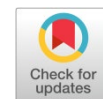


Available online at www.synsint.com

Synthesis and Sintering

ISSN 2564-0186 (Print), ISSN 2564-0194 (Online)



Perspective

From self-healing surfaces to living interfaces: A material–cell biology perspective on next-generation biomaterials

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ABSTRACT

Self-healing surfaces are undergoing a fundamental transition from passive materials that merely repair cracks toward active interfaces capable of sensing, responding, and restoring function within complex biological environments. This perspective proposes a shift from conventional crack-repairing materials to bioadaptive self-healing interfaces, in which dynamic material chemistry is integrated with cellular and molecular processes. We examine how dynamic covalent and supramolecular networks, nanocomposites, hydrogels, and stimuli-responsive materials can be coupled with cell-material interactions, extracellular matrix (ECM) remodeling, mechanotransduction, redox regulation, immune signaling, and tissue regeneration. Particular attention is given to the distinction between structural healing and biological or functional recovery, highlighting that closure of a crack or recovery of mechanical strength does not necessarily indicate restoration of the original biointerface. On this basis, we propose a multidimensional framework encompassing geometrical, mechanical, chemical, biological, and functional healing, together with a damage repair biology evaluation strategy that compares pristine, damaged, and healed interfaces. Emerging concepts including ECM-inspired networks, cell-interactive hydrogels, conductive and antibacterial self-healing surfaces, and stimuli-responsive biointerfaces are discussed as routes toward adaptive materials that can dynamically communicate with surrounding cells. Finally, a research roadmap is proposed for developing multifunctional surfaces capable of sensing environmental changes, reorganizing their molecular architecture, restoring interfacial properties, and regulating cellular responses. This perspective positions self-healing interfaces as dynamic communication layers between engineered materials and living systems, providing a framework for the next generation of regenerative and biofunctional surfaces.

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KEYWORDS

Self-healing materials
Bioadaptive interfaces
Dynamic polymer networks
Cell-material interactions
Tissue regeneration



1. Introduction

Surfaces represent the primary interface through which engineered materials interact with their surrounding environments. Surface damage caused by mechanical abrasion and scratching, as well as exposure to corrosive media, can compromise material integrity and progressively impair functional performance before substantial degradation of the

bulk material occurs [1–8]. Such damage is particularly important in protective polymeric coatings, where surface defects may disrupt the barrier function and expose the underlying substrate to corrosive agents. Beyond corrosion protection, preserving surface integrity is also essential for maintaining the mechanical, adhesive, electrical, and biological performance of functional polymeric materials. These considerations have motivated growing interest in self-healing

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Received 2 June 2026; Received in revised form 27 September 2026; Accepted 27 September 2026.

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<https://doi.org/10.53063/synsint.2026.63352>

materials that can repair surface damage and potentially extend service life by restoring material continuity and functionality. Conventional coatings generally protect an underlying substrate by acting as a passive barrier against environmental exposure. However, the formation of cracks or other defects can compromise this protective barrier, potentially accelerating localized degradation. Self-healing materials are designed to address this limitation through mechanisms that enable the recovery of damaged structures or functions. Depending on the material design, healing may occur through intrinsic mechanisms or extrinsic healing agents, and may be triggered by damage or external stimuli, or proceed autonomously under suitable conditions [1–5]. Recent studies have demonstrated self-healing capabilities across a broad range of material systems, including polymeric protective coatings, superhydrophobic surfaces, conductive hydrogels for wearable sensing, flexible bioelectronic materials, and biomedical hydrogels designed for tissue repair and regeneration [3–10]. Self-healing materials are commonly designed using two broad strategies: extrinsic and intrinsic approaches. In extrinsic systems, healing agents incorporated into the material are released or activated in response to damage, facilitating the repair of cracks or other defects. In contrast, intrinsic self-healing relies on reversible interactions or dynamic bonds within the material network, which enable damaged regions to reconnect under suitable conditions. These interactions may include dynamic covalent bonds, hydrogen bonding, and ionic interactions, depending on the material composition and design. Such mechanisms have been investigated in polymeric coatings and hydrogels, where they contribute to the recovery of structural integrity and functional performance [1–7]. Although this progress is substantial, most self-healing studies continue to define healing primarily in terms of a material parameter: crack closure, tensile strength recovery, elastic recovery, electrical conductivity restoration, or corrosion resistance. This materials-centric definition is highly useful but incomplete when self-healing surfaces are intended for interaction with biological systems. Biological tissues provide a fundamentally different model. Skin, bone, cartilage, blood vessels, and connective tissues continuously adapt their structure and function through interactions among cells, extracellular matrix, soluble factors, mechanical forces, and biochemical signals. Repair therefore involves not only restoration of physical continuity but also coordinated cellular responses. Cells sense substrate stiffness, ligand density, topography, viscoelasticity, electrical properties, and molecular composition through membrane receptors, focal adhesions, cytoskeletal networks, and mechanotransduction pathways. Thus, from a biological perspective, an interface is not simply a passive surface.

This observation leads to the central proposition of this perspective: The next generation of self-healing surfaces should be designed as dynamic biological interfaces rather than merely crack-repairing materials.

Such a surface should ideally satisfy four simultaneous requirements: first, it should repair physical damage; second, it should restore its original surface chemistry and functionality; third, it should preserve or reconstruct a cell-compatible microenvironment; and fourth, it should actively regulate biological responses when interacting with living systems. This perspective therefore connects two traditionally separated research domains: materials self-healing and cellular self-repair. Rather than reviewing these areas independently, we propose a materials biology framework for designing surfaces capable of interacting dynamically with cells and tissues.

2. From material self-healing to biological self-repair

Self-healing materials are designed to recover structural integrity and/or functional performance following damage. In synthetic polymeric systems, this recovery may involve reversible bond formation, dynamic intermolecular interactions, molecular mobility, interfacial reconnection, or the activation of incorporated healing agents. Depending on the material design, these mechanisms may be triggered by thermal energy, near-infrared irradiation, pH variations, or other environmental conditions. Such approaches have been investigated in protective coatings, polymer nanocomposites, flexible electronic devices, and hydrogel-based wound dressings. Although self-healing synthetic materials can restore selected structural or functional properties, their repair mechanisms and outcomes depend on the composition, network architecture, and operating conditions of the material [11–20]. This distinction suggests that self-healing can be viewed at multiple hierarchical levels.

Table 1 highlights that self-healing cannot be considered an isolated phenomenon occurring at a single length scale; rather, healing emerges from a cascade of interconnected processes extending from molecular interactions to tissue-level function. At the molecular scale, reversible covalent bonds, hydrogen bonding, ionic interactions, and other dynamic associations determine the ability of a material to reorganize after damage. These molecular events influence chain mobility, network rearrangement, and the restoration of local structure at the nanoscale. At the microscale, the cumulative effects of these molecular processes become evident as crack closure, interfacial reconnection, pore recovery, or reorganization of heterogeneous domains. The restored microstructure subsequently determines the recovery of interaction. Thus, changes originating from molecular-scale chemistry

Table 1. Comparison between synthetic self-healing and biological repair.

Level	Synthetic self-healing surface	Biological counterpart	Key design implication	Refs.
Molecular	Reversible covalent/non-covalent bonds	Protein–protein and receptor–ligand interactions	Dynamic chemistry	[4, 11, 12]
Nanoscale	Polymer chain rearrangement, nanofiller interactions	Cytoskeletal remodeling and ECM organization	Dynamic nanoscale architecture	[10, 13, 14]
Microscale	Crack closure and network reconstruction	Cell migration and matrix remodeling	Spatially controlled repair	[3, 15, 16]
Surface	Recovery of wettability, adhesion, or barrier function	Re-establishment of cell–ECM interface	Functional surface recovery	[7, 17, 18]
Tissue scale	Recovery of mechanical integrity	Regeneration and remodeling	Multi-scale design	[19–21]
Functional	Recovery of conductivity, corrosion resistance, or sensing	Recovery of physiological signaling	Function must be restored, not merely structure	[6, 11, 22]

can propagate upward to influence surface recognition and cellular behavior. This multiscale relationship becomes particularly important when moving from material self-healing toward biological self-repair. At the surface and cellular levels, the recovered material provides the physical and chemical environment in which proteins, extracellular matrix components, and cell-adhesion receptors interact. Consequently, incomplete molecular or nanoscale recovery may result in persistent changes in surface chemistry or mechanics even when macroscopic crack closure appears complete. At the tissue scale, these local cellular and interfacial responses accumulate to influence cell organization, tissue integration, remodeling, and ultimately functional recovery. In this sense, the molecular scale provides the chemical basis for healing, the nanoscale and microscale translate these interactions into structural recovery, the surface scale governs biological recognition, and the tissue scale represents the integrated biological outcome. This hierarchical coupling is central to the transition from conventional self-healing materials toward bioadaptive self-healing interfaces.

The major conceptual difference is therefore that biological repair is multiscale, feedback-controlled, and function-oriented. This provides an important lesson for materials science: a self-healing material should ideally not be evaluated solely by whether a crack disappears, but by whether the original function of the interface has been restored.

3. Molecular design of self-healing surfaces

3.1. Bridging polymer chemistry with cell-material interactions

The molecular mechanisms responsible for intrinsic self-healing also directly influence how a material surface is presented to biological systems. Dynamic covalent bonds, reversible noncovalent interactions, chain mobility, and network rearrangement can continuously alter surface chemistry, molecular accessibility, hydration, and mechanical

properties following damage and during subsequent healing. These changes are particularly relevant at the cell-material interface, where adsorbed proteins and extracellular matrix components determine the availability of ligands recognized by cell-adhesion receptors such as integrins. Thus, restoration of the polymer network alone does not necessarily guarantee restoration of the biological interface. A self-healing surface must also recover the chemical and physical cues required for appropriate protein adsorption, integrin engagement, and downstream cellular adhesion and signaling. From this perspective, polymer self-healing chemistry can be considered an upstream determinant of cell material interactions: molecular-level reversibility governs the recovery of surface properties, while the recovered surface properties subsequently regulate biological recognition and cellular responses. Establishing this connection provides a conceptual bridge between intrinsic material self-healing and the cell-mediated processes discussed in the following sections.

3.2. Intrinsic self-healing

Intrinsic self-healing is particularly attractive for biological and biomedical applications because it can enable repeated repair without relying on a finite reservoir of encapsulated healing agents. This approach commonly relies on reversible interactions or dynamic bonds within the material network, allowing damaged regions to reconnect under suitable conditions. Reported mechanisms include dynamic covalent bonding, such as disulfide and acylhydrazone bonds, as well as reversible noncovalent interactions, including hydrogen bonding. The effectiveness of these mechanisms depends on the material composition, network architecture, and environmental conditions [4, 5, 11, 17, 23]. As schematically illustrated in Fig. 1, reversible dynamic bonding can provide a molecular basis for restoring the integrity of damaged interfaces through repeated bond dissociation and reformation. In addition, non-covalent interactions, particularly

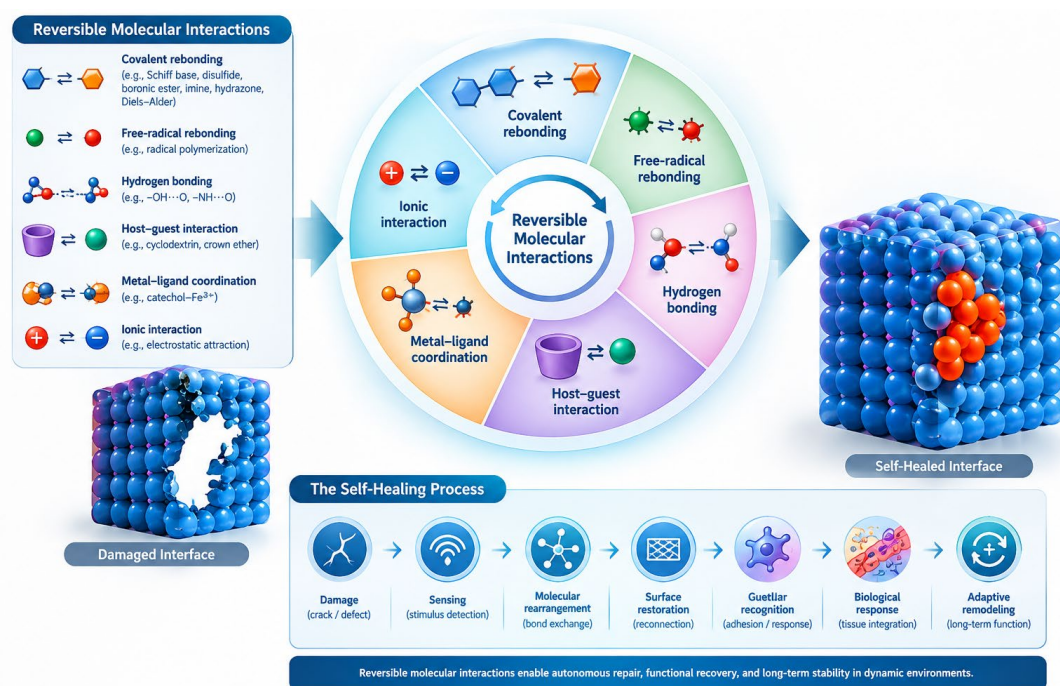


Fig. 1. Reversible molecular interactions underlying intrinsic self-healing mechanisms.

hydrogen bonding and ionic interactions, can promote molecular rearrangement and facilitate the recovery of structural integrity and functional performance. The effectiveness of these mechanisms depends on the chemical composition, network architecture, and environmental conditions of the material [4, 11]. Fig. 1 further highlights these reversible non-covalent interactions, showing how hydrogen bonding, ionic interactions, metal-ligand coordination, and host-guest interactions can contribute to the reconstruction of the interfacial network following damage. For biomedical surfaces, the reversibility of these interactions becomes particularly important because healing must occur under aqueous and often physiological conditions. The challenge is therefore not simply to maximize bond reversibility, but to achieve a balance between bond lifetime, mechanical strength, healing kinetics, water stability, and cytocompatibility. Accordingly, the combination of reversible covalent and non-covalent interactions can provide a versatile molecular strategy for designing intrinsically self-healing biomedical interfaces, in which damaged regions can undergo molecular reorganization and recover their structural continuity without requiring an externally supplied healing agent.

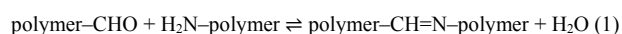
3.3. Extrinsic self-healing

Extrinsic self-healing systems rely on embedded reservoirs of healing agents that are released upon damage to facilitate the repair of the affected region. These reservoirs may include microcapsules or other carrier structures containing suitable healing agents, which can be released when the surrounding material is damaged [2, 24–27]. This strategy has shown promise in protective coatings, particularly for mitigating corrosion following mechanical damage. Microcapsule-based systems can release encapsulated healing agents at damaged regions, thereby helping restore the protective function of the coating [27–30]. However, an important limitation emerges when these systems are transferred to biological surfaces. The release of a healing agent must be compatible with cells, proteins, immune cells, and surrounding tissue. Therefore, the biological translation of extrinsic self-healing requires a shift from the concept of “healing-agent release” toward biologically controlled release.

4. Dynamic covalent chemistry as a bridge between materials and biology

Dynamic covalent chemistry provides an effective strategy for developing self-healing hydrogels by enabling reversible cross-linking while maintaining network integrity. Schiff-base reactions, in particular, form dynamic covalent bonds that support hydrogel self-healing, making these materials promising candidates for biomedical applications, including tissue engineering [17].

A biologically relevant self-healing network can be conceptually represented as:



The reversibility of this interaction enables network rearrangement after mechanical disruption.

However, a critical question remains: How dynamic should the network be?

Balancing mechanical integrity and self-healing capability remains a major challenge in hydrogel design. Excessively restricted molecular mobility may hinder the reformation of network connections, whereas

insufficiently stable networks may compromise mechanical strength. Recent studies have demonstrated that advanced network architectures can help overcome this trade-off. For example, researchers have developed double-network hydrogels that combine self-healing behavior with improved mechanical performance, while nanoconfinement through polymer entanglements has enabled the fabrication of stiff hydrogels with self-healing efficiencies up to 90% [19, 20]. This is particularly relevant to biology because many tissues simultaneously exhibit strength, toughness, viscoelasticity, and regenerative capacity.

5. The cell-material interface: Where materials science meets cell biology

A surface intended for biological use interacts with proteins before it directly interacts with most cells. Following immersion in physiological fluids, proteins adsorb onto the material and form a dynamic interfacial layer. Cells subsequently interact with this protein-modified surface through integrins, cadherins, proteoglycans, and other receptors. Consequently, the biological response to a self-healing surface can be divided conceptually into four stages:

Surface chemistry → Protein adsorption → Receptor engagement → Cellular response

Changes in self-healing chemistry may therefore influence biological behavior indirectly. For example, a damaged polymer surface may expose hydrophobic domains, nanoparticles, catalysts, or healing agents. After healing, the chemical composition and nanoscale morphology may differ from the original state. Even when the crack has visually disappeared, the biological interface may not have been completely restored.

This leads to a key research gap:

Mechanical healing efficiency does not necessarily equal biological healing efficiency.

A material can exhibit 90% recovery in tensile strength while showing substantially different protein adsorption, cell adhesion, or inflammatory behavior after healing.

The incorporation of these parameters into self-healing studies could transform the field from conventional materials characterization toward biointerface characterization.

6. Extracellular matrix-inspired self-healing surfaces

The extracellular matrix is an especially useful biological model because it is itself dynamic. Collagen, hyaluronic acid, proteoglycans, fibronectin, laminin, and other components undergo continuous synthesis, degradation, crosslinking, and remodeling. Self-healing hydrogels based on hyaluronic acid, gelatin, chitosan, alginate, oxidized polysaccharides, and other biomacromolecules therefore provide an opportunity to reproduce some of the dynamic characteristics of ECM (extracellular matrix) [11–20, 24, 31–33]. For example, a self-healing hyaluronic acid hydrogel containing dynamic acylhydrazone and ionic interactions demonstrated rapid healing under physiological conditions [24]. Similarly, chitosan-based systems incorporating dynamic covalent interactions and bioactive glass have been designed to combine self-healing, mechanical properties, injectability, and cytocompatibility [23]. These examples suggest that the most biologically relevant self-healing surfaces may not necessarily be completely synthetic. Instead, hybrid bio-synthetic networks may provide a more effective route.

Table 2. Material parameters and their potential cellular consequences.

Materials parameter	Possible biological consequence	Relevant cellular process	Suggested characterization
Surface roughness	Changes protein adsorption and cell attachment	Focal adhesion formation	AFM, profilometry
Surface energy	Modifies protein adsorption	Integrin-mediated adhesion	Contact-angle measurement
Stiffness	Alters mechanotransduction	YAP/TAZ, FAK signaling	AFM, rheology
Viscoelasticity	Affects cell spreading and migration	Cytoskeletal remodeling	Stress relaxation
Dynamic bond density	Controls remodeling rate	Cell-matrix adaptation	Spectroscopy, rheology
Charge	Influences protein and membrane interactions	Adhesion, membrane signaling	Zeta potential
Nanotopography	Regulates cell morphology	Cytoskeletal organization	AFM/SEM
ROS generation/scavenging	Influences oxidative stress	NF- κ B, apoptosis, proliferation	ROS assays
Electrical conductivity	Influences electroactive cells	Neural/cardiac signaling	Electrochemical analysis
Wettability	Controls protein adsorption and cell attachment	Adhesion and spreading	Contact angle

A possible architecture is:

Rigid substrate $\rightarrow$ mechanically reinforced interlayer $\rightarrow$ dynamic polymer network $\rightarrow$ ECM-mimetic surface $\rightarrow$ cell-interactive ligands
Such a multilayer structure could allow each layer to perform a different function.

7. Self-healing hydrogels as cellular interfaces

Hydrogels are particularly attractive because their high water content and three-dimensional polymer networks can reproduce some physical characteristics of soft tissues [11–16]. Their self-healing behavior can arise from reversible chemical bonds or physical interactions. Importantly, hydrogels can also be engineered to encapsulate cells, proteins, nanoparticles, growth factors, and drugs [11–20]. Several recent studies have demonstrated the biological potential of self-healing hydrogels. Self-healing systems have been investigated for bone regeneration, wound healing, cartilage regeneration, injectable implants, cell delivery, and antibacterial applications [13–20, 24, 31–33]. In a study, a self-healing hydrogel based on oxidized pectin grafted with dopamine as a gallic acid carrier has been used for burn wound treatment, demonstrating the potential of self-healing biomaterials in wound care [34]. A particularly important direction is the integration of corrosion protection and material healing. A self-healing coating can protect metal substrates from corrosive damage while maintaining its protective properties. Gharieh et al. demonstrated a self-healing nanocomposite coating based on zinc-doped polyaniline incorporated into an epoxy matrix, achieving effective corrosion protection and healing of scratched coatings [19]. This highlights an important distinction between two concepts: self-healing material, in which the material repairs damage to itself, and corrosion-protective self-healing material, which combines damage repair with sustained protection against environmental degradation. The second concept is particularly relevant to the long-term protection of metals in harsh environments.

8. Surface self-healing and cell adhesion

Cell adhesion is controlled by a combination of biochemical ligands, surface chemistry, topography, stiffness, and mechanical properties. A self-healing event can modify all of these parameters simultaneously. For example, if a scratch causes polymer chains to rearrange and exposes a hydrophobic domain, the subsequent healing process may

restore mechanical continuity but not necessarily reproduce the original surface energy.

Therefore, future studies should distinguish among:

- geometrical healing
- mechanical healing
- chemical healing
- biological healing
- functional healing

A complete self-healing surface should ideally restore all five.

This framework represents one of the central propositions of this perspective.

9. Self-healing and mechanobiology

Mechanobiology provides another major bridge between materials science and cell biology. Cells do not simply respond to chemical composition. They also sense mechanical properties through focal adhesions and the cytoskeleton. Changes in substrate stiffness and viscoelasticity can influence cell morphology, migration, proliferation, differentiation, and gene expression. This creates an unusual opportunity for self-healing materials. Instead of designing a surface with a fixed mechanical modulus, it may be possible to design a mechanically adaptive surface whose stiffness changes in response to damage or cellular activity.

For example:

Damage $\rightarrow$ local bond dissociation $\rightarrow$ increased chain mobility $\rightarrow$ self-healing $\rightarrow$ restoration of stiffness

This process could potentially be coupled to:

Cell adhesion $\rightarrow$ mechanical loading $\rightarrow$ mechanosensing $\rightarrow$ remodeling of the surface

Such feedback would transform the interface from a passive material into a dynamic system. Recent work on stiff self-healing hydrogels is particularly relevant because it demonstrates that high modulus and self-healing do not necessarily need to be mutually exclusive [35].

10. Redox biology and self-healing materials

Reactive oxygen species (ROS) play dual roles in biology. Moderate ROS concentrations participate in signaling, while excessive oxidative stress can damage proteins, lipids, DNA, and cellular membranes. This is highly relevant to self-healing biomaterials because many healing environments are characterized by oxidative stress, particularly chronic

Table 3. Proposed hierarchy of self-healing efficiency for biointerfaces.

Healing level	Main question	Typical metric
Geometrical	Has the crack closed?	Crack width/area recovery
Mechanical	Has strength returned?	Tensile or modulus recovery
Chemical	Has surface chemistry returned?	FTIR/XPS/contact angle
Biological	Has cellular compatibility returned?	Cell viability/adhesion/proliferation
Functional	Has the original biological/material function returned?	Corrosion, sensing, antibacterial or tissue-specific assay

wounds. Self-healing hydrogels with antioxidant functions have therefore received increasing attention [18, 32]. Feng et al. developed an adhesive self-healing hydrogel with antioxidant functionality and demonstrated biological effects associated with regulation of oxidative stress and fibrosis-related pathways [7].

This suggests a broader concept:

A self-healing surface should ideally respond not only to mechanical damage but also to the biochemical environment surrounding the damage.

In other words, future surfaces could be dual-responsive:

Mechanical damage + biochemical damage → adaptive healing response

For example:

- crack → triggers network reconstruction;
- low pH → activates healing chemistry;
- elevated ROS → activates antioxidant components;
- bacterial infection → activates antimicrobial response;
- inflammatory signals → modify surface properties.

Such multifunctionality would move self-healing materials closer to biological systems.

11. Antibacterial self-healing surfaces

Bacterial contamination is a major problem for both conventional coatings and biomedical devices. A major limitation of conventional antibacterial coatings is that surface damage can remove the active layer and expose the underlying substrate. Self-healing antibacterial surfaces attempt to solve this problem by combining antimicrobial activity with autonomous repair. Recent examples include self-healing polyurethane coatings, zwitterionic hydrogel coatings, conductive hydrogels containing photothermal components, and nanocomposite wound dressings [22, 25, 26, 32]. The biological challenge is that antibacterial activity must be balanced against cytocompatibility. A material capable of killing bacteria may also damage mammalian cells if its mechanism is insufficiently selective.

Consequently, future research should evaluate:

Antibacterial activity + mammalian cell viability + inflammatory response + healing efficiency rather than antibacterial activity alone.

12. Self-healing conductive surfaces and bioelectronics

Self-healing materials are particularly attractive for bioelectronics because flexible and wearable devices experience repeated deformation, stretching, bending, and mechanical damage [6, 10, 13, 19, 22, 29].

Self-healing hydrogels can simultaneously provide:

- ionic conductivity;
- electronic conductivity;
- stretchability;
- adhesion;
- self-healing;
- biocompatibility;
- sensing functionality.

Self-healing bioelectronics can therefore be considered an important intermediate between materials engineering and cell biology. The 2025 study by Gharieh et al. demonstrated the potential of self-healing nanocomposite coatings for corrosion protection, where the material acts as a protective barrier for metals in harsh environments [19]. A particularly interesting future direction is the development of cell-compatible self-healing electrodes that maintain stable electrical interfaces despite mechanical deformation.

Such materials could potentially be used for:

- neural interfaces;
- cardiac monitoring;
- electrophysiological sensing;
- wearable biosensors;
- electronic skin;
- implantable sensors.

13. Nanomaterials as functional components of self-healing surfaces

Nanomaterials can contribute to self-healing surfaces in several ways. Carbon nanotubes (CNTs), graphene derivatives, MXenes, metal nanoparticles, semiconductor nanoparticles, nanoclays, mesoporous silica, and magnetic nanoparticles can act as mechanical reinforcements, conductive networks, photothermal agents, reservoirs, or stimuli-responsive components [9, 10, 20, 27, 28, 35, 36]. However, biological applications introduce additional requirements.

Nanoparticles must be evaluated in terms of:

- particle release;
- cellular uptake;
- oxidative stress;
- inflammation;
- biodegradation;
- long-term accumulation;
- protein corona formation.

Thus, the simple addition of nanoparticles to increase mechanical strength may not necessarily produce a biologically optimal self-healing surface. The preferred strategy may be interface-localized nanostructuring, where nanoparticles remain confined within the

Table 4. Stimulus-responsive self-healing and biological opportunities.

Stimulus	Materials response	Potential biological relevance	Major concern
Heat	Chain mobility/increased diffusion	Physiological or externally controlled healing	Thermal damage
NIR light	Photothermal heating	Localized remote healing	Phototoxicity/temperature
pH	Bond exchange/release	Wound/cellular microenvironment	Limited pH window
ROS	Oxidation/reduction chemistry	Chronic wound environment	Excessive ROS
Mechanical stress	Dynamic bond rearrangement	Wearable/implantable devices	Fatigue
Electrical stimulus	Electrochemical response	Neural/cardiac interfaces	Electrochemical stability
Magnetic field	Magnetic heating or actuation	Remote control	Nanoparticle safety
Enzymes	Bioresponsive degradation/reconstruction	Cell/tissue-specific response	Specificity

polymer network rather than being freely released into the biological environment.

14. Stimuli-responsive self-healing surfaces

Self-healing can be activated by several stimuli, including heat, light, pH, electrical fields, magnetic fields, mechanical stress, and chemical signals [1–10]. Photothermal self-healing is particularly attractive because the healing response can potentially be spatially controlled. Photothermal nanoparticles convert light into localized heat, increasing polymer chain mobility or activating reversible interactions [8, 10]. pH-responsive healing is another promising mechanism. Recent work has demonstrated intrinsic self-healing coatings based on pH-dependent solid–liquid transitions [15]. For biological interfaces, the use of physiological stimuli is especially interesting.

The most advanced future systems may combine two or more stimuli to prevent unwanted activation.

15. Toward “living” self-healing surfaces

Based on Fig. 2, the central proposal of this perspective is the development of a new category of materials that can be termed living-interface-inspired self-healing surfaces. The concept is not that the material itself becomes alive. Rather, the material is designed to reproduce selected principles of living systems:

- dynamic adaptation;
- reversible molecular interactions;
- environmental sensing;
- spatially localized responses;
- feedback;
- hierarchical repair;
- preservation of biological function.

A hypothetical four-layer architecture can be proposed:

Layer 1 – Structural substrate

Provides mechanical support and dimensional stability.

Layer 2 – Dynamic self-healing layer

Contains reversible covalent or supramolecular networks.

Layer 3 – Bioactive interfacial layer

Controls protein adsorption, wettability, adhesion, antimicrobial activity, and cell attachment.

Layer 4 – Cellular signaling layer

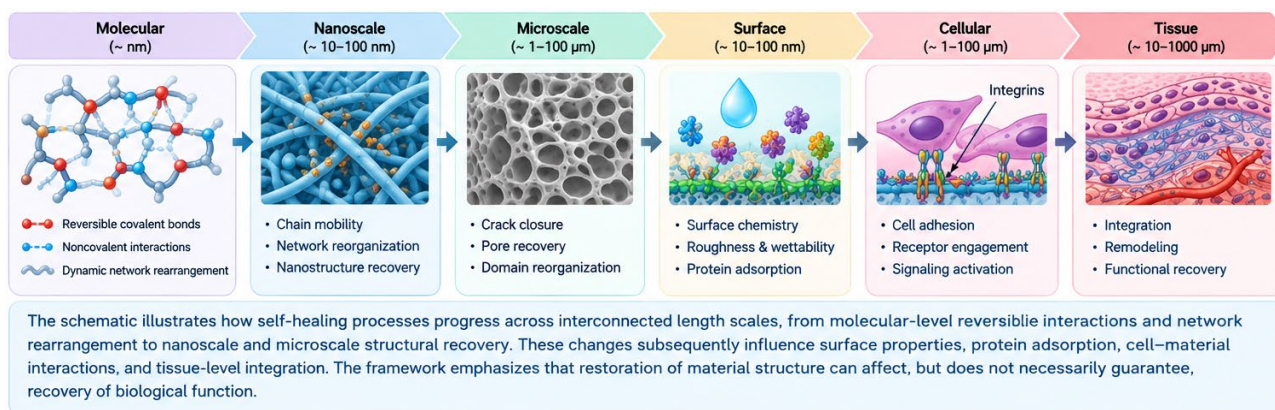
Provides biochemical or mechanical cues capable of regulating cell behavior.

The interaction among these layers can be conceptualized as:

Damage → sensing → molecular rearrangement → surface restoration → cellular recognition → biological response → adaptive remodeling

This is fundamentally different from conventional crack-healing systems, in which:

Damage → healing agent release → crack closure
is generally the dominant sequence.

**Fig. 2.** Conceptual architecture of living-interface-inspired self-healing and self-regulating surfaces.

16. From “self-healing” to “self-regulating” surfaces

The next major step beyond self-healing may therefore be self-regulation. A self-healing material responds to damage. A self-regulating material responds to damage and adjusts its properties according to environmental conditions.

A biologically integrated self-regulating surface could potentially respond to:

- mechanical stress;
- pH;
- ROS;
- temperature;
- bacterial signals;
- cell adhesion;
- inflammatory mediators;
- electrical activity.

For example, a wound-interface material could theoretically detect elevated ROS, release an antioxidant component, mechanically repair a crack, maintain moisture, inhibit bacterial growth, and support cell migration.

This concept combines several fields:

Materials science + polymer chemistry + nanotechnology + surface engineering + cell biology + mechanobiology + bioelectronics and therefore represents a particularly rich research direction.

17. Characterization: Why conventional self-healing metrics are not enough

One of the most important limitations in the field is the absence of a universal standard for measuring self-healing performance. Existing studies use crack closure, tensile recovery, modulus recovery, electrical recovery, corrosion resistance, or visual microscopy. Panahi et al. emphasized that different characterization methods can produce different interpretations of healing efficiency [13]. For biological interfaces, this problem becomes even more important. A surface may show excellent crack closure but poor cell adhesion after healing. Another material may recover only 80% of its mechanical strength but restore almost completely its biological functionality. Therefore, future studies should report a multidimensional healing index rather than a single healing percentage.

A possible conceptual equation is:

$$HI_{\text{total}} = w_G H_G + w_M H_M + w_C H_C + w_B H_B + w_F H_F \quad (2)$$

where:

- H_G = geometrical healing;
- H_M = mechanical healing;
- H_C = chemical healing;
- H_B = biological healing;
- H_F = functional healing;
- w_i = application-dependent weighting factors ($\sum w_i = 1$; $0 \leq w_i \leq 1$).

This equation is proposed as a conceptual framework rather than a universal standardized metric.

Fig. 3 illustrates a conceptual multidimensional framework for evaluating self-healing performance beyond conventional single-parameter measurements. The framework integrates geometrical, mechanical, chemical, biological, and functional healing, recognizing that recovery of one property does not necessarily indicate complete restoration of the material–biological interface. The schematic also highlights the diversity of conventional characterization methods, including crack closure, tensile and modulus recovery, electrical recovery, corrosion resistance, and microscopic analysis, which may lead to different interpretations of healing efficiency. The proposed multidimensional healing index combines these five healing dimensions using application-dependent weighting factors, providing a conceptual approach for comparing materials according to the specific requirements of biomedical applications rather than assigning a single universal healing percentage.

Fig. 4 presents a comprehensive characterization framework for assessing self-healing performance across both material and biological dimensions. The framework links each evaluation category to appropriate characterization techniques and corresponding primary outputs, ranging from morphological recovery, chemical restoration, mechanical strength, wettability, electrical conductivity, and corrosion protection to antibacterial activity, cytocompatibility, cell adhesion, cell migration, mechanobiological signaling, inflammation, oxidative stress, and tissue regeneration. This integrated approach emphasizes that the performance of self-healing biomedical interfaces should not be evaluated using a single parameter; instead, complementary physicochemical, mechanical, and biological measurements are required to determine whether structural recovery is accompanied by restoration of interfacial and biological functions.

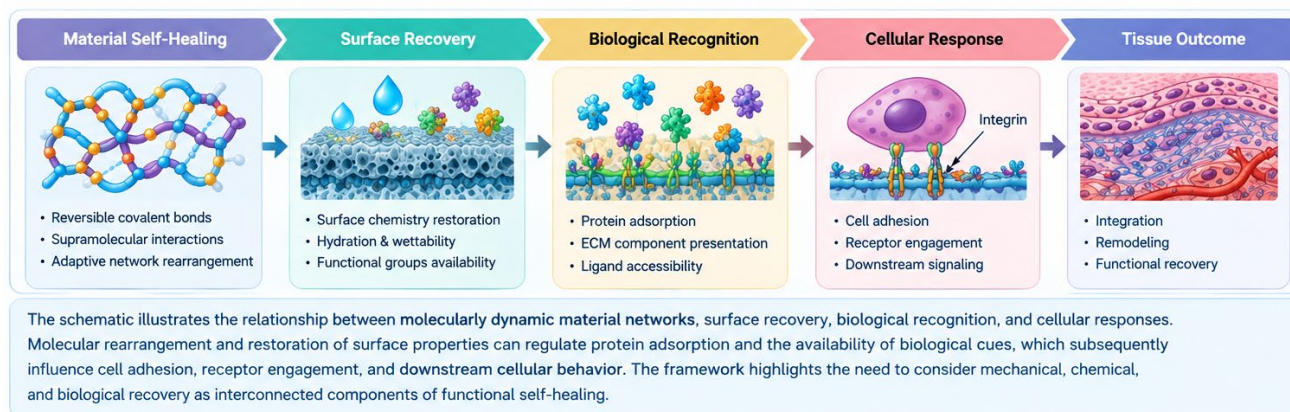


Fig. 3. A multidimensional framework for evaluating self-healing performance in biomedical interfaces.

Table 5. Proposed characterization framework for biofunctional self-healing surfaces.

Category	Recommended technique	Primary output
Morphology	SEM, AFM, optical microscopy	Crack closure
Chemistry	FTIR, Raman, XPS	Chemical restoration
Mechanical	Tensile, nanoindentation, rheology	Modulus/strength recovery
Surface	Contact angle, surface energy	Wettability recovery
Electrical	EIS, four-point probe	Conductivity recovery
Barrier	EIS, salt spray	Corrosion protection
Antibacterial	Colony count, live/dead staining	Antimicrobial recovery
Cytocompatibility	MTT/Alamar blue, live/dead	Cell viability
Cell adhesion	Fluorescence microscopy	Adhesion/spreading
Cell migration	Scratch assay, transwell	Migration
Mechanobiology	YAP/TAZ, FAK, vinculin	Mechanical signaling
Inflammation	IL-6, TNF- α , NF- κ B	Immune response
Oxidative stress	ROS assays	Redox regulation
Tissue function	Histology, immunostaining	Regeneration

18. A new experimental design strategy

Based on the literature discussed above, we propose that future research should follow a sequential design strategy.

Stage 1: Material design

Select a polymer system with reversible interactions.

Stage 2: Mechanical optimization

Optimize the balance between stiffness, toughness, elasticity, and healing rate.

**Fig. 4.** Multidimensional characterization framework for evaluating self-healing performance from material integrity to biological functionality.

Stage 3: Surface engineering

Control roughness, wettability, surface energy, charge, and ligand density.

Stage 4: Biological functionalization

Introduce ECM-derived molecules, peptides, polysaccharides, growth-factor-binding domains, or cell-adhesion motifs.

Stage 5: Cellular evaluation

Measure viability, adhesion, spreading, proliferation, migration, differentiation, and inflammatory response.

Stage 6: Damage–repair–biology cycle

Instead of characterizing only pristine materials, compare:

Pristine → Damaged → Healed

for all biological parameters. This last stage is particularly important. A study should ask:

Does the healed surface reproduce the biological properties of the original surface?

rather than only:

Has the crack disappeared?

19. Applications at the materials–biology interface

The proposed framework could be relevant to several emerging application areas.

19.1. Wound dressings

Self-healing hydrogels can maintain structural integrity despite deformation of the wound. Incorporation of antibacterial, antioxidant, conductive, or drug-delivery functions can further improve their potential [18, 21, 24, 25, 32, 37].

19.2. Implant coatings

Implant surfaces experience mechanical stresses and biological interactions. Self-healing coatings could reduce surface degradation while maintaining a cell-compatible interface.

19.3. Tissue engineering

Self-healing matrices can provide a dynamic environment for cell encapsulation and tissue regeneration [13, 19, 23, 35].

19.4. Neural interfaces

Self-healing conductive hydrogels may help maintain electrical contact during mechanical deformation [14–16, 20].

19.5. Cardiac biointerfaces

Because cardiac tissues undergo continuous mechanical deformation, self-healing conductive materials may be particularly relevant for electrophysiological monitoring.

19.6. Antibacterial medical devices

Self-healing zwitterionic and antimicrobial coatings may help maintain biological functionality after mechanical damage [22, 25].

19.7. Corrosion protection of biomedical and engineering devices

For metallic substrates, self-healing coatings can restore barrier properties after damage [1, 2, 27–30].

20. Critical challenges

Despite rapid progress, several fundamental challenges remain. First, the trade-off between mechanical strength and self-healing remains unresolved in many systems. Highly crosslinked networks often provide strength but suppress chain mobility, whereas highly dynamic networks may heal rapidly but exhibit insufficient mechanical stability [4, 5, 11, 35]. Second, many reported healing processes require external stimuli that may be difficult to implement in vivo. Third, the long-term fate of nanoparticles and healing agents remains a concern for biomedical applications. Fourth, most studies evaluate healing after a single damage event. Real biological and engineering surfaces experience repeated damage. Fifth, the distinction between structural healing and functional healing is still insufficiently addressed. Sixth, cellular responses are often evaluated only in the pristine material. The biological behavior of the damaged and subsequently healed surface should also be investigated. Seventh, standardized protocols are needed for comparing healing efficiency across different materials [7]. Finally, translation from laboratory-scale films and hydrogels to large-area coatings, complex geometries, sterilizable medical devices, and long-term implants remains challenging.

21. Future perspective: The next decade of self-healing surfaces

The field may evolve through five major transitions.

Transition 1: From crack closure to function restoration

Future research should ask whether mechanical, chemical, electrical, optical, antimicrobial, and biological functions are simultaneously restored.

Transition 2: From passive healing to environmental sensing

Materials should recognize the local environment and activate healing only when necessary.

Transition 3: From synthetic networks to hybrid biological–synthetic networks

Synthetic polymers can provide mechanical durability, while biomolecules can provide cell recognition and biological functionality.

Transition 4: From single-cycle healing to regenerative interfaces

Materials should maintain their performance over multiple damage–healing cycles.

Transition 5: From materials to adaptive systems

The ultimate objective is not simply a material that heals itself but a surface that can:

Sense → respond → repair → communicate with cells → adapt

This framework could create a new class of materials situated between conventional engineering surfaces and biological tissues.

22. Proposed research roadmap

A particularly promising research platform would consist of a multifunctional nanocomposite surface containing:

- a dynamic polymer network;
- ECM-mimetic components;
- mechanically reinforcing nanomaterials;
- antioxidant functionality;
- antibacterial functionality;
- cell-adhesion ligands;
- a stimulus-responsive healing mechanism;
- and, where appropriate, an electrically conductive phase.

The experimental workflow could be:

Substrate preparation → surface functionalization → dynamic polymer synthesis → nanoparticle incorporation → ECM-mimetic functionalization → mechanical characterization → controlled damage → healing → surface characterization → protein adsorption → cell adhesion → proliferation → migration → mechanotransduction → inflammatory response → repeated damage/healing cycles.

The most important experimental comparison would involve three groups:

- pristine surface;
- damaged surface;
- healed surface.

If the healed surface demonstrates comparable mechanical, chemical, and biological properties to the pristine surface, a stronger claim of true multifunctional self-healing can be justified.

23. A conceptual model for “bioadaptive self-healing surfaces”

Based on the literature discussed in this perspective, a new conceptual model can be proposed:

Damage → Sensing → Dynamic molecular response → Structural healing → Surface functional recovery → Cellular recognition → Biological adaptation

This model integrates material and biological responses into a single process. In such a system, the surface is not considered a static boundary between material and biological environment. Instead, it becomes a dynamic communication layer. This concept may be particularly important for regenerative medicine because the interface between an implant and tissue frequently determines the long-term success of the device.

24. Conclusions

Self-healing materials have traditionally been evaluated based on their ability to restore structural integrity after damage. However, for biomedical and biointegrated applications, effective healing should extend beyond crack closure and mechanical recovery to include the restoration of surface chemistry, biological compatibility, and application-specific functions. Molecularly dynamic mechanisms, including reversible covalent bonds, supramolecular interactions, and adaptive network rearrangement, provide an important basis for achieving this broader form of recovery. A key perspective of this work is that material self-healing and biological responses are closely interconnected across multiple length scales. Molecular and nanoscale recovery can influence surface properties, protein adsorption, cell adhesion, and receptor-mediated signaling, ultimately affecting tissue-level integration and function. Therefore, mechanical healing should not be considered equivalent to biological healing. Future self-healing materials should be designed as dynamic and bioadaptive interfaces capable of restoring both material properties and relevant biological functions. Overall, the transition from conventional self-healing materials toward bioadaptive and self-regulating surfaces provides a promising framework for next-generation biomaterials. Integrating molecular design, surface engineering, biological characterization, and application-specific functional recovery may enable self-healing systems that do not simply repair damage but actively adapt to their biological environment.

CRedit authorship contribution statement

Zeinab Amiri Far: Formal Analysis, Writing – review & editing.

Erfan Mohammadzadeh: Conceptualization, Writing – original draft, Writing – review & editing.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Declaration of competing interest

The authors declare no competing interests.

Funding and acknowledgment

This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors used artificial intelligence (AI)-assisted tools, including large language models (LLMs), to improve the linguistic quality of the manuscript and assist in drafting and refining selected scientific descriptions. AI tools were not used to generate scientific data or to make independent scientific decisions. All scientific interpretations, perspectives, conclusions, and final editorial decisions were carefully verified and approved by the authors, who take full responsibility for the content and integrity of the manuscript.

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