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Quorum-sensing-responsive materials: Toward living smart interfaces in biomedical systems

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ABSTRACT

Quorum-sensing-sensitive materials are emerging as innovative platforms with significant clinical potential, particularly in the areas of infection diagnosis, targeted antimicrobial therapy, and wound management. By leveraging bacterial communication molecules such as acylhomoserine lactones and autoinducer peptides, these smart materials can detect early pathogenic activity before overt clinical symptoms appear. By sensing quorum-signaling thresholds associated with virulence activation or biofilm formation, the materials can trigger controlled antimicrobial release, modulate local immune responses, or modify surface properties to prevent bacterial adhesion. Such "living" interfaces offer a dynamic alternative to traditional passive biomaterials, enabling real-time, infection-specific therapeutic effects with reduced systemic drug exposure. This review summarizes the clinical significance, mechanism-driven design principles, and translational challenges of quorum-sensing-sensitive materials, highlighting their potential to address antibiotic resistance, improve patient outcomes, and support precision infection control in modern healthcare.

1. Introduction

Historically, materials research has concentrated on the synthesis and characterisation of materials exhibiting passive qualities, such as mechanical strength, thermal conductivity, and chemical inertness. In the 21st century, however, the desire has changed to "smart" or "responsive" materials that can change and adapt to changes in the environment. At this time, getting ideas from biology has become a very useful method. Nature has created systems that are very efficient, use little energy, and can organize themselves over the course of 4 billion years of development. Quorum Sensing (QS) is one of the most advanced of these biological inspirations. This system, prevalent in bacteria, fungi, and certain human cells, enables individual cells to "vote" and trigger a synchronized gene expression pattern when reaching a crucial population threshold [1]. This process begins with the production and release of a signaling molecule, such as Acyl-Homoserine Lactones (AHLs) for Gram-negative bacteria, which builds up in the environment as the population density rises. When the concentration of this signaling molecule reaches a specific level, it binds to a receptor protein that is similar to a transcription factor called LuxR. The complex attaches to the promoter regions of target genes and starts processes like bioluminescence, virulence factor secretion, biofilm formation, and antibiotic synthesis [2]. Adding this well-known biological process to materials science gives materials a new "layer of function" [3]. The material is no longer just a building block; it is now a living thing that "listens" to the microbes surrounding it, "interprets" their signals, and "responds" in a

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set way [4,5].

Bacteria are not solitary organisms; instead, they frequently operate as coordinated communities capable of responding to environmental cues in a collective manner. One example of this type of community behaviour is QS, a regulatory system that depends on population density and modulates gene expression in response to the buildup of signaling molecules known as autoinducers (AIs). Initially discovered in the bioluminescent marine bacterium *Vibrio fischeri* [6], QS has since been recognized as a ubiquitous phenomenon across diverse bacterial taxa, regulating a variety of physiological functions including virulence, biofilm formation, motility, sporulation, antibiotic production, and genetic competence [1,7,8].

Gram positive and Gram-negative bacteria possess different QS mechanisms (Fig. 1). In Gram-negative bacteria, QS is predominantly mediated by AHLs. These small, diffusible molecules are synthesized by LuxI-type enzymes and detected by LuxR-type transcriptional regulators [8]. One of the significant examples is the LuxI/LuxR systems in *V. fischeri*, where AHL-mediated QS activates the expression of bioluminescence genes at high cell densities. AHLs consist of a conserved homoserine lactone ring linked to an acyl side chain of varying length and substitution (e.g., 3-oxo or 3-hydroxy groups), which determines specificity. The LuxI enzyme uses S-adenosylmethionine (SAM) and acyl-acyl carrier proteins (acyl-ACPs) as precursors to synthesize AHLs. Once secreted into the extracellular milieu, AHLs accumulate in proportion to cell density. When a threshold concentration is reached, they re-enter the cell and bind their cognate LuxR receptor. This complex then modulates the transcription of QS-regulated genes by interacting with promoter regions containing specific DNA-binding motifs, such as the lux box [9]. In this way, AHL-based QS systems regulate a range of behaviours including biofilm maturation, secondary metabolite production, conjugation, and host interaction. Notably, *P. aeruginosa* utilizes two hierarchically organized AHL systems (LasR/LasI and RhlR/RhlI) to control virulence and antibiotic resistance [10].

Unlike their Gram-negative counterparts, Gram-positive bacteria employ small, modified oligopeptides as QS signals, often referred to as autoinducing peptides (AIPs). The mechanism of AIPs and their role on QS system is depicted in Fig. 2. AIPs are sensed via two-component signal transduction systems (TCS) consisting of a membrane-bound histidine kinase and a cytoplasmic response regulator [11]. AIPs are ribosomally synthesized as precursor peptides and undergo post-translational modifications, such as cyclization, methylation, or thiolactone formation, before being exported via ABC transporters. The mature peptides accumulate extracellularly and bind to a specific sensor histidine kinase (HK). Upon ligand binding, the HK auto phosphorylates and transfers the phosphate to the response regulator (RR), which then activates or represses transcription of target genes. QS via oligopeptides controls a wide array of processes. In *S. aureus*, the accessory gene regulator (agr) system regulates toxin production, biofilm dispersal, and immune evasion [12]. In *Bacillus subtilis*, different oligopeptide systems control sporulation, competence, and allolysis, underscoring the diversity and complexity of QS in this bacterial clade [13].

AI-2 is a unique signaling molecule implicated in interspecies communication, produced by both Gram-negative and Gram-positive bacteria. Unlike AHLs and AIPs, AI-2 is a product of the activated methyl cycle and synthesized by the LuxS enzyme from S-ribosylhomocysteine [14]. The AI-2 precursor, 4,5-dihydroxy-2,3-pentanedione (DPD), spontaneously cyclizes to form a family of furanone-based molecules that can complex with boron, forming the active signal in some species (e.g., *V. harveyi*). Different bacteria have evolved distinct AI-2 detection systems for example *V. harveyi* uses LuxP (periplasmic binding protein) and LuxQ (sensor kinase) and *E. coli* employs the Lsr (LuxS-regulated) transporter system, which internalizes and phosphorylates AI-2 to modulate transcription via LsrR [15].

Although the precise physiological roles of AI-2 remain under investigation, it has been associated with biofilm formation, virulence regulation, and metabolic cooperation. Its presence across diverse taxa suggests a potential role as a "universal language" in microbial communities [16]. In addition to canonical AHL, AIP, and AI-2 systems, several bacteria utilize non-classical QS signals, further expanding the chemical lexicon of microbial communication. *P. aeruginosa* synthesizes

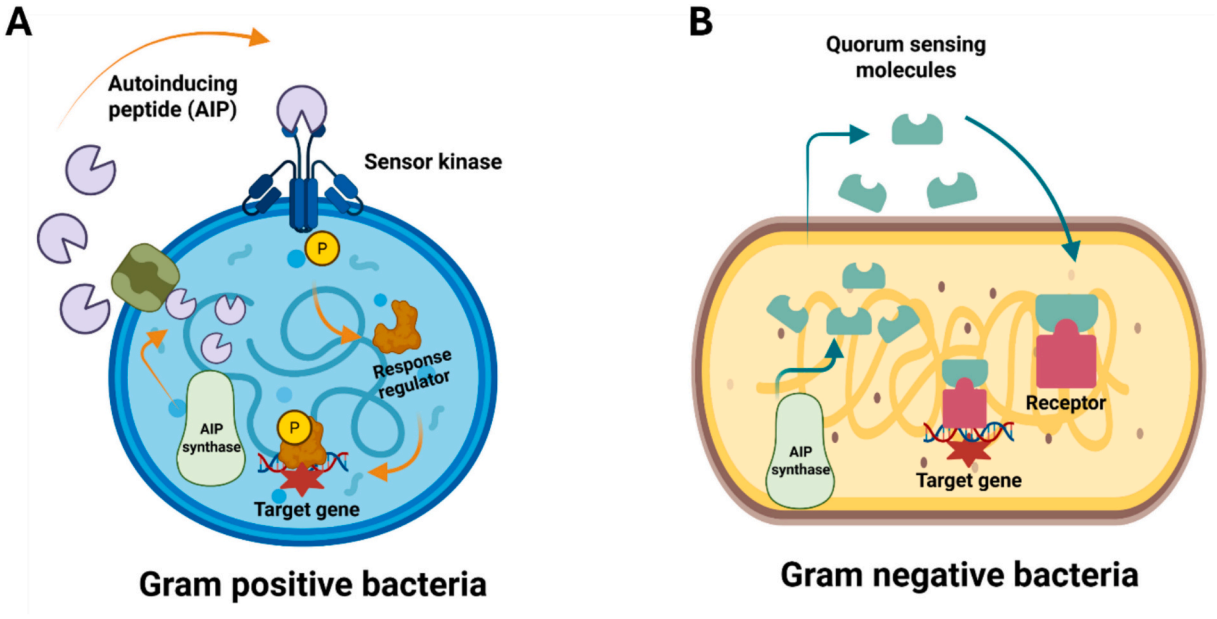

Fig. 1. Quorum Sensing Mechanisms in Gram-Positive and Gram-Negative Bacteria. A) In Gram-positive bacteria QS is mediated by autoinducing peptides (AIPs), which are synthesized by AIP synthase and secreted into the extracellular environment. Once a threshold concentration is reached, AIPs are detected by a membrane-bound sensor kinase, initiating a phosphorylation cascade involving a response regulator. This phosphorylated regulator then activates the transcription of target genes. B) QS in Gram-negative bacteria involves the synthesis of small diffusible signaling molecules (QS molecules) by AI (autoinducer) synthase. These molecules freely diffuse across the membrane and accumulate in the environment. At high cell densities, they re-enter the cell and bind to specific intracellular or membrane-bound receptors, triggering the expression of target genes involved in various group behaviours. This highlights the key differences in signal molecule types, detection mechanisms, and regulatory pathways between Gram-positive and Gram-negative bacterial quorum sensing systems. http://biorender.com.

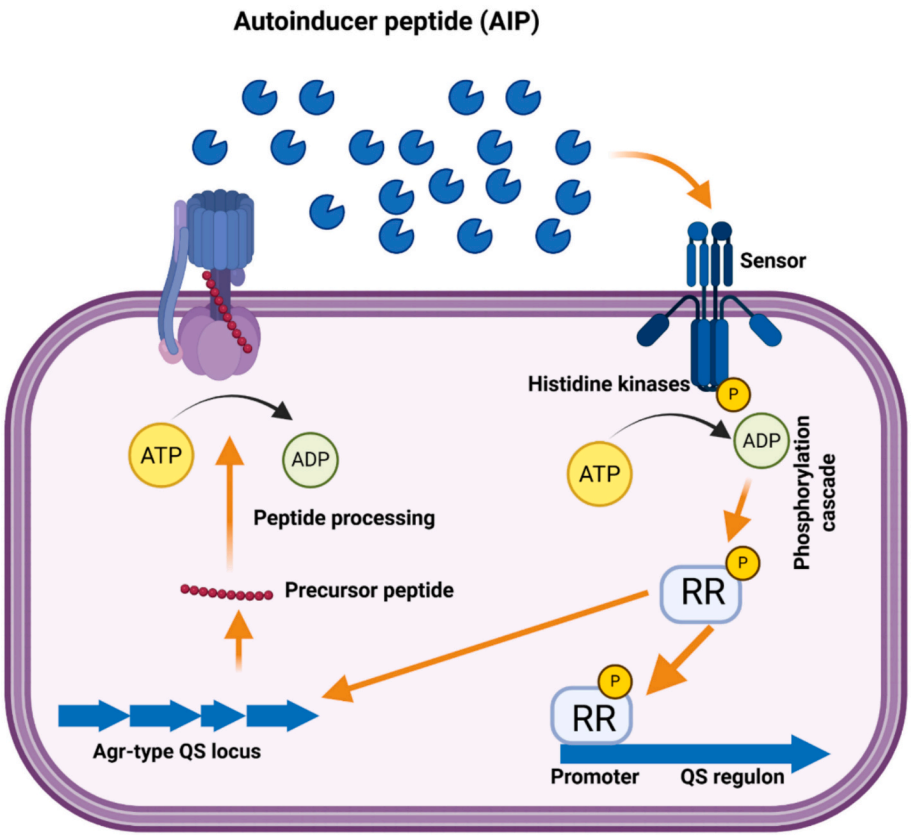

Fig. 2. Quorum Sensing Mechanism in Gram-Positive Bacteria via Agr-Type System. This diagram illustrates the steps involved in QS in Gram-positive bacteria using an Agr-type system, emphasizing peptide-mediated signaling. The quorum sensing locus encodes a precursor peptide that is processed and exported out of the cell via an ATP-binding cassette (ABC) transporter, consuming ATP in the process. The processed autoinducer peptide (AIP) accumulates in the extracellular environment. Once a threshold concentration is reached, it binds to a membrane-bound sensor histidine kinase (HK). Binding of AIP activates the HK, leading to autophosphorylation using ATP. The phosphate group is then transferred to a response regulator (RR) protein. The phosphorylated RR binds to specific promoter regions, initiating the transcription of QS-regulated genes, collectively known as the QS regulon. Activation of the QS regulon includes upregulation of the Agr-type QS locus, enhancing the production of precursor peptides and reinforcing the signaling loop. This system allows the bacterial population to coordinate gene expression in response to cell density, regulating processes such as virulence, biofilm formation, and sporulation. http://biorender.com.

2-heptyl-3-hydroxy-4(1H)-quinolone (PQS) via the PqsABCDE operon. PQS functions in conjunction with AHL systems to control virulence factors, iron acquisition, and biofilm maturation [17]. Diffusible signal factor (DSFs) is a family of cis-2-unsaturated fatty acids involved in QS in plant pathogens such as *Xanthomonas* spp. and *Burkholderia cenocepacia*. The RpfF/RpfC system detects DSF signals and regulates motility, biofilm formation, and host interaction [18].

The molecular diversity of QS signaling systems ranging from species-specific AHL and AIP circuits to the more universally conserved AI-2 highlights the evolutionary adaptability of bacterial communication networks. With the increasing prevalence of antibiotic resistance, quorum quenching (the disruption or inhibition of QS pathways, QQ) has emerged as a promising avenue for antimicrobial therapy. Targeting QS could attenuate bacterial virulence without exerting selective pressure for resistance, making it an attractive strategy for drug development. Future studies should aim to unravel the ecological relevance of QS in polymicrobial environments, elucidate signal crosstalk between species, and explore the potential roles of QS-like systems in host-microbe interactions beyond pathogenesis.

Biofilm-related infections represent a major challenge in the biomedical field, largely due to the inherent resistance of the extracellular polymeric matrix, which reduces the effectiveness of conventional antibiotics and contributes to the escalation of antimicrobial resistance. This issue is particularly critical in the context of medical devices and implants, where bacterial biofilms can firmly establish and persist, rendering traditional treatment strategies insufficient and difficult to manage [19,20]. Infections related with biofilms pose a significant challenge to healthcare, primarily due to the prevalence of antibiotic resistance and the common colonization of medical implants. Therefore, the implementation of preemptive surface coatings that possess anti-biofilm characteristics is essential. However, traditional antifouling coatings merely postpone the initial adhesion of bacteria and are ineffective in preventing the long-term development of biofilms [21]. The surfaces of synthetic materials are particularly susceptible to the colonization of pathogenic bacteria, which can result in the formation of biofilms and ultimately lead to device failure in both biomedical and industrial contexts. However, the complete removal of mature biofilms that develop on these surfaces poses a significant challenge due to the intricate nature of their chemical composition and physical structure. Consequently, preventing biofilm formation is regarded as a more effective strategy for addressing issues related to biofilms [22].

In this review, we comprehensively examine the emerging field of quorum-sensing-sensitive materials, focusing on their clinical relevance, underlying mechanisms, and design strategies that enable responsive and targeted antimicrobial action. We discuss how these smart platforms exploit bacterial communication pathways to achieve early detection of infection, controlled therapeutic release, and prevention of biofilm formation. In addition, current limitations and translational challenges—including material stability, specificity, scalability, and regulatory considerations—are critically evaluated. By integrating recent advances and outlining future perspectives, this review aims to highlight the potential of quorum-sensing-responsive systems as next-generation tools

for combating antimicrobial resistance and advancing precision infection management.

2. Quorum sensing and its role in biofilm formation, virulence, and antibiotic resistance

2.1. Biofilm formation

QS serves as a central regulatory mechanism that coordinates a wide range of microbial behaviours, especially those requiring community-wide participation. Among these behaviours, biofilm formation, virulence expression, and antibiotic resistance are of critical clinical and ecological significance. The ability of bacteria to synchronize these functions in a population-density-dependent manner not only promotes survival in fluctuating environments but also contributes to the persistence and resilience of pathogenic communities, particularly in host-associated infections. Highlights how bacterial populations synchronize gene expression in response to changes in population density through the accumulation of signaling molecules is presented in Fig. 3. Biofilms are structured microbial communities embedded in a self-produced extracellular polymeric substance (EPS) matrix that adheres to biotic or abiotic surfaces. QS plays a pivotal role at multiple stages of biofilm development, including initial attachment, microcolony formation, maturation, and dispersal.

In *P. aeruginosa*, the LasI/LasR and RhlI/RhlR QS systems regulate the production of EPS components such as Pel, Psl, and alginate, which are essential for biofilm architecture and mechanical stability [23]. The Pseudomonas quinolone signal (PQS) further modulates biofilm maturation by affecting rhamnolipid synthesis and iron acquisition [24]. Similarly, in Gram-positive bacteria like *S. aureus*, the agr system negatively regulates biofilm formation, promoting biofilm dispersal via the expression of proteases, nucleases, and surfactants [25]. QS-mediated biofilm formation confers enhanced tolerance to environmental stresses, including desiccation, oxidative stress, immune responses, and antimicrobial agents, making biofilms a key survival strategy in both environmental and host-associated niches.

2.2. Virulence regulation

One of the most well-characterized roles of QS is its control over virulence factor production, allowing pathogens to delay the expression of costly or host-damaging traits until a sufficient population density is reached, thereby optimizing resource use and evasion of host immune surveillance. In *P. aeruginosa*, QS regulates the expression of a wide array of virulence factors, including elastase (LasB), pyocyanin, exotoxin A, and hydrogen cyanide, through the hierarchical Las and Rhl systems [26]. The QS system also influences the type III secretion system (T3SS) and motility traits that are essential for acute infection. In *S. aureus*, the agr QS system governs the expression of numerous toxins, such as α-hemolysin (Hla), phenol-soluble modulins (PSMs), and superantigens, all of which contribute to immune evasion and tissue damage [11]. QS-regulated virulence is not limited to intraspecies signaling. Molecules like AI-2 and indole can mediate interspecies communication, modulating competitive or cooperative behaviours within polymicrobial

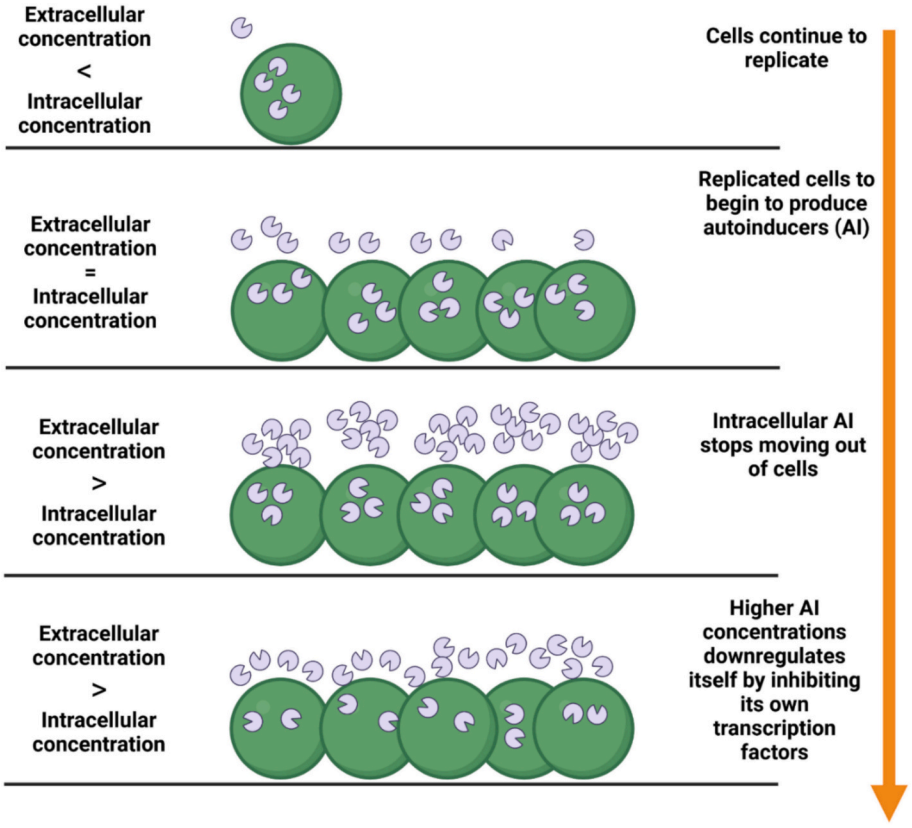

Fig. 3. Dynamics of Autoinducer Accumulation and Quorum Sensing Regulation. Illustration depicts the stepwise process of quorum sensing based on autoinducer (AI) concentration gradients during bacterial population growth. When the bacterial population is low, intracellular AI concentration is higher than extracellular concentration. Cells continue to replicate, and AIs are not yet at a threshold level to trigger quorum sensing. As the population increases, more cells produce AIs, and the extracellular AI concentration begins to rise, eventually reaching equilibrium with the intracellular concentration. With further cell replication, extracellular AI concentration exceeds intracellular concentration, triggering quorum sensing. This signals bacteria to alter gene expression, such as stopping movement or initiating group behaviours. At high AI concentrations, quorum sensing is activated, and the system downregulates AI production via negative feedback by inhibiting its own transcription factor. The extracellular and intracellular AI concentrations balance once more as the population stabilizes. http://biorender.com.

communities. Some QS signals can even influence host cells, modulating immune responses, apoptosis, and epithelial barrier integrity [27]. A schematic representation of bacterial AHL production, the uptake of signaling molecules by the bacterial receptor, and gene expression is shown in Fig. 4.

2.3. Role of QS on antibiotic resistance and tolerance

Although QS does not directly cause classical antibiotic resistance via mutations or acquisition of resistance genes, it contributes to antibiotic tolerance and persistence, especially within biofilms or during chronic infection. QS-regulated biofilm formation plays a major role in impeding antibiotic penetration, creating heterogeneous microenvironments (e.g., oxygen or nutrient gradients), and promoting the formation of persister cells—dormant variants that survive antibiotic treatment [28]. QS can upregulate the expression of multidrug efflux pumps and detoxification enzymes. In *P. aeruginosa*, QS controls the MexAB-OprM efflux system, contributing to multidrug resistance [29]. Similarly, QS-regulated catalases and superoxide dismutases help detoxify oxidative stress induced by certain antibiotics. Certain QS systems trigger general stress responses (e.g., SOS response), which can enhance survival under antibiotic exposure and promote the horizontal transfer of resistance genes via transformation, conjugation, or transduction [30].

2.4. Clinical and therapeutic implications

The QS regulation of biofilms, virulence, and antibiotic tolerance underscores its importance in chronic and device-associated infections, such as cystic fibrosis lung infections, endocarditis, chronic wounds, and urinary tract infections. These insights have fueled the development of QSIs and quorum quenching (QQ) strategies aimed at disrupting communication pathways rather than killing bacteria directly. QSIs such as furanones, AHL analogs, or natural plant compounds—are being explored for their ability to attenuate virulence, reduce biofilm formation, and restore antibiotic efficacy without exerting selective pressure for resistance [31].

To summarize, QS is intricately linked to some of the most medically and ecologically relevant bacterial behaviours. By synchronizing gene expression across a population, QS enhances the ability of bacteria to form structured communities (biofilms), express virulence in a coordinated fashion, and resist or tolerate antimicrobial agents. These connections place QS at the heart of microbial pathogenesis and persistence, making it an attractive target for novel anti-infective strategies. Continued exploration of QS pathways and their interconnections with stress responses, metabolism, and host interactions will be crucial for developing innovative approaches to combat bacterial infections in an era of rising antimicrobial resistance.

3. QS signal recognition systems

In recent years, QS-based smart material systems have become a significant research area for dynamically monitoring and directing microbial behaviour. These materials, thanks to their designs that can be activated or respond to signaling molecules based on microbial population density, can prevent biofilm formation or support beneficial microbial activities. Therefore, QS-sensitive or QS-mimicking surfaces and nanostructures hold critical potential not only in preventing infections but also in maintaining the biophysical balance of host-microbe interactions. In this regard, the intersection between biomaterials science and microbial ecology paves the way for the development of next-generation functional material systems that suppress pathogenicity, modulate immune responses, and optimize symbiotic relationships.

Biomaterials science and surface engineering are emerging as important tools for regulating host-microbe interactions. Smart surfaces, in particular, that can influence QS mechanisms or mimic this signaling, can reduce the risk of infection by controlling microbial colonization. Furthermore, functional material systems capable of sensing biological signals and responding to environmental conditions can be designed to suppress pathogenicity or promote the stability of beneficial microbial communities. Thus, future material-based approaches may reveal that QS is a decisive factor in modulating not only microbial communication but also host defense dynamics. QS-based smart materials are fundamentally composed of systems capable of recognizing specific signaling molecules with high sensitivity and selectivity. These systems typically incorporate biological components, such as receptors and enzymes, which are either embedded within the material's matrix or immobilized on its surface. In this context, material platforms capable of recognizing or neutralizing fundamental QS signals, such as AHL, are gaining prominence. Some key design approaches for QS-aware smart systems are discussed below:

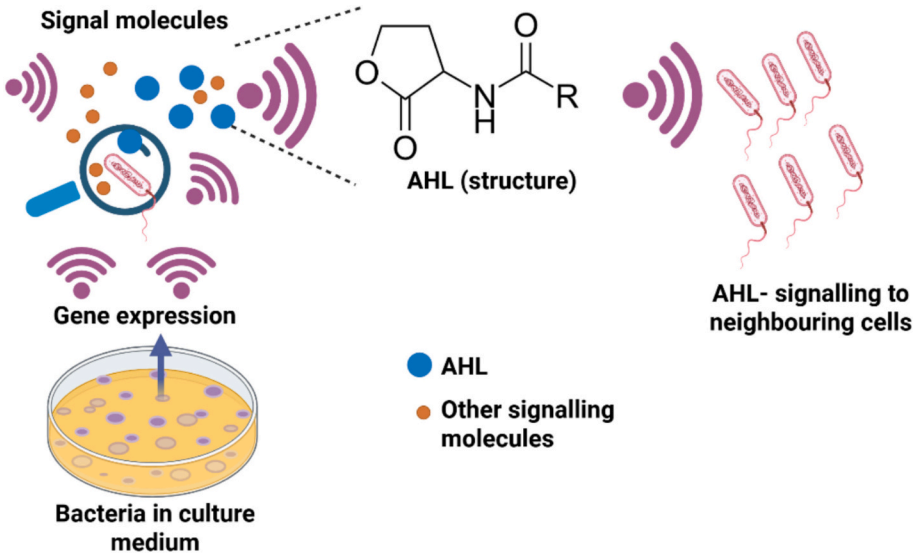

Fig. 4. Schematic representation of bacterial quorum sensing via acyl-homoserine lactone (AHL) signaling. Bacteria produce and release AHL signal molecules into the culture medium. As cell density increases, AHL accumulates and diffuses into neighbouring cells, where it binds to a receptor protein. The ligand–receptor complex activates gene expression, leading to coordinated population-level responses. http://biorender.com

3.1. Biosensor polymers sensitive to AHLs

Biosensor polymers are mixed materials that have both a biological recognition element (in this case, an AHL receptor) and a way to send signals [32]. To keep the receptor's natural structure and function, it is very important to design these polymers correctly. Some receptor immobilization strategies are as follows:

3.1.1. Physical arrest

LuxR-like receptor proteins or entire cells (e.g., genetically modified bacterial strains that respond to a specific AHL and express a reporter gene, such as GFP) can be encapsulated in porous matrices, including hydrogels, sol-gels, or polymeric membranes [33]. This approach is easy to use, however it has several problems, such the receptor leaking over time or the diffusion kinetics being slow.

3.1.2. Covalent binding

Receptor proteins can be chemically attached to polymeric substrates that possess functionalised surfaces (containing amine, carboxyl, or epoxy groups) [34]. This mitigates receptor leakage and overall enhances stability. A self-assembled monolayer (SAM) on a gold surface can act as a binding platform for a LuxR protein.

3.1.3. Aptamer based systems

Nucleic acid aptamers, which exhibit high affinity for certain AHL molecules, can be chosen and synthesized as an alternative to protein receptors [35]. Aptamers exhibit greater stability than proteins and can be readily changed and incorporated into diverse polymeric frameworks. Upon binding of an AHL, the aptamer experiences a conformational shift that can be utilized to provide an electrochemical, visual, or mechanical signal.

3.2. Signal transduction mechanisms

The biosensor polymer must transduce the AHL recognition event into a discernible signal for human interpretation. This is accomplished by multiple methods [36–38]:

3.2.1. Electrochemical detection

The binding of an AHL to an immobilized receptor results in alterations to the electrical properties, specifically impedance and surface potential, at the polymer/solution interface. Techniques such as electrochemical impedance spectroscopy (EIS) and voltammetry enable the detection of these changes at nanomolar levels [39]. *A comparative overview of the analytical performance of these QS sensing platforms in complex biological fluids is provided in* Table 1. *Such comparison is essential for guiding the selection of appropriate sensor technologies toward clinical applications where sample matrix interference and stability are major challenges.*

3.2.2. Optical detection (color change/fluorescence)

One of the most common methods. Here, a fluorescent reporter system is embedded into the polymer matrix. For example, *E. coli* cells encapsulated in a hydrogel can be engineered to express green fluorescent protein (GFP) in the presence of AHL [48,49]. When the signaling molecule is detected, the hydrogel begins to emit a bright green light. Instead of fluorescence, there are also systems that provide color change (from red to blue) via AHL binding-sensitive, color-changing chromophores or aggregation/dispersion of gold nanoparticles [50].

3.2.3. Piezoelectric detection

A polymer or aptamer that is sensitive to AHL is used to cover the surface of a quartz crystal resonator (QCM - Quartz Crystal Microbalance). When the AHL is connected, the increase of mass at the nanoscale causes the crystal's resonance frequency to change in a way that can be measured [40,51].

These biosensor polymers are the foundation of very sensitive, rapid, and field-deployable detectors for food quality assessment, clinical diagnosis (including urinary tract infections), and environmental surveillance [52].

3.2.4. Clinical translation notes

- For rapid point-of-care (POC) diagnosis in wound exudate or urine: Piezoelectric (QCM-MIP) and electrochemical aptamer-based sensors offer the best balance of speed, sensitivity, and stability [40,44,45].
- For long-term implant coatings: MIP-based or enzyme-linked QQ surfaces are more stable than whole-cell bioreporters [42,45,46].
- Whole-cell systems remain valuable for mechanistic studies but are not yet suitable for direct use in purulent or bloody samples due to viability and interference issues [39,43].
- Combining two orthogonal methods (e.g., colorimetric screening + electrochemical confirmation) may improve specificity in complex media [41,42,47].

3.3. Enzyme-controlled quorum quenching (QQ) constructs

One method to incorporate QS mechanisms into materials science involves the disruption of bacterial communication through the inactivation of signaling molecules. The process referred to as “Quorum Quenching” represents a highly effective approach for the development of anti-biofilm surfaces [53]. Conventional biocidal surfaces are designed to kill bacteria; however, QQ surfaces function by keeping bacteria in a “silent” state. This mechanism inhibits virulence and biofilm formation while avoiding the selective pressure that can contribute to the development of antibiotic resistance [54]. The most critical step in

Table 1
Comparison of QS signal detection techniques in complex biological fluids [39–47].

Detection Method	Example QS Target	Limit of Detection (LOD)	Response Time	Stability in Biological Fluids (e.g., pus/blood)	Key Clinical Limitation
Electrochemical (EIS/ Voltammetry)	AHLs (e.g., C12-HSL)	1–10 nM	10–30 min	Moderate (protein fouling on electrode surface)	Requires surface regeneration; fouling in whole blood
Fluorescent (whole-cell bioreporter)	AHLs, AI-2	0.1–1 μM	1–4 h	Low (cell viability loss; signal interference by heme)	Not suitable for real-time; long response time
Colorimetric (AuNP aggregation)	AHLs	10–100 nM	30–60 min	Low–Moderate (salt-induced aggregation in serum)	Limited to transparent or diluted samples
Piezoelectric (QCM-MIP)	AHLs (e.g., C6-HSL)	0.5–5 nM	5–15 min	High (MIP stability; minimal fouling)	Requires careful regeneration; humidity sensitivity
Aptamer-based (optical/ electrochemical)	AHLs, AI-2	1–50 nM	15–30 min	High (aptamers stable in serum)	Limited availability of high-affinity aptamers for QS signals
Molecularly Imprinted Polymers (MIPs)	AHLs	0.1–1 nM	5–20 min	Very High (chemically robust)	Binding reversibility; potential cross-reactivity

Abbreviations: EIS: Electrochemical Impedance Spectroscopy; QCM: Quartz Crystal Microbalance; MIP: Molecularly Imprinted Polymer; AuNP: Gold Nanoparticle; AHL: Acyl-Homoserine Lactone; AI-2: Autoinducer-2.

material-based applications of this approach is the stable integration of enzymes, such as AHL, that hydrolyze or chemically modify QS signals into the material. This allows the surface to actively deactivate the bacterial communication network by continuously converting the signaling molecules present in the medium. Enzymes commonly used in QQ applications and their immobilization strategies are detailed below.

- Immobilization of QQ Enzymes:

AHL-Lactases: These enzymes catalyse the hydrolysis of the homoserine lactone ring within the AHL molecule, resulting in its inactivation. AHL-lactases, such as the enzyme AiiA derived from Bacillus species, are capable of being immobilized on the surfaces of polymeric coatings, catheters, or subsea structures [55].

AHL-Acylases: These enzymes break the acyl chain of AHL and stop the signaling molecule from working again [56].

Oxidases/Reductases: Some enzymes can break down or oxidise AHLs, which changes their structure.

- Engineering QQ Structures: The performance of materials incorporating QQ enzymes is contingent upon the efficiency of enzyme immobilization, as well as the stability and longevity of the enzyme [57]. Polymeric membranes and thin-film coatings provide a fundamental platform for the immobilization and stable operation of QQ enzymes; in addition, nanocarrier systems and self-organizing substrates (SAMs) offer additional advantages in terms of controlled enzyme release, surface adsorption, and preservation of biocatalytic activity. These multilayered approaches enhance the effectiveness of the QQ mechanism by providing both high enzyme loading capacity and long-term functional activity in surface-based applications. Therefore, the interaction of enzymes with surfaces, their structural integrity, and functional continuity become critical design parameters for successfully integrating the QQ mechanism into materials. Optimizing the enzyme-material interface ensures not only the efficient degradation of signaling molecules but also the long-term preservation of biocatalytic activity. Various engineering strategies have been developed to address these requirements, and different material platforms have been adapted for the stable immobilization of QQ enzymes.
- Polymeric Membranes and Coatings: Polymers such as polyurethane, polyacrylonitrile or chitosan can form porous membranes or thin film coatings to accommodate QQ enzymes. These membranes can be integrated into medical implants or water purification systems [58].
- Nanocarriers: Liposomes, polymeric nanoparticles, and silica nanoparticles serve as vehicles for the transport and controlled release of QQ enzymes, as well as for their attachment to surfaces. This offers safeguarding to the enzyme and enhances its functionality [59].
- Self-Assembled Substrates (SAMs): Self-assembled sheets can be used to consistently attach QQ enzymes to gold or silica surfaces. This makes a smooth surface with a lot of enzyme loading and easy access [60].

These QQ constructions provide a long-term answer to the problem of antibiotic resistance by stopping bacteria from becoming pathogenic instead of killing them [54].

3.4. Classification of QS-responsive materials

The convergence of quorum sensing (QS) mechanisms with materials science has yielded a new class of biointerfaces that can be systematically classified according to their functional interaction paradigm with the microbial microenvironment. Unlike traditional passive biomaterials, these systems establish bidirectional or unidirectional communication with bacteria, enabling dynamic responses to population-density-dependent cues. Based on the complexity of signal processing and actuation, three distinct categories emerge: (i) passive biosensing platforms, (ii) active quorum-quenching (QQ) interfaces, and (iii) closed-loop theranostic systems. The classification of QS-responsive materials is shown in Fig. 5.

3.4.1. Passive biosensing materials (signal-to-reading converters)

These platforms are designed for non-intervening surveillance. They function as analytical transducers that capture and report QS signal molecules without perturbing the native microbial community. The recognition layer typically employs high-affinity biorecognition elements—such as LuxR-type receptor proteins, nucleic acid aptamers, or molecularly imprinted polymers (MIPs)—that selectively bind autoinducers (e.g., AHLs, AI-2, or AIPs). Upon ligand binding, a conformational or chemical change is transduced into a quantifiable output signal (electrochemical, piezoelectric, fluorescent, or colorimetric) with sensitivity often reaching nanomolar to picomolar levels. Importantly, these materials operate as non-actuating sentinels, making them ideal for early infection diagnosis, food safety monitoring, and environmental surveillance where minimal microbial disturbance is desired [39,40].

3.4.2. Active quorum-quenching materials (signal interrupters)

Moving beyond passive detection, this category encompasses materials that actively disrupt bacterial communication networks. The working principle relies on either (a) enzymatic degradation of autoinducers via immobilized QQ enzymes (e.g., AHL-lactonases, AHL-acylases, or oxidoreductases) or (b) competitive inhibition of signal receptors using QS inhibitors (QSIs) such as halogenated furanones, AHL analogs, or natural plant-derived compounds. These surfaces continuously convert or block signaling molecules, effectively maintaining the bacterial population in a “silent” (pre-virulent) state. Critically, because QQ materials do not kill bacteria directly, they exert minimal selective pressure, thereby reducing the risk of resistance evolution. This paradigm is particularly valuable for long-term implant coatings, urinary catheters, and water treatment membranes where biofilm prevention is paramount [53,54].

3.4.3. Integrated feedback (Theranostic) materials – closed-loop systems

The most advanced class, these materials embody biomimetic intelligence by combining sensing, computation, and actuation into a single self-regulating platform. They incorporate molecular logic gates (AND, OR, NOT) that process multiple QS signal inputs and trigger a therapeutic output only when predefined threshold conditions are met. Upon detection of a critical autoinducer concentration (indicative of established infection), the material undergoes a physicochemical transition—such as hydrogel swelling, bond cleavage, or nanoparticle disassembly—to release a precise dose of antimicrobial agents (antibiotics, antimicrobial peptides, or reactive oxygen species). This response is spatiotemporally controlled and reversible: once the bacterial burden decreases and QS signal levels fall below the threshold, the material ceases drug release. Such closed-loop systems enable on-demand therapy, minimize systemic off-target effects, and align with the principles of precision medicine. Representative applications include infection-responsive wound dressings, smart drug-eluting stents, and self-regulating intrauterine devices [61–63].

4. QS-controlled material responses

The development of materials and agents with enhanced quality stands as a pivotal tenet of the “Quality by Design” (QbD) framework. This principle encompasses not only the clinical conditions that the new product is intended to address but also its pharmacokinetics, pharmacodynamics, and potential toxicity [64,65]. QbD emphasizes the importance of “need-based smart design” at the core of material development, proving particularly beneficial in domains such as biomaterials, drug-delivery systems, and functional polymers. Within this methodology, the critical quality attributes that influence material

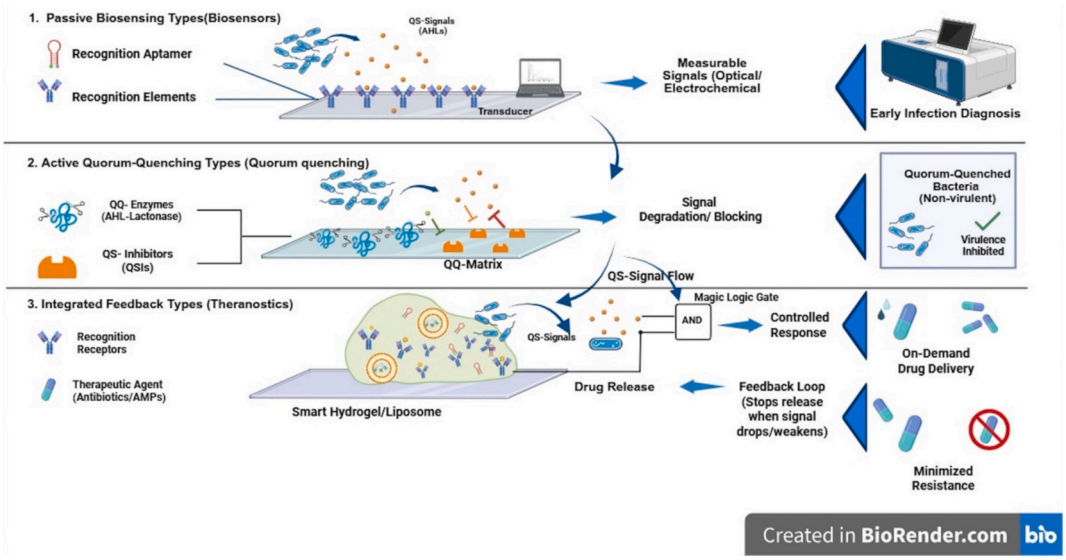

Fig. 5. Quorum sensing–targeted biosensing and therapeutic strategies. (1) Passive biosensing systems (biosensors): Recognition elements such as aptamers or antibodies capture QS molecules (e.g., AHLs) and convert binding events via a transducer into measurable optical or electrochemical signals, enabling early infection diagnosis. (2) Active quorum-quenching systems: Quorum-quenching (QQ) enzymes (e.g., AHL-lactonases) and QS inhibitors (QSIs) are incorporated into a matrix to degrade or block QS signals, disrupting signal propagation and reducing bacterial virulence. (3) Integrated feedback systems (theranostics): Smart hydrogel or liposome platforms combine QS recognition with therapeutic payloads (e.g., antibiotics or antimicrobial peptides). Upon detection of QS signals, logic-gated activation (e.g., AND gate) triggers-controlled drug release, followed by a feedback loop that halts release as signal levels decrease, enabling on-demand therapy and minimizing resistance. http://biorender.com.

performance—such as mechanical strength, porosity, biocompatibility, and release behaviour—are identified from the outset, allowing for a systematic optimization of the entire process to achieve these established goals. This paradigm shift in material development moves away from trial-and-error methods toward purpose-driven engineering, ensuring that the final product aligns perfectly with its intended use, whether that involves controlled diffusion for drug delivery, infection-responsive characteristics in wound dressings, or heightened selectivity in sensing systems. Consequently, QbD fosters more predictable manufacturing processes, diminishes variability, and guarantees consistent functional performance in real-world applications.

Quorum sensing represents an intricate communication system that allows microbial communities to collectively react to environmental stimuli. The incorporation of this mechanism into biomaterial design has facilitated the creation of sophisticated systems capable of detecting and responding to chemical signals from microorganisms. Materials governed by QS can adaptively modify their surface characteristics, permeability, or biological activation in accordance with the density of microbial populations. Consequently, these systems can deliver multifunctional responses, such as triggering preventive defenses during the initial phases of infection, inhibiting biofilm development, or fostering beneficial interactions among microbes. This innovative approach elevates biomaterial engineering from a mere passive defense mechanism to a dynamic platform that actively engages with microbial signaling.

The most intriguing new things are happening with dynamic material responses that happen after sensing, in addition to signal recognition. This changes the material from a static thing into a "living" system that interacts with its surroundings [4].

4.1. Color change and surface energy modification

Color change and surface energy modification approaches demonstrate the functional diversity of smart materials responsive to QS signals. Color-based systems provide intuitive, energy-free visual output that directly communicates the status of infection or microbial activity to the user. Dynamic adjustment of surface energy, on the other hand, allows for control of the material's interaction with the biological environment, offering more active functions such as inhibiting bacterial attachment, reducing biofilm formation, or directing cell behaviour. Considering these two features together, QS-responsive platforms can be designed not only as sensing but also as semi-living interfaces that adapt to environmental conditions and change behaviour as needed. This offers a significant advantage, particularly for environmentally sensitive applications such as wound dressings, implant coatings, and environmental biosensors.

- Color Change: The fluorescent reporter systems we talked about before can be used to detect things, but they can also be used to show how the material itself reacts. For instance, a band-aid can change color to signify when harmful germs are present [39] The principle of structural color is used in more advanced systems. You can put materials like photonic crystals or inverse opal hydrogels into AHL-sensitive polymer networks. When AHL binds to the network, it makes it expand or shrink, which changes the material's lattice constant and the hue of the light it reflects [66]. This gives a very accurate visual cue that doesn't need a label.
- Surface Energy Modification: The surface energy (hydrophilicity/hydrophobicity) of a material determines characteristics including cell adhesion, protein adsorption, and wetting. This property can be changed in real time with QS. For instance, it can be added molecules (such peptides or oligomers) to the surface of a polymer that alter shape when AHL is present. The surface may be hydrophobic before it binds to AHL. When AHL is found, the conformational shift reveals hydrophilic groups, which makes the surface hydrophilic [67]. This can help release bacteria that have already attached themselves ("anti-fouling") or be used to manage cell adherence.

4.2. pH, viscosity or permeability responses

QS signals can induce significant alterations in the macroscale physicochemical characteristics of the material.

- pH Response: Genetically modified microbes or enzyme systems can be set up to start metabolic pathways that make acid or base when

they sense AHL. If this pH change happens in "smart" hydrogels that are sensitive to pH (such polyacrylic acid), it might trigger a big volumetric phase transition in the material, like rapid swelling or collapse [61]. You can use this to control how drugs are released: AHL signals are sent out by pathogens that build up at the site of an infection. These signals make the hydrogel swell and release the antibiotic inside. The signal goes away and the hydrogel closes when the infection becomes better. The QS-induced pH change typically arises from the engineered expression of metabolic enzymes (e.g., glucose oxidase, urease, or lactate dehydrogenase) under the control of QS-responsive promoters (e.g., LuxI/LuxR system). Upon detection of threshold concentrations of autoinducers (e.g., AHLs), genetically modified microbes embedded in the hydrogel initiate the transcription of these enzyme genes. For example, glucose oxidase catalyzes the oxidation of glucose to gluconic acid and hydrogen peroxide, locally lowering the pH from neutral to acidic (pH 4.0–5.5). Conversely, urease expression leads to ammonia production and an alkaline shift (pH 8.0–9.0). This localized pH alteration directly affects the ionization state of pH-sensitive polymer side chains (e.g., carboxyl groups in poly(acrylic acid) or amino groups in chitosan). At a critical pH (pKa), the polymer undergoes a conformational change: protonation/deprotonation alters hydrogen bonding and electrostatic repulsion, driving a macroscopic volume phase transition (swelling or collapse). In the case of hydrogels containing acid-labile crosslinkers (e.g., acetal or hydrazone bonds), the pH drop triggers bond hydrolysis, leading to network disintegration and consequent release of encapsulated therapeutics. Importantly, this process is reversible if the pH-sensitive moiety is designed with buffering capacity, allowing the gel to re-form once the bacterial burden decreases and the pH returns to physiological levels [61,68–70]. Such QS-pH-gelation coupling represents a self-regulated, energy-independent actuation mechanism that is particularly attractive for on-demand drug delivery in infected wounds or implant-associated biofilms.

- Viscosity Response: QS can change the viscosity of suspensions or hydrogels. A polymer solution with AHL in it may have structures that either cross-link and gel or, on the other hand, unlink and turn into a liquid. These "liquid-gel" changes are perfect for 3D bioprinting: During printing, the material stays thin, but it quickly gels when synthetic AHL molecules are added to the medium after printing. This keeps the structure strong [71–73].
- Permeation Response: QS can change how permeable polymeric membranes or microcapsules are. When AHL is present, a polymer membrane that swells or alters the size of its pores can modify how it lets molecules pass through [62]. This could be utilized in "smart filtration" systems or tiny medication carriers that deliver drugs directly to the right place. The capsule only lets out its contents when harmful bacteria are present because of their QS signaling. A

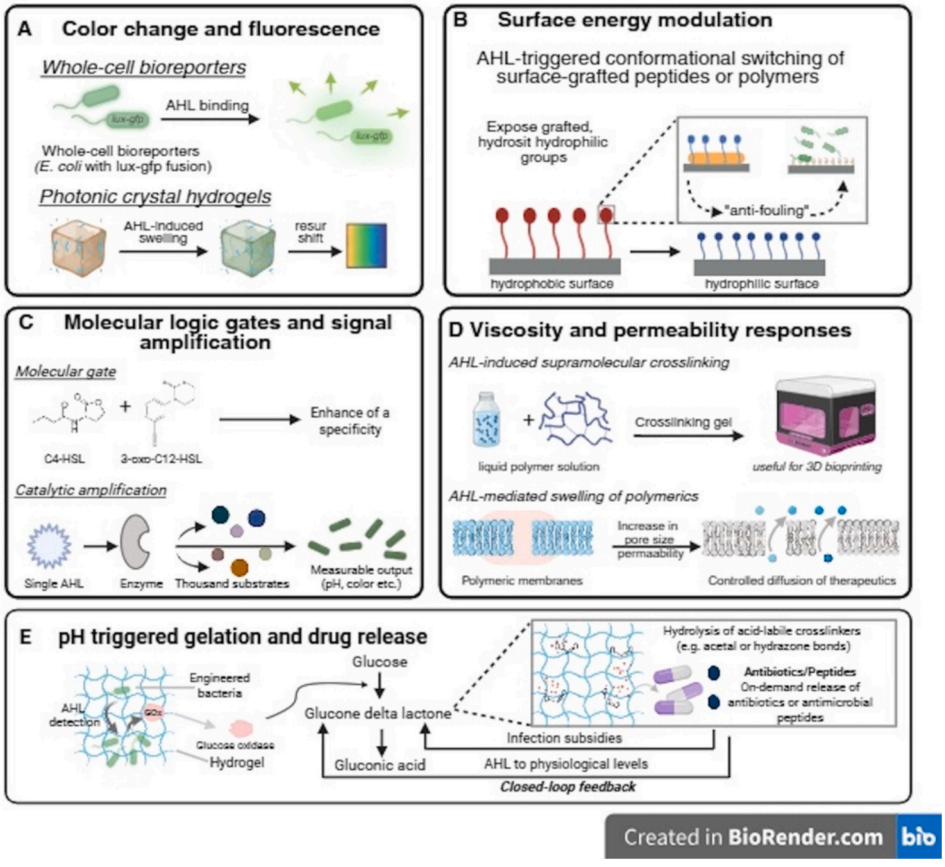

Fig. 6. Comprehensive schematic of QS-controlled material response mechanisms. (A) Color change and fluorescence. Whole-cell bioreporters produce fluorescence upon AHL binding, while photonic crystal hydrogels undergo AHL-induced swelling that shifts reflected color. (B) Surface energy modulation. AHL-triggered conformational switching of surface-grafted peptides or polymers exposes hydrophilic groups, converting hydrophobic surfaces to hydrophilic, anti-fouling states. (C) Molecular logic gates and signal amplification. Combinatorial recognition of distinct AHLs enables molecular gating for enhanced specificity; catalytic amplification converts low AHL inputs into amplified, measurable outputs (e.g., pH or color changes). (D) Viscosity and permeability responses. AHL-induced supramolecular crosslinking transforms liquid polymer solutions into gels, while AHL-mediated swelling of polymeric membranes increases pore size and permeability, enabling controlled diffusion (e.g., for drug delivery or 3D bioprinting). (E) pH-triggered gelation and drug release. Engineered bacteria detect AHLs and convert glucose to gluconic acid via glucose oxidase, lowering pH and hydrolyzing acid-labile crosslinkers within hydrogels. This triggers on-demand release of antibiotics or antimicrobial peptides and establishes a closed-loop feedback system that attenuates infection as AHL levels return to baseline. http://biorender.com.

comprehensive schematic representation of the QS-controlled material response mechanisms is shown in Fig. 6.

This mechanism integrates five distinct categories of stimuli-responsive behaviour enabled by quorum sensing (QS) signals. Whole-cell bioreporters (e.g., *E. coli* with a lux–gfp fusion) emit green fluorescence upon AHL binding [39]. Alternatively, photonic crystal hydrogels undergo structural color changes due to AHL-induced swelling or shrinking [74]. In another approach, AHL-triggered conformational switching of surface-grafted peptides or polymers exposes hydrophilic groups, converting a hydrophobic surface into a hydrophilic one and thereby releasing adhered bacteria (antifouling) [75,76]. Engineered bacteria embedded within a hydrogel can produce glucose oxidase upon AHL detection. Subsequent glucose oxidation generates gluconic acid, lowering the local pH from 7.4 to 4.0–5.5. This pH decrease protonates carboxyl groups on poly (acrylic acid) chains, leading to hydrogel swelling or hydrolysis of acid-labile crosslinkers (e.g., acetal or hydrazone bonds). As a result, encapsulated antibiotics or antimicrobial peptides are released on demand [61,69,76]. This process is reversible: as the infection subsides and AHL levels decrease, the pH returns to physiological values and the gel reforms, enabling closed-loop feedback. In addition, AHL-induced supramolecular crosslinking (e.g., cyclodextrin–adamantane host–guest interactions) can convert a liquid polymer solution into a gel, which is useful for applications such as 3D bioprinting. Alternatively, AHL-mediated swelling of polymeric membranes can increase pore size and permeability, allowing controlled diffusion of therapeutics [62]. Logical gating can further enhance specificity: for example, an AND gate requires the simultaneous presence of two distinct AHL signals (e.g., C4-HSL and 3-oxo-C12-HSL) to trigger a response [77]. Finally, catalytic amplification enables signal enhancement, whereby a single AHL molecule activates an enzyme that converts many substrate molecules, producing a large measurable output such as a color change or pH shift [40,78]. Together, these strategies illustrate how QS signals can be transduced into diverse macroscopic material responses, enabling self-regulated and infection-specific actuation in biomedical applications.

4.3. Molecular logic gates and signal amplification

This is the most advanced and promising field of QS-material integration. In this case, the substance is more than just a basic detector or responder; it is a "biochemical computer" that can make complicated choices [79].

Molecular Logic Gates: The fundamentals of Boolean logic (AND, OR, NOT) can be utilized in QS systems. This enables a material to react just in the presence of a particular combination of signals, significantly enhancing selectivity and safety [77].

- AND Gate: A substance can be made to only react (such releasing a medication or changing color) when TWO distinct AHL signals (like C4-HSL AND 3-oxo-C12-HSL) are present at the same time. This restricts the response to the presence of a certain type of pathogen capable of generating several signals, hence preventing false positives [80].
- OR Gate: If either of two separate AHLs is present, a response happens. This helps find more types of infections.
- NOT Gate: Can be put into action by blocking the response when an inhibitor (such a QQ enzyme) is present.

Genetically modified cells can have these logic gates programmed into them as genetic circuits. These circuits can then be put into a hydrogel matrix [81]. Alternatively, signal integration can be achieved in pure chemical systems by employing various receptors and signaling pathways organized on a surface.

4.4. Signal amplification

Natural QS systems exhibit significant amplification, where a signal of even a few nanomolars induces substantial alterations in the expression of several genes. In materials science, this amplification principle is emulated such that a minor signal trigger elicits a substantial material reaction.

- Catalytic Amplification: You can make systems that let an AHL molecule "turn on" an enzyme's activity. After that, this enzyme can process thousands of substrate molecules, which can cause a measurable change (like a color change or the formation of gas bubbles) or a physical change (like a big drop in pH) [82–84]. This makes sensitivity much higher.
- Cascade Reactions: It can be used chemical or enzymatic cascades that have non-linear response curves. The first detection of AHL causes the release of a second messenger molecule, which then starts a third reaction that causes a sudden change in a material's properties [78].This makes the signal act like a "threshold" since nothing happens while it is below a particular level, but when it is beyond that level, there is a full and robust response.
- Systems that can make copies of themselves: A very powerful idea that is more theoretical. An AHL signal can start the making of a peptide or polymer, which can then cause self-assembly. This process of putting things together is catalytic, which means that existing fibrils speed up the process of putting together new monomers. This leads to quick changes in the material on a large scale, such the fast creation of a gel [85].

5. Materials science at the interface of quorum sensing and microbial behaviour

The integration of materials science with biological systems offers a unique and powerful approach to understanding and controlling microbial communication. As QS underpins critical microbial behaviours such as biofilm formation, virulence regulation, and antibiotic resistance, material-based strategies have been increasingly employed to probe, interfere with, and exploit these signaling systems. Simultaneously, QS principles are influencing the design of smart, adaptive, and biomimetic materials that emulate biological complexity.

This section discusses the bidirectional relationship between materials science and QS: (i) how engineered materials are used to study and modulate QS systems and (ii) how insights from QS and microbial collective behaviour are informing the development of responsive and bioinspired materials. Traditional microbiological approaches to studying QS often lack the spatial and temporal resolution required to capture the nuances of microbial signaling. Advances in nanomaterials, microfabrication, and biosensing platforms now enable more precise investigations of QS dynamics.

5.1. QS-sensing materials (passive detection)

Materials in this category are designed to detect and report QS signals without interfering with bacterial behaviour. They function as analytical transducers that capture autoinducers (AHLs, AI-2, or AIPs) using high-affinity biorecognition elements such as LuxR-type receptors, nucleic acid aptamers, or molecularly imprinted polymers (MIPs). Upon ligand binding, a conformational or chemical change is transduced into a quantifiable output signal (electrochemical, piezoelectric, fluorescent, or colorimetric) with sensitivity often reaching nanomolar to picomolar levels. These non-actuating sentinels are ideal for early infection diagnosis, food safety monitoring, and environmental surveillance where minimal microbial disturbance is desired. Representative examples include AHL-sensitive QCM-MIP sensors [40] and whole-cell bioreporters (e.g., *E. coli* with lux-gfp fusion) encapsulated in hydrogels [39].

5.2. QS-interfering materials (active quorum quenching)

These materials actively disrupt bacterial communication by degrading or blocking QS signals. Two primary mechanisms are employed: (a) enzymatic degradation of autoinducers using immobilized QQ enzymes (e.g., AHL-lactonases, AHL-acylases, or oxidoreductases), or (b) competitive inhibition of signal receptors using QS inhibitors (QSIs) such as halogenated furanones, AHL analogs, or natural plant-derived compounds. By continuously converting or blocking signaling molecules, these surfaces maintain the bacterial population in a "silent" (pre-virulent) state. Critically, because QQ materials do not kill bacteria directly, they exert minimal selective pressure, reducing the risk of resistance evolution. This paradigm is particularly valuable for long-term implant coatings, urinary catheters, and water treatment membranes where biofilm prevention is paramount.

5.3. QS-mimetic materials (synthetic communication systems)

This category encompasses materials that emulate the principles of bacterial QS – namely autonomous signal generation, diffusion, threshold sensing, and synchronized response – rather than merely responding to natural QS signals. These synthetic or hybrid systems do not interfere with bacterial QS; instead, they replicate its logic in engineered constructs. Key examples include:

- Hydrogel-based artificial cells: Embedded with synthetic QS-like circuits (e.g., genetic oscillators or enzyme cascades), these protocells exhibit collective swelling, self-healing, or regulated release in response to environmental stimuli, mimicking bacterial community behaviours [86].
- Chemically communicating soft matter: Microgel droplets or liposome-based protocells loaded with signal-producing and signal-receiving chemistries can activate programmed responses (e.g., dye release or gelation) once a critical local concentration of a diffusible chemical cue is achieved, analogous to the quorum threshold in bacteria [87].
- Engineered living materials (ELMs): Genetically modified bacteria embedded in polymeric or hydrogel matrices can be programmed with synthetic QS circuits to coordinate group-level behaviours such as color change, therapeutic release, or self-healing, offering programmable spatiotemporal control [88].

These systems are inspired by but distinct from natural QS; they do not require the presence of bacteria and can be designed to operate in isolation or in hybrid environments.

5.4. QS-responsive biosensors and microdevices

Materials-based biosensors incorporating fluorescent probes, electrochemical transducers, or nanoparticles have been developed to detect autoinducers such as AHLs, AI-2, or peptide signals in real time [89]. These platforms utilize functionalized surfaces (e.g., gold nanoparticles, graphene oxide) to selectively capture QS molecules and quantify them with high sensitivity. Microfluidic devices fabricated from biocompatible polymers like PDMS allow for controlled spatial confinement and gradient generation, enabling researchers to observe cell–cell communication, signal diffusion, and QS threshold responses under physiologically relevant conditions [90]. Molecularly imprinted polymers (MIPs) have been designed to selectively recognize and sequester QS signals. These "smart polymers" mimic antibody–antigen interactions and can be used to disrupt QS by scavenging autoinducers from microbial communities [91].

One of the most promising applications at the QS-materials interface lies in (QQ), the disruption or inhibition of QS pathways using engineered materials. Surfaces coated with QS inhibitors (QSIs)—such as synthetic AHL analogs, plant-derived flavonoids, or enzymes like AHL-lactonases—can inhibit QS in situ and prevent biofilm formation on medical devices, implants, and industrial surfaces [92]. These materials offer a non-bactericidal approach to infection control, minimizing the risk of resistance development. Advanced materials like responsive hydrogels and layer-by-layer assembled polyelectrolyte films can release QSIs in a stimuli-responsive manner, such as upon bacterial adhesion or pH shifts, enabling on-demand QQ [93].

Metallic and carbon-based nanoparticles (e.g., AgNPs, ZnO, graphene oxide) can modulate QS through multiple mechanisms, including autoinducer degradation, signal receptor blocking, and membrane perturbation [94]. These nanomaterials often exhibit synergistic effects when combined with antibiotics or anti-biofilm agents. For example, gold nanoparticles functionalized with AHL analogs have been shown to competitively inhibit QS receptors in *P. aeruginosa*, reducing virulence factor expression and biofilm maturation [95].

5.5. QS-inspired material design

While materials are increasingly used to control QS, the underlying principles of QS are also inspiring novel material systems that mimic collective behaviour, signal integration, and dynamic responsiveness. QS demonstrates how simple organisms can coordinate complex behaviours using chemical signaling. This has inspired the design of materials that can communicate chemically, enabling distributed sensing, autonomous responses, and emergent functionalities in synthetic systems. For instance, hydrogel-based artificial cells embedded with QS-like circuits can exhibit collective swelling, self-healing, or regulated release in response to environmental stimuli, mimicking bacterial community behaviours [86]. Incorporating QS genetic circuits into engineered microbial consortia or synthetic cells enables programmable behaviours in living materials. Such systems are being explored for applications ranging from smart wound dressings that sense infection to biosensors that signal contamination via colorimetric changes [96]. The integration of QS-regulated gene expression with 3D-printed or electrospun scaffolds opens up new possibilities for living materials capable of adapting to their surroundings, coordinating repair, or modulating tissue regeneration in real time.

The convergence of QS and materials science is increasingly moving toward hybrid living-synthetic systems, where engineered bacteria embedded in smart materials perform functions such as biosensing, self-assembly, or therapeutic delivery. Key challenges are maintaining microbial viability within synthetic matrices, engineering stable signal exchange across material boundaries, ensuring safety and containment in clinical or environmental applications. Nonetheless, the development of engineered living materials (ELMs) that respond to QS signals represents a frontier with profound implications for healthcare, environmental remediation, and soft robotics.

5.6. Smart materials that respond to or mimic quorum sensing

The development of smart materials or engineered systems that can sense, respond to, and adapt based on environmental stimuli has opened new avenues in biomedicine, environmental sensing, synthetic biology, and bioelectronics. A particularly innovative direction involves materials that either respond to microbial QS signals or are engineered to mimic the principles of QS, such as decentralized communication, threshold-based activation, and coordinated behaviour. By integrating QS mechanisms into material systems, researchers aim to create bio-responsive coatings, drug delivery platforms, artificial biofilms, and living materials that exhibit programmable and collective behaviours akin to microbial communities. Materials that respond to microbial QS signals are typically engineered to detect autoinducers (e.g., AHLs, AI-2, or oligopeptides) and trigger a functional change—such as releasing antimicrobials, changing optical properties, or initiating degradation—once the microbial population reaches a critical density.

One of the most prominent applications of QS-responsive materials is

in infection-responsive drug delivery. These systems remain inert under normal conditions, but activate in response to bacterial QS molecules, particularly during infection, where pathogen density is high. For instance, hydrogels functionalized with AHL-sensitive elements have been developed to release antibiotics or QQ agents only when N-acyl homoserine lactones (AHLs) reach a threshold concentration, thereby minimizing off-target toxicity and delaying resistance development [97]. Moreover, nanoparticles encapsulating antibiotics, coated with AHL-degrading enzymes (e.g., lactonases) or QS-sensitive gatekeepers, have demonstrated enhanced activity in biofilm-rich infections, releasing drugs only when QS is active [98]. Smart materials have also been designed as biosensors that detect QS signals and report on microbial density or infection status. For instance, Fluorescent polymeric films or colorimetric hydrogels can change optical properties in response to AHLs, enabling real-time detection of bacterial QS in clinical or environmental samples [99]. Electrochemical sensors embedded in responsive materials detect AI-2 or peptide signals and generate quantifiable outputs such as voltage changes or electrical resistance, facilitating point-of-care diagnostics [100].

For antimicrobial purpose, surfaces modified with QS-responsive coatings can inhibit bacterial attachment or release QQ agents when autoinducer levels increase. For instance, coatings that release lactonase enzymes upon detection of AHLs can pre-emptively disrupt biofilm formation [101].

5.7. Materials that mimic QS behaviour

Beyond sensing QS signals, materials scientists are increasingly interested in mimicking the principles of QS namely autonomous signal generation, diffusion, threshold sensing, and synchronized response—to create programmable, collective behaviours in synthetic systems. Engineered bacteria embedded within polymeric, or hydrogel matrices can be programmed with synthetic QS circuits, allowing the material to act as a living, communicative system. These “engineered living materials” (ELMs) can not only sense environmental conditions (e.g., toxins, pH, light) and coordinate a group-level response, such as producing color changes, releasing therapeutics, or self-healing [88] but also can exhibit threshold-dependent behaviours, mimicking QS-like gene regulation. For instance, producing antimicrobial peptides only when bacterial load surpasses a certain density. Such systems harness QS-like principles for spatiotemporal control and community-wide coordination in synthetic constructs.

Researchers have extended the QS paradigm to non-biological, chemical communication networks, creating chemically communicating soft matter systems. Microgel droplets or liposome-based protocells can be loaded with signal-producing and -receiving chemistries that simulate QS communication. These systems emit and sense chemical cues, activating programmed responses once a critical local concentration is achieved [102]. For example, a material can be designed to release a dye or therapeutic only when a collective quorum of artificial “cells” has received a signal similar to coordinated virulence expression in bacteria. Hydrogels containing reaction–diffusion networks or feedback-controlled gene circuits have been developed to mimic QS-like behaviours such as signal propagation, threshold activation, and pattern formation. These systems can dynamically reorganize or release functional agents in a manner analogous to microbial colony coordination [87].

Smart materials that respond to or mimic QS are finding applications in multiple domains. In biomedicine, infection-responsive coatings for implants and catheters, targeted drug delivery systems, and smart wound dressings that adapt to pathogen load. Whereas, in synthetic biology, building blocks for living biofactories, biosensors, or programmable tissues that communicate via synthetic QS systems. For environmental monitoring: responsive materials that signal microbial contamination or metabolic activity in water systems or industrial processes. In addition to that it can be used for dissecting microbial social behaviour, communication range, and the role of QS in polymicrobial communities.

Smart materials that respond to or mimic QS represent a novel and exciting class of functional systems at the intersection of materials science, microbiology, and synthetic biology. Whether through direct sensing of microbial communication signals or by emulating the decentralized, density-dependent behaviours of microbial populations, these materials hold promise for next-generation applications in precision therapeutics, adaptive biointerfaces, and programmable synthetic ecosystems. Continued advances in materials design, biological circuit engineering, and interfacial science will accelerate the realization of responsive and intelligent material systems inspired by the microbial world.

Despite their potential, several challenges remain in the development and deployment of QS-responsive or QS-mimetic smart materials. Autoinducers can be unstable or subject to environmental degradation, complicating signal interpretation. Achieving precise, tunable thresholds for signal detection is essential for avoiding false positives or premature activation. Embedding engineered microbes or synthetic circuits within materials requires careful balancing of biocompatibility, nutrient diffusion, and safety constraints. Future efforts should be focused on modular, plug-and-play platforms for integrating QS components into materials, the use of machine learning for material–signal optimization, and the exploration of multi-signal systems that mimic the complexity of microbial communication networks.

5.8. Biomedical applications of QS-responsive materials

Modern healthcare is severely endangered by the problem of infections associated with biofilms developing on medical implants and chronic wounds that cannot be effectively treated with regular antibiotics (Arciola et al., 2018). Biofilm is a structured community of bacteria enclosed in an extracellular matrix that is over 1000 times more resistant to antibiotics than free planktonic organisms (Hall & Mah, 2017; Juszczuk-Kubiak, 2024). Although current treatment approaches are based on administering high doses of broad-spectrum antibiotics to the body, these drugs are ineffective against biofilms and antibiotic-resistant bacteria are still a major problem [103].

The global antimicrobial resistance emergency has forced biomaterials to evolve from their basic structural role into active materials which engage with biological systems [104]. Smart materials that change their properties through specific triggers including pH changes and enzyme exposure and light activation show great potential as solutions [105].

Among these triggers, bacterial QS signals are particularly attractive because they possess the following properties:

1. The different bacterial species and strains generate unique QS molecule classes that include AHLs and autopeptides and AI-2 [8].
2. The concentration of QS signals directly links to bacterial population density because it signals the start of virulence and biofilm development [106].
3. The infection site becomes the target for treatment because the signals accumulate at high levels in this specific area which prevents systemic side effects [61].

Biomedical material applications developed by leveraging these unique properties of QS mechanisms, which prevent, diagnose, and treat infections, are expected to stand out among the next generation of materials.

5.8.1. Infection-sensitive drug delivery systems

The drug release mechanism of QS-responsive systems operates differently from conventional drug delivery systems because it depends on the activity and presence of pathogenic bacteria. The “theranostic” (diagnostic and therapeutic) method provides personalized treatment

while reducing the development of drug resistance. Here, it is necessary to take a holistic approach to the human microbiome and immune system.

5.8.2. Antibiotic release with signal detection

The operation of these systems relies on QS signal molecules which trigger drug or antimicrobial agent release mechanisms. The "cap" or "switch" mechanism detects the QS signal to perform this function. A drug carrier system that includes nanoparticles or hydrogels or liposomes contains biological components such as enzymes or receptor proteins or aptamers which detect and bind to QS signals. The binding process creates structural damage to the carrier which leads to swelling or destruction of the carrier structure and subsequent release of the therapeutic agent [62].

Advantages:

- The system demonstrates high specificity because it identifies only the specific signal from the target pathogen without interfering with the beneficial commensal bacteria [107–109].
- The system operates as a self-regulating system because drug release halts when the QS signal becomes weak and the infection reaches a controlled state which avoids drug overdose [5,110–112].
- The tiny dimensions of nanoparticles allow them to reach deep into biofilm structures for delivering targeted antibiotics [113,114].

5.8.3. Biofilm-detecting nanoparticle systems

Biofilms establish two types of barriers which protect against traditional nanoparticles through physical and chemical means. The design of QS-responsive nanoparticles aims to solve this specific problem.

- The surface of nanoparticles can receive peptide or polymer coatings which enable them to attach to biofilm matrices or penetrate biofilm structures. The "targeting" approach allows nanoparticles to reach infected tissue more effectively [114]
- The most advanced systems use dual-trigger systems which enable detection of multiple biofilm-related signals (e.g., low pH and high AHL concentration) at the same time. The Boolean command functions as "AND" logic to boost response accuracy by removing all incorrect positive results [77]. For example, a nanoparticle can be designed to release its antibiotic only when the pH of the environment falls below 6.0 and the 3-oxo-C12-HSL signal exceeds a certain threshold. The regulation exists in multiple possible configurations.
- Nanoparticles show promise as delivery systems for AiiA lactase enzymes and antibiotics through QQ agents. The QQ enzyme breaks down bacterial communication and causes the biofilm structure to become less stable. Then, the released antibiotic can more effectively eliminate the now-vulnerable bacteria [63,115,116].

5.8.4. AHL-compatible liposomes and hydrogels

The lipid bilayer structure of liposomes creates vesicles which contain a water-soluble core. To make them responsive to AHL, specially designed lipids (e.g., mimicking LuxR protein binding sites) that undergo a conformational change upon binding to an AHL molecule can be integrated into the lipid layer of the liposome. The modification results in liposome instability which causes the antibiotics to escape from the structure [117–119]. Peptides that create channels through lipid bilayers become active when AHL binds to liposome surfaces can be used as an alternative.

AHL-responsive hydrogels function as cage-like polymer networks which contain water and serve as the best possible delivery system for targeted drug release. AHL-responsive hydrogels are often formulated in two methods:

- Volume Change: The polymer chains of the hydrogel may contain cross-linkers covalently bound to AHL. The use of AHL-lactase enzymes in hydrogel matrices enables these matrices to degrade AHLs which they encounter in their surroundings. The process breaks down cross-linkers which results in network expansion and drug release from the hydrogel [4]
- Cell-Based Systems: The system contains genetically modified bacterial cells which produce antibiotics and drug-activating enzymes after detecting specific AHL signals. Scientists place these "living" cells within a hydrogel matrix structure. The hydrogel serves as a protective framework which safeguards cells during the process of nutrient and QS signal exchange. The embedded cells start producing therapeutic proteins after infection which they generate directly at the site of infection [33]. This will create a long-term, self-regulating therapy system.

5.8.5. Smart implant surfaces and wound dressings

Medical implants together with chronic wounds create conditions that enable biofilm formation. The surfaces of these devices could receive "programmable digital eyes" through QS-responsive materials which activate defense systems only when threats are identified.

- QS-Triggered Antimicrobial Coatings: The coatings function to silently eliminate bacteria that try to establish colonies on implants through their natural communication methods. The system contains Antimicrobial Peptide (AMP) Release which operates as a natural defense system that generates wide-range antimicrobial substances without showing signs of resistance development. A QS-triggered coating can encapsulate an AMP within a polymeric matrix that degrades or changes in the presence of a QS signal. The AHL-responsive hydrogel coating expands when AHL concentrations rise which activates AMP release [120–122]. This ensures that AMP is only released when there is a heavy bacterial load, thereby reducing potential toxicity and the development of resistance to AMP. The production of Reactive Oxygen Species (ROS) serves as a mechanism for certain coatings to generate ROS-based bacterial killing through AHL activation of photosensitizing molecules. The coating activates these molecules through a low-intensity light source when it detects QS signals to produce lethal ROS [123]. The system implements an additional security mechanism through its combination of physical light triggers with biological QS signals.
- Biocompatible, Temporarily Activated Surfaces: The method operates differently from permanent biocidal surfaces because it creates temporary and reversible changes to surface characteristics. The method prevents tissue reactions from occurring while preventing bacterial adhesion.
- Surface Energy Modulation: The surface energy of a material determines how well bacteria will stick to it because hydrophobic and hydrophilic surfaces affect bacterial adhesion differently. Molecular switches integrated into QS-responsive polymers allow these materials to transform their structure when AHL binds to the system. The surface usually exhibits hydrophobic properties which enable bacterial cells to stick to it. The polymer chains transform their structure to show their concealed hydrophilic groups after detecting a QS signal which leads to fast surface hydrophilic behaviour [75,124–126]. The change disrupts the first stage of biofilm development by removing bacteria that have already adhered to the surface. Once the risk of infection has passed, the surface can return to its original hydrophobic state.
- Self-Assembled Peptide Scaffolds (SPS): The SPS method uses self-assembling peptide nanofibers that create weak structures which become stabilized through the addition of QS signal molecules. The multiplication of bacteria and rising QS signal levels cause the peptide nanofibers to develop into a denser and more rigid structure. The method produces structural reinforcement of the surface which blocks bacterial growth yet enables antimicrobial peptides to escape from the material [85,126–128]. Essentially, the material adapts to the severity of the bacterial threat.

5.8.6. Preclinical and emerging application scenarios

The materials show potential according to research conducted on animal subjects although they remain outside standard medical practice.

a) Smart Wound Dressings: The bacteria *Pseudomonas aeruginosa* and *Staphylococcus aureus* commonly infect diabetic foot ulcers which develop into chronic wounds. The AHL-responsive hydrogel wound dressing fights infection through two mechanisms which include detecting *P. aeruginosa* AHL signals to release antibiotics and simultaneously releasing a QQ enzyme that blocks bacterial communication and virulence expression [26,129]. Such a covering can also provide a visual warning by changing color in the event of an infection [39].
b) Orthopedic and Dental Implants: The prosthetic devices of hips and knees and dental implants are susceptible to biofilm infections. A QS-triggered coating applied to the surface of these implants can provide proactive protection from the moment the implant is placed. The wound remains at high risk for bacterial contamination throughout the healing process in the initial stages following surgery. The coating operates as a bacterial detection system which prevents infection progression by releasing antimicrobial peptides in the local area [120]. Once tissue healing is complete and the bacterial load has decreased, the coating ceases to be effective.
c) Urinary Catheters: Catheter-associated urinary tract infections are one of the most common hospital-acquired infections. The AiiA enzyme immobilization process for QQ coating on catheter surfaces generates a protective layer which prevents bacterial communication and biofilm development [53,130,131].
d) QS-Based Smart Solutions for Women's Birth Control Implants: Women's reproductive implants and devices represent a particularly promising application area for QS)-based smart materials, as this region carries a high risk of biofilm-related infections and complications.

- Intrauterine Devices (IUDs): Although IUDs are an effective method of birth control, they may increase the risk of pelvic inflammatory disease (PID) in the first few months following insertion. The infections occur when bacteria use the cervical route to ascend and develop biofilms which include *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.
- Dual-Action, Self-Regulating IUD: The polymeric structure of a traditional IUD (e.g., copper-containing or hormone-releasing) is coated with a two-layer smart coating. The outermost layer consists of QS-Sensor and QQ-Releasing which functions as a hydrogel that detects AHL signals produced by Gram-negative bacteria including *E. coli* and *Gardnerella vaginalis*. At the onset of a bacterial infection, the accumulation of AHL in the environment alters the structure of this hydrogel, triggering the controlled release of embedded QQ enzymes (such as AiiA lactase) [132–134]. The enzymes function to prevent bacteria from forming biofilm structures.
- Inner Layer (pH-Responsive and Antimicrobial-Releasing): The disruption of vaginal flora which causes bacterial vaginosis leads to an elevated pH level that shifts from acidic to basic. The secondary layer expands or disintegrates when pH levels increase which enables antimicrobial drugs (clindamycin or metronidazole) and pH-reducing probiotic metabolites such as lactic acid to pass through [135–137].

Research conducted in laboratory settings demonstrates that dual-trigger coatings outperform copper-based coatings in preventing bacterial biofilm development when tested against various bacterial strains [138,139]. The coated RIA devices proved successful in animal studies with rats by delivering antimicrobial agents directly to the uterine area to reduce endometritis severity during infections.

5.8.7. Synthetic meshes used in pelvic organ prolapse (POP) and urinary incontinence surgery

The medical application of vaginal meshes for pelvic organ prolapse treatment results in major biofilm-related adverse reactions. Mesh infections together with chronic pain and tissue erosion and serious complications that need mesh removal can happen.

- QS-Triggered Self-Healing Mesh Coating: The polypropylene mesh surface receives a biopolymer coating of chitosan or hyaluronic acid derivatives which performs two essential functions. The polymeric mesh provides delivery of small compounds which include furanone derivatives and halogenated furanones that function as natural quorum-quenching agents [138,140]. The compounds block LuxR-like receptor activation of AHL signals which prevents the activation of target genes and keeps bacteria in a non-virulent silent state.

  The polymeric coating includes RGD peptides which serve as cell adhesion peptides to enhance the mesh integration with human tissue that surrounds the mesh [141,142]. The QS inhibition establishes a silent infection space which allows these cells to survive near the mesh as they construct new tissue matrix. The research shows that human fibroblasts both stick to and multiply on these mesh surfaces which have been treated with specific coatings. The mesh surfaces coated with specific materials prevent both *Staphylococcus aureus* and *E. coli* from forming biofilms [143,144]. In animal models, coated meshes have been reported to produce less inflammatory response compared to uncoated meshes and to develop a higher quality connective tissue capsule around them.
- Fallopian Tube Stents Used in Fertility (Infertility) Treatment: The stents placed to open blocked fallopian tubes or to keep them open after surgery can develop biofilm formation which is the main reason for tube blockage.
- Biofilm-Resistant Fallopian Tube Stents: The biodegradable polymer stent constructed from polylactic acid (PLA) includes a molecular cap system which degrades after detecting a QS signal. An antibiotic (e.g., doxycycline) or a QQ enzyme is covalently bound to the polymeric structure of the stent via an ester bond that hydrolyzes in the presence of an AHL signal [61,145–148]. The therapeutic agent becomes available when bacterial accumulation starts in the fallopian tube and AHL concentration surpasses the threshold value which causes the ester bonds to break. The stent contains growth factors such as Epidermal Growth Factor- EGF that stimulate fallopian tube epithelial cells to migrate and proliferate. The stent promotes natural tube tissue repair through its degradation process [149]. The research shows that EGF-releasing stents improve both survival rates and migration speed of fallopian tube epithelial cells in cell culture experiments. Biofilm models demonstrate that antibiotic release triggered by AHL creates an expanded protective layer on stent surfaces which prevents biofilm formation [150–153].
- Surgical Suture Materials: The sutures used for gynecological procedures such as cesarean sections and hysterectomies create a risk for surgical site infections. Biosensor bacteria that emit fluorescence when a QS signal is detected (representing a shift toward cell-free systems) or color-changing chromophores are integrated into the structure of absorbable suture materials such as Vikril or polylactic acid [4,39].

  During the postoperative phase, if an infection develops in the wound and QS signals are generated, the sutures start emitting green fluorescence or undergo a visible color change (e.g., from white to red). This gives a physician an early and visual warning long before the infection produces systemic symptoms, while it is still at a superficial stage. The suture can also stimulate the release of a local anesthetic (bupivacaine) or antibiotic (tricyclic glycerol monocaprylate) along with the color change [154]. This alleviates the pain in the patient and controls the infection at its source. Fluorescent reporter stitches were shown in mouse models to identify skin infections 24-48 h before symptoms arise [155]. It has been

demonstrated that sutures that provide controlled release of antibiotics accelerate the wound healing process and eliminate the need for systemic antibiotics.

The QS-based solutions for the use of women's reproductive implants are proactive and preventive and not reactive. Such intelligent materials do more than cure infection, they identify it early and they even prevent it from developing in the initial stages. Despite sound preclinical findings, rigorous biocompatibility, long-term safety, and interaction with the complex human microbiome need to be fully established before such a technology can enter routine clinical implementation. However, these scenarios can provide an extraordinarily inspiring roadmap for minimizing implant-associated complications in women's health and enhancing patient outcomes.

6. Challenges and future directions for biomedical applications

The clinical translation of this technology (the transition from the laboratory to the clinic) also brings with it a number of challenges.

- Biocompatibility and Safety: The method of synthetic biology is the new generation of entirely synthetic, cell-free QS circuits as an alternative to GMOs (genetically modified organisms) [79]. There is also concern about the long-term cytotoxicity of released antimicrobial agents and polymeric carriers if it is not carefully study these.
- Complex Microbiome: The human body has complex QS networks. A substance that targets a certain microbial pathogen must be highly specific so as not to inadvertently respond to messages from commensal flora. New strategies often require the combining of several signals, and this may be very difficult to do successfully [77]
- Diversity of Signals and Resistance Development: Bacteria utilize different QS signals (AHLs, autopeptides, AI-2). Therefore, it is challenging to design a universal QS-responsive material. Moreover, bacteria are capable of exhibiting resistance through learning not to produce QS signals or by changing signal structure [156]. So, combination therapies, which involve QS inhibition plus traditional antibiotics, are perhaps a more resilient strategy.
- Production and Scale-Up: The reproducible and cost-effective production of these complex, hybrid biomaterials will be a significant engineering achievement in the transition to industrial production [157].

7. Future perspectives

The convergence of QS, synthetic biology, and materials science is opening new paradigms in the development of responsive, adaptive, and programmable biointerfaces. As research continues to evolve beyond static materials and passive systems, several future directions stand out for their transformative potential. These include QS-responsive artificial cells, CRISPR-integrated smart materials, living hybrid materials, and the translation of these innovations into clinical and regulatory frameworks.

7.1. Artificial cell systems responsive to QS signals

Artificial cells—synthetic vesicles, liposomes, or hydrogel-based compartments capable of mimicking basic functions of living cells—are being engineered to sense and respond to QS signals. These cell-mimetic systems can act as decoders of microbial communication, triggering internal reactions such as signal amplification, enzyme release, or fluorescent reporting when exposed to autoinducers like AHLs or AI-2.

Future developments are likely to focus on coupling artificial cells with reaction–diffusion systems, enabling spatial sensing and coordinated behaviour similar to microbial colonies. Integrating feedback loops and logic gates, allowing artificial cells to exhibit threshold-dependent responses to complex QS signal mixtures. Deploying QS-responsive synthetic cells for targeted antimicrobial release, real-time infection monitoring, or biosensing in polymicrobial environments. These systems will serve as platforms to study interkingdom communication, simulate microbial behaviour in controlled environments, and ultimately perform in vivo functions such as smart diagnostics or programmable therapeutics.

7.2. Smart materials integrated with CRISPR-based control systems

The integration of CRISPR-based gene regulation with smart materials represents a powerful strategy for precise, programmable biological responses. CRISPR interference (CRISPRi) and activation (CRISPRa) systems can be embedded into engineered cells within materials to modulate gene expression in response to QS signals or material-derived cues.

Emerging opportunities include materials functionalized with QS ligands that trigger CRISPR-controlled transcriptional programs inside embedded or neighbouring cells. 3D-printed scaffolds or responsive hydrogels incorporating microbial consortia with QS-controlled CRISPR systems, enabling spatially localized therapeutic delivery or regeneration cues. CRISPR-based QS circuits that enable programmable pattern formation, synthetic morphogenesis, or antimicrobial resistance suppression via targeted gene silencing. The programmable nature of CRISPR allows smart materials to move beyond passive response, enabling dynamic, user-defined control of biological systems interfacing with synthetic substrates.

7.3. The concept of 'living materials' and cell–material hybrids

The notion of "living materials"—hybrid systems composed of synthetic matrices embedded with engineered, metabolically active cells—represents a fundamental shift from inert biomaterials toward autonomous, evolvable, and self-sustaining constructs.

Future research will expand the capabilities of living materials by developing QS-based communication networks within embedded cell populations to enable coordinated responses, such as self-healing, color change, or pathogen neutralization. Engineering multi-cellular consortia within materials that can perform distributed tasks, such as sensing, computing, and actuation, inspired by microbial community dynamics. Creating mechanically robust, biocompatible scaffolds that support long-term viability and tunable exchange between cells and the external environment.

Applications range from smart implants, living wound dressings, and self-regulating bioreactors, to environmentally responsive building materials. However, maintaining long-term cellular function, preventing overgrowth, and ensuring biosafety remain key challenges for clinical translation.

7.4. Priorities for regulation and clinical translation

As these technologies advance toward real-world applications, addressing regulatory, ethical, and translational challenges becomes increasingly urgent. Unlike conventional pharmaceuticals or devices, QS-responsive systems and living materials blur the line between biology and technology, posing unique hurdles for evaluation and approval.

Key priorities include establishing safety and efficacy standards for engineered living systems, particularly those containing genetically modified organisms or CRISPR-regulated functions. Defining containment strategies for embedded microbes, such as kill switches, auxotrophy, or environmental responsiveness, to prevent unintended proliferation. Developing standardized protocols for manufacturing, sterilization, and quality control of bio-integrative materials. Engaging with regulatory agencies (e.g., FDA, EMA) early in development pipelines to facilitate the approval of QS-targeted therapeutics, smart diagnostics, and hybrid implants. Ensuring ethical considerations are

addressed, including transparency in genetic engineering, patient consent, and environmental release protocols. Cross-disciplinary efforts between materials scientists, synthetic biologists, clinicians, and policymakers will be crucial to translate QS-inspired smart systems from lab-scale innovations to safe, reliable, and impactful clinical tools.

The integration of QS with advanced materials design is catalyzing a new generation of bioresponsive, programmable, and autonomous systems. Artificial cells that decode microbial signals, CRISPR-regulated materials that process biological inputs, and hybrid living constructs capable of community-level responses are all on the horizon. To realize the full potential of these innovations, future work must balance technical ingenuity with responsible governance, ensuring that emerging technologies are not only powerful but also safe and accessible for medical and environmental applications.

7.5. Integration into different industries

QS- based materials possess the capacity to transform multiple industries (Fig. 7). These are as follows:

- Smart Drug Delivery Systems: QS-controlled microcapsules or nanoparticles can only release the medicine at the site of infection when QS signals from pathogenic bacteria tell them to [62]. This makes targeting more accurate and lowers the risk of negative effects throughout the body.
- Food Safety and Packaging: "Smart packaging" can tell when certain spoilage bacteria are making AHLs and change color as a sign that the food is going bad [158]. This gives consumers and retailers real-time quality management.

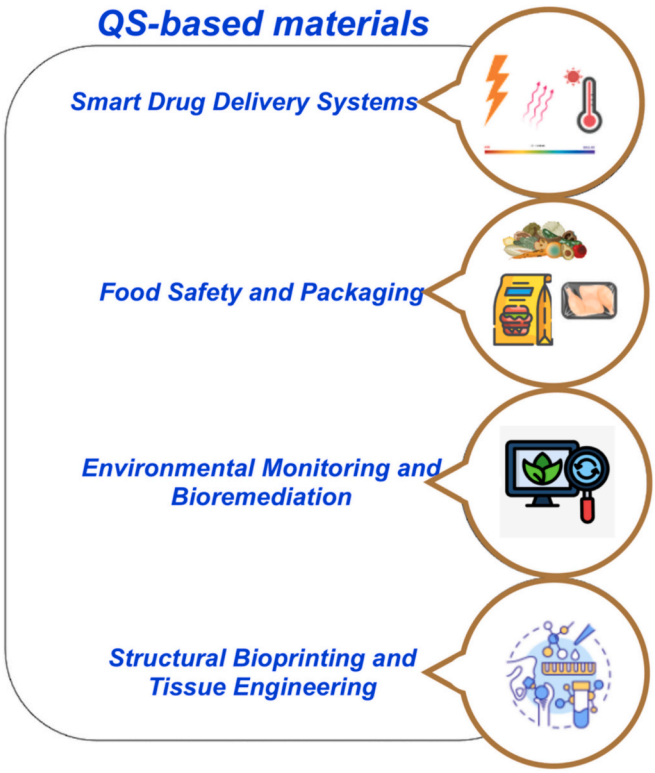

Fig. 7. QS- based materials and integration into different industries. Schematic overview highlighting key application areas of QS-based materials. These include (i) smart drug delivery systems responsive to external stimuli (e.g., temperature, light, or chemical signals), (ii) food safety and packaging for monitoring freshness and preventing contamination, (iii) environmental monitoring and bioremediation through detection and degradation of pollutants, and (iv) structural bioprinting and tissue engineering for constructing functional biological systems.

- Environmental Monitoring and Bioremediation: QS-based biosensors can find certain infections or pollutants in water or soil [39]. They can also be utilized to improve bioremediation processes by getting bacterial communities to work together to break down pollutants [159]
- Structural Bioprinting and Tissue Engineering: QS-sensitive hydrogels can be used as 3D cell culture scaffolds. They can be strengthened structurally or release differentiation factors when the cells reach a certain density and make their own QS signals, which is like how tissues organize themselves [160].

Fig. 7 illustrates the translational potential of quorum-sensing (QS)-based smart materials beyond traditional biomedical uses. In smart drug delivery systems, QS signals can trigger localized antibiotic release from engineered microcapsules or nanoparticles [62]. In food safety and smart packaging, AHL-producing spoilage bacteria induce visible color changes in responsive polymer films, enabling real-time quality monitoring [158]. In environmental monitoring and bioremediation, QS-based biosensors detect pathogens or pollutants in water and soil, while engineered QS circuits enhance the performance of microbial consortia for pollutant degradation [39,161,162]. In structural bioprinting and tissue engineering, QS-responsive hydrogels exhibit density-dependent stiffening or controlled release of differentiation factors, thereby mimicking aspects of natural tissue organization [160].

8. Challenges and limitations

This area is still being worked on and has a lot of key problems to solve:

- Biocompatibility and Immune Response: When living cells or big biological molecules (such enzymes and receptors) are put into the body, the host's immune system may react in ways that are not good [163]. This risk can be lowered by using synthetic receptors or aptamers [164].
- Stability, Longevity, and Stabilizing Surface-Immobilized Enzymes: Biological parts can break down over time because of physical factors like temperature and pH, or because of proteases. We need synthetic compounds that aren't biological but act like AHL or more stable versions of enzymes [165,166]. Tackling the prolonged inactivation of AHL lactonase and acylase on material surfaces is essential for industrial application. Successful approaches to overcome this challenge involve enzyme engineering aimed at enhancing thermal and chemical stability, sophisticated covalent immobilization techniques, encapsulation methods, and integration into protective coatings [167,168]. Recent studies provide a comprehensive overview of following approaches to address this bottleneck.

8.1.1. Enzyme engineering and selection

Enzyme stability can be improved prior to immobilization through rational design and protein engineering approaches such as PROSS (Protein One-Stop Shop Server), which generate variants with enhanced thermal and chemical robustness. These engineered enzymes exhibit increased resistance to organic solvents and improved compatibility with surface coatings. Additionally, selecting naturally robust homologs, such as thermoacidophilic lactonases from *Alicyclobacillus acidoterrestris* (AaL), provides inherent stability across a wider pH and temperature range [169–171].

8.1.2. Robust enzyme immobilization strategies

Advanced immobilization techniques move beyond simple adsorption to enhance enzyme retention and long-term stability on material surfaces. Covalent immobilization provides strong and durable

attachment, minimizing enzyme leaching and preserving structural integrity over time. Oriented covalent linking, often achieved using affinity tags such as sortase-mediated systems, ensures that enzymes are immobilized in a favorable orientation, maintaining accessibility of their active sites. Multipoint covalent attachment, enabled by supports like epoxy-functionalized polymethacrylates or silanized carriers (e.g., SBA-15), further stabilizes enzymes by restricting conformational flexibility and reducing denaturation. In addition, cross-linked enzyme aggregates (CLEAs) offer a carrier-free and cost-effective approach, avoiding catalyst dilution while enhancing enzymatic activity and stability. Collectively, these strategies significantly improve storage performance and operational durability under industrial conditions [168,172–175].

8.1.3. *Smart surface coatings and functional materials*

Integrating enzymes into biocompatible coatings is an effective strategy to preserve their activity and enhance durability on material surfaces. Encapsulation or entrapment within matrices such as sol–gel systems, alginate beads, or hybrid nanocarriers provides protection against proteolytic degradation and harsh environmental conditions. Bio-inspired polymeric coatings, including acrylic, silicone, and polyurethane systems, enable stable incorporation of enzymes like lactonases while maintaining high quorum-quenching activity for extended periods (up to 250 days). In addition, responsive materials—such as pH-sensitive chitosan—allow dynamic control by triggering enzyme release or optimizing activity in the presence of bacterial biofilms. These approaches collectively improve functional stability and adaptability under real-world conditions [168,176–179].

8.1.4. *Enhancing reusability and operational longevity*

Immobilization of enzymes on solid supports improves their stability by shielding them from harsh environmental conditions such as temperature fluctuations, pH changes, and proteolytic degradation, while also enabling convenient recovery and reuse. Magnetic separation strategies, where AHL-degrading enzymes such as AiiA lactonase are adsorbed onto magnetic silica or nanoparticle systems, allow efficient recovery using external magnets and maintain substantial catalytic activity (around 60% or higher) over multiple reuse cycles. In parallel, encapsulation of whole quorum-quenching bacteria such as *Pseudomonas* sp. YH-1 within sodium alginate beads provides cellular protection and sustains long-term activity, enabling multiple operational cycles in membrane bioreactors and effectively reducing biofouling [167,180–184].

- Specificity and Cross Talk: Natural QS systems can sometimes demonstrate cross-reactivity between AHLs that have similar structures. Engineering is necessary to guarantee a high degree of specificity [185]. Also, in complicated microbial communities with multiple species, there might be several different QS signals at the same time, which can cause undesired responses.
- Delay Times: Because natural QS depends on gene transcription and protein synthesis, it can take minutes or hours for a response to be sent. This may not be appropriate for applications that need quick diagnosis or action. Pure chemical methods can cut down on this wait time [83,159].

9. Conclusion

The incorporation of QS processes into materials science constitutes a vibrant and interdisciplinary research domain situated at the convergence of synthetic biology, chemistry, and materials engineering [3,4]. This approach has the potential to provide materials with a new level of "intelligence" and "functionality," ranging from basic signal recognition systems to advanced materials that can make intricate judgments and alter their macro-scale properties in real time.

This strategy provides durable and sophisticated answers to global issues, including antibiotic resistance, hospital-acquired infections, and difficulties in point-of-care diagnostics [54,61]. People no longer think of materials as just "building blocks." Instead, they perceive them as living things that "listen," "understand," and "act" in an active conversation with their surroundings [60,61,111].

The difficulties that lie ahead in terms of stability, biocompatibility, and specificity seem intimidating, yet they appear to be conquerable through progress in synthetic biology, nanotechnology, and polymer chemistry. In the future, there will be wound dressings that can tell if they are infected and treat them, "smart" filters that can sense and clear pollution, and tissue scaffolds that can help cells organize themselves. Quorum Sensing is going to be a big part of this revolution in smart materials.

Quorum sensing-responsive materials present a fast-paced and dynamic domain at the intersection of biomaterials science and infection biology. These materials deploy bacteria's own language of communication to fight back against them, which gives them unparalleled specificity and timing precision in antimicrobial therapy. Innovative technologies like infection-responsive drug delivery systems and smart implant surfaces are set to create a sustainable approach to the antimicrobial resistance crisis, delivering the medication only where and when required. The feasibility of these basic concepts has been repeatedly shown through ongoing research. Advances in materials engineering and synthetic biology will be used to develop these systems for enhanced stability, biocompatibility, and efficacy in complex in vivo settings. Fully integrated "theranostic" wound management platforms are the next step for the future with the ability to diagnose the presence of a specific pathogen, to release the relevant antibiotic at the correct dose and monitor recovery, or implant surfaces preventing lifelong infection. Such smart materials have the ability to transform infectious disease treatment and usher in a period of precision and personalized medicine.

CRediT authorship contribution statement

Santosh pandit: Conceptualization, Investigation, Writing – original draft, Visualization, Funding acquisition. Demet Erdönmez: Writing – original draft, Investigation. Duygu Polat: Writing – original draft, Writing – review & editing. Burcu Önal Acet: Writing – original draft, Writing – review & editing. Mustafa Dolaz: Writing – original draft, Writing – review & editing. Mehmet Odabaşı: Writing – original draft, Writing – review & editing. Ivan Mijakovic: Writing – review & editing, Funding acquisition. Ömür Acet: Investigation, Writing – original draft, Writing – review & editing, Visualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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