^{-1} , with a maximum compressive strain of 85%.

For the fiber pull-out test, fiber membranes were cut into rectangular strips ($30 \times 4 \times 0.2\text{ mm}^3$), adhered to non-stretchable double-sided adhesive tape, and immersed in monomer for polymerization. During testing, the fiber specimen was clamped in the upper grip of the testing machine, while the hydrogel matrix containing the fiber was secured in the lower grip. The fiber was pulled out at a speed of 10 mm min^{-1} .

For the pure shear test, hydrogel samples measuring $60 \times 20 \times 0.5\text{ mm}^3$ were prepared. The testing area between the grips was $60 \times$

(f) The schematic illustration of the sciatic nerve location, transecting the sciatic nerve, and reconnecting the disconnected nerve with PSB/PCL-PSB composite hydrogel. (g) Schematic representation of rat ankle joint movements under electrical stimulation. (h) The ankle joint movement when stimulating the sciatic nerve with a voltage of 1 V. (i) Electrical signals are recorded when the sciatic nerve is stimulated with 1 V under different conditions. (j) The photograph of the appearance of the PCL-PAAm composite hydrogel and PSB/PCL-PSB composite hydrogel 4 weeks after in vivo implantation. (k) Electrical signal amplitude recorded using different hydrogel electrodes within 4 weeks of implantation. (l) Quantitative analysis of signal amplitude changes over 4 weeks.

15 mm². A pre-crack (~15 mm long) was introduced at the edge of one sample using a blade, while the other sample remained intact. Both samples were stretched uniaxially at 20 mm min⁻¹ until failure. The elastic energy density function $w(\lambda)$ was calculated by integrating the stress-strain curve up to the maximum stretch ($\lambda_{\max}$) at crack instability propagation. Fracture toughness (I') was determined as $w(\lambda_{\max}) \times H$, where H is the sample height between the grips.

For the fatigue test, samples of the same dimensions and initial notch length as those used in the fracture toughness test were subjected to cyclic tensile loading at a speed of 10 mm min⁻¹ for 2000 cycles. The notch length was recorded throughout the cycles.

For the puncture test: A 500 μ m thick hydrogel film was secured to a circular ring fixture with an inner diameter of 10 mm. An 0.8 mm diameter stainless steel rod was then positioned above the center of the hydrogel and pressed down at a constant speed of 5 mm min⁻¹ to gradually puncture the hydrogel.

4.6 | Anti-Swelling Test

The ESR of the hydrogel relative to its initial state was determined using a dimensional measurement method. The hydrogel was molded into a disc, and its initial diameter (r_1) and height (h_1) were recorded. It was then immersed in PBS solution for two days to reach swelling equilibrium, after which the resulting diameter (r_2) and height (h_2) were measured. The ESR was calculated using Equation (1).

$$ESR(\%) = \frac{r_2^2 \times h_2}{r_1^2 \times h_1} \times 100\% \quad (1)$$

4.7 | Anti-Adhesion Tests

4.7.1 | Protein Adhesion Test

BSA and lysozyme (Ly) were employed as a model protein to evaluate protein adsorption on PSB/PCL membranes with different degrees of phase separation. The membranes were cut into circular discs (6 mm in diameter, thickness < 40 μ m) and immersed in a 5 mg/mL protein solution, followed by incubation at 37°C for 2 h. After incubation, the samples were rinsed three times with PBS and subsequently sonicated for 1 h in a 2 wt% sodium dodecyl sulfate (SDS) solution to desorb surface-bound proteins. The amount of adsorbed protein was then determined using the BCA assay according to the manufacturer's instructions, and the absorbance was measured at 562 nm. The PCL fiber membrane (without antifouling properties) served as the control group, and the absorbance value for this group was normalized to 100%. The relative protein adsorption capacity of other samples was calculated by comparing their absorbance values with that of the control group.

Using BSA and Ly as model proteins, the protein adsorption behavior on the surfaces of PSB and PSB/PCL-PSB hydrogels was evaluated. The hydrogels were cut into circular discs (6 mm in diameter, 1 mm in thickness), and the testing method was

the same as described above. Here, the PCL-PAAm composite hydrogel was used as the control group, and its absorbance value was normalized to 100%. The relative protein adsorption capacity was determined by comparing the absorbance values of the PSB and PSB/PCL-PSB hydrogels with those of the PCL-PAAm control group.

4.7.2 | Cell Adhesion Test

Sterilized hydrogels were cut into dimensions of 5 $\times$ 5 $\times$ 0.5 mm³ and added to an L929 cell suspension (1×10^5 cells mL⁻¹). PCL-PAAm composite hydrogel served as the control. After 24 and 48 h of incubation, the medium was removed, and the hydrogels were gently rinsed with PBS. The hydrogels were then transferred to new 24-well plates and incubated with 1 mL of Calcein-AM solution (diluted 1:1000) for 30 min. Subsequently, the cells were washed twice with PBS, and cell adhesion was visualized using a confocal laser scanning microscope (Leica SP8).

4.7.3 | Bacterial Adhesion Test

The antibacterial adhesion capacity of the hydrogels was evaluated using two representative bacterial strains: *E. coli* and *S. aureus*. Both strains were cultured at 37°C for 12 h and then diluted to a concentration of 1×10^5 CFU·mL⁻¹ using sterile PBS. Hydrogel samples, each 6 mm in diameter, were incubated in the diluted microbial suspensions in a 48-well culture plate at 37°C for 4 h. After incubation, the samples were gently washed three times with 1 mL of PBS and subjected to ultrasound treatment. A 100 μ L aliquot of the resulting solution was then spread onto Luria-Bertani agar plates and incubated for 12 h. The number of colonies of *E. coli* and *S. aureus* was counted, with PCL-PAAm composite hydrogel serving as the control.

4.8 | In Vitro and In Vivo Biocompatibility Tests

4.8.1 | Cell Cytotoxicity

Cell cytotoxicity was evaluated using the methylthiazolylidiphenyl-tetrazolium bromide (MTT) assay. Sterilized PSB and PSB/PCL-PSB hydrogels were cut into dimensions of 5 $\times$ 5 $\times$ 0.5 mm³ and soaked in Dulbecco's Modified Eagle Medium (DMEM) to achieve equilibrium. L929 cells were seeded into 24-well plates at a density of 1×10^5 cells mL⁻¹ and incubated overnight. The hydrogels were then added to the medium and co-incubated with the cells for 24 and 48 h. Following incubation, the hydrogels were removed, and 80 μ L of MTT solution (5 mg mL⁻¹) was added to each well and incubated for 2 h. The supernatant was carefully discarded, and 600 μ L of dimethyl sulfoxide was added to each well to dissolve the MTT-formazan crystals. The absorbance was finally measured at $\lambda = 490$ nm using a microplate reader. L929 cells cultured in DMEM without hydrogels served as the control. Cell viability (%) was calculated according to Equation (2).

$$Cell\ viability\ (\%) = \frac{A_{sample} - A_{blank}}{A_{control} - A_{blank}} \times 100\% \quad (2)$$

Calcein-AM and propidium iodide (PI) co-staining cells: L929 cells were stained with Calcein-AM and PI (1:1000) for 30 min, washed twice with PBS, and observed with a confocal laser scanning microscope.

4.8.2 | Hemocompatibility

The hydrogel samples were immersed in 1 mL of fresh sheep blood and incubated at 37°C for 6 h. After incubation, the hydrogels were removed, and the samples were centrifuged at 3000 rpm for 10 min. Sheep blood mixed with PBS and deionized water served as negative and positive controls, respectively. The absorbance of the supernatants was measured at 570 nm. The hemolysis percentage (%) was calculated using Equation (3).

$$\text{Hemolysis (\%)} = \frac{A_{\text{sample}} - A_{\text{negative}}}{A_{\text{positive}} - A_{\text{negative}}} \times 100\% \quad (3)$$

4.8.3 | In Vivo Biocompatibility

In vivo biocompatibility was assessed by implanting PSB/PCL-PSB composite hydrogel samples into the subcutaneous tissue on the backs of SD rats. After 4 weeks of implantation, the subcutaneous tissues and major organ tissues were harvested and analyzed using H&E staining. Additionally, blood samples were collected from the rats for blood biochemistry and blood routine tests.

4.9 | Electrical Test

The resistance of the hydrogel was evaluated using a universal testing machine in conjunction with an electrochemical workstation (2450). The sample was subjected to a fixed displacement rate while the resistance (R) was recorded continuously throughout the strain application. The relative change in resistance was calculated as $\Delta R/R_0$, where $\Delta R = R - R_0$, with R_0 denoting the resistance of the original hydrogel and R representing the resistance of the deformed hydrogel. Additionally, the conductivity of the hydrogel was measured using a four-probe tester (KDK-KDY-1).

4.10 | In Vivo EMG Test

The experimental subjects were SD rats (male, 8 weeks old, 180–200 g) without any disease. The rats were kept in the animal center of Beijing Institute of Nanoenergy and Nanosystems in a pathogen. General anesthesia and analgesia procedures were administered according to the Experimental Animal Guide provided by the Animal Resources Committee. All experimental procedures were reviewed and approved by the University Animal Resources Committee (2025013LZ).

The SD rats were anesthetized, and two skin incisions were made: one on the neck and another on the head. To record EMG signals, two hydrogel electrodes were implanted into the right neck muscle through the neck incision. The electrode wires were tunneled subcutaneously using blunt dissection techniques,

and the incision was sutured closed. For head fixation, a second incision was made to expose the skull. Two small holes were drilled into the skull, where anchoring screws were inserted. A head connector was then secured to the screws using bone cement, firmly attaching the plastic connector to the skull. After recovery, the head connector was connected to the Micro-4 system (Cambridge Electronic Design Limited) to record EMG signals as the animal moved freely within its cage.

4.11 | In Vivo Sciatic Nerve Stimulation

SD rats were used to create a model of sciatic nerve defect. The rats were first anesthetized, and their legs were shaved. Access to the sciatic nerve was achieved by carefully dissecting the lateral femoral muscle and the biceps femoris muscle, which were then severed to create a 5 mm gap in the nerve. The damaged sciatic nerve was bridged using a hydrogel (500 μm thick) and secured in place with sutures. For electrical stimulation, an isolated waveform generator (DG1022), a double-hook electrode, a cuff electrode, and a protractor were employed to measure and record the angle of ankle flexion. To evaluate the signal transmission efficiency of the hydrogel, double-hook electrodes were positioned at the upper end of the hydrogel for stimulation, while cuff electrodes were placed at the lower end to capture the resulting signals.

One month after surgery, sciatic nerve tissue was harvested, fixed in 4% paraformaldehyde for 24 h, dehydrated in a gradient of ethanol, cleared with xylene, and embedded in paraffin. The tissue was sectioned into 5- μm -thick slices and stained with H&E, Masson's, and Sirius Red to assess inflammation and fibrosis. Immunofluorescence staining for TNF- α and COL1A1 was also performed. Fluorescence intensity was quantified using ImageJ and normalized to the control group.

4.12 | Statistics and Reproducibility

All experiments were repeated independently with similar results at least three times.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supporting File 1: adma74810-sup-0001-SuppMat.docx.

Supporting File 2: adma74810-sup-0002-MovieS1.mp4.

Supporting File 3: adma74810-sup-0003-MovieS2.mp4.