ChemComm

Chemical Communications

rsc.li/chemcomm

ROYAL SOCIETY
OF CHEMISTRY
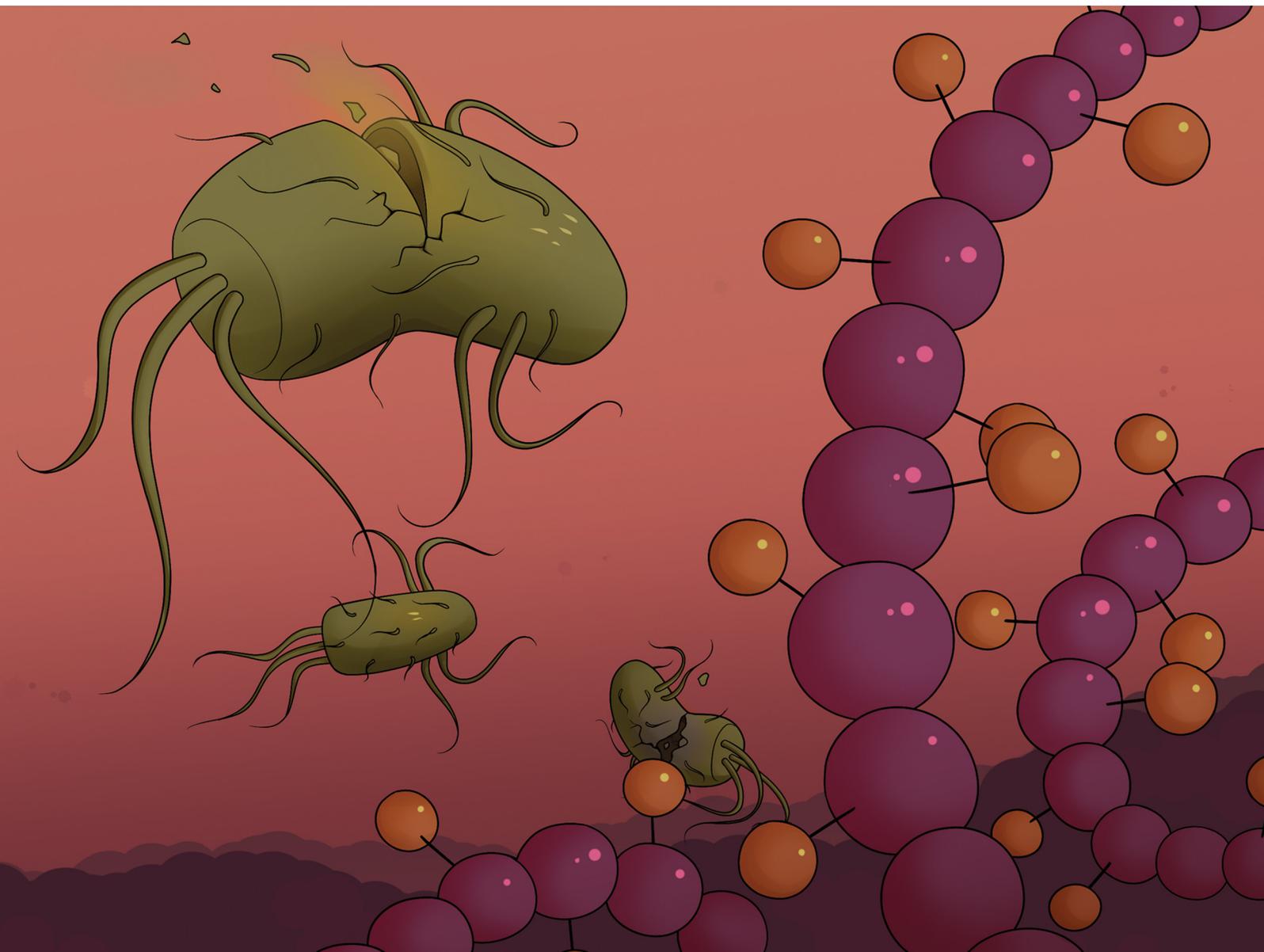
FEATURE ARTICLE
Michael D. Schulz *et al.*
Recent developments in antimicrobial polymers for biofilm
inhibition

Check for updates

Recent developments in antimicrobial polymers for biofilm inhibition

Gillian A. Kropp, †[ab] Cassell N. McMillian,†[ab] Jonathan D. Mase,[ab] Sanjana Kandagiri,[a] Elizabeth S. Nowak [de] and Michael D. Schulz ⋆[abc]

Biofilm-associated infections continue to present a formidable clinical challenge, as surface-adhered microbial communities exhibit remarkable tolerance toward conventional antibiotics. Polymeric materials have emerged as a versatile platform for combating biofilms, offering chemical tunability and enabling diverse antimicrobial strategies. This feature review article highlights recent advances in polymeric materials designed to prevent biofilm-associated infections by resisting bacterial adhesion (passive inhibition) or exerting bactericidal effects (active inhibition). These approaches include antifouling surfaces, polymer–nanoparticle composites, and bioinspired materials. Particular attention is given to how polymer structure and functionality (*e.g.*, hydrophobicity, charge, and network architecture) govern bacterial adhesion and viability at interfaces. Emerging glycomaterials are also discussed, where glycan motifs are integrated with nanoparticles or cationic domains to enhance biofilm penetration and antimicrobial efficacy. Collectively, these studies underscore the potential of polymeric materials to modulate microbe–surface interactions, thereby guiding the design of next-generation antibiofilm materials.

a Department of Chemistry, Virginia Tech, Virginia, USA. E-mail: mdschulz@vt.edu
b Macromolecules Innovation Institute, Virginia Tech, Virginia, USA
c Translational Biology, Medicine, and Health Graduate Program, Virginia Tech, Virginia, USA
d Division of Infectious Diseases, Carilion Clinic, Virginia, USA
e Virginia Tech Carilion School of Medicine, Virginia, USA
† Equal contribution.

Introduction

The human body hosts trillions of microbes, including bacteria, viruses, fungi, and archaea.[1] This diverse community, collectively known as the microbiome, exists in a balanced symbiosis with the host. Bacteria are especially influential and abundant. They line our skin as an additional protective barrier and immune regulator,[2,3] form biofilms in the oral cavity,[4–6] and densely populate the gastrointestinal tract, where they support digestion,[7,8] nutrient absorption, and metabolite

Gillian Kropp received her PhD in Chemistry in 2025 from Virginia Tech under the supervision of Michael Schulz, where her research focused on functional polymer composites for medical and engineering applications. She earned her BS degree from SUNY Binghamton University in 2021, conducting research on nanomaterial-based platforms for cancer biomarker detection in the lab of Chuan-Jian Zhong. Her research interests center on the development of medical devices, biomaterials, and peptide-based materials.

Gillian A. Kropp

Cassell McMillian received his BS in Biochemistry in 2022 from Virginia Tech, where he conducted undergraduate research with Dr. Kevin Edgar on polysaccharide-based copolymers as compatibilizers in polymer blends. He is currently pursuing a PhD under the supervision of Michael Schulz in the Department of Chemistry at Virginia Tech. His research focuses on antibacterial glyco-materials and the synthesis and mechanical characterization of polybutadiene-based materials.

Cassell N. McMillian

production.[9] However, even minor disruptions to this balance can have profound consequences, as microbial species can rapidly proliferate and cause disease. The 20th century saw a dramatic reduction in bacterial infections due to the development of antibiotics and improved sanitation. Today, many bacterial infections can be treated with short courses of antibiotics, which disrupt key processes such as cell wall synthesis, protein production, or nucleic acid replication.[10] Yet two challenges limit their long-term effectiveness. First, because bacteria reproduce rapidly, even a few surviving cells can acquire mutations and develop resistance. Second, bacteria can transition from free-floating (planktonic) cells to surface-attached biofilms—a multicellular state that protects them from antibiotics and immune cells while anchoring them to surfaces such as tissues or medical devices (Fig. 1).[11,12]

Biofilms are particularly problematic in clinical settings. On indwelling medical devices, such as urinary catheters, they
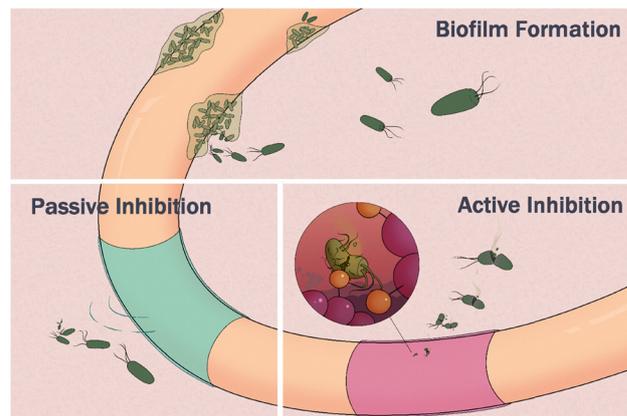

Fig. 1 Free-floating bacteria can aggregate into larger biofilms on indwelling medical hardware surfaces (*e.g.*, catheters, shunts, *etc.*) and then disperse to form new colonies. Polymers can disrupt this process through either passive (antifouling) or active (bactericidal) inhibition mechanisms.

Jonathan Mase received his bachelor's degree in Biochemistry from Bowling Green State University in 2015. Under the supervision of Alexis Ostrowski, he designed photo-responsive materials that released nitric oxide. He then moved to the Texas Heart Institute where he worked with Doris Taylor, exploring the role of stem cell therapy in treating cardiovascular disease. He joined the lab of Michael Schulz at Virginia Tech in 2019, where he currently investigates the design of glycopolymers to inhibit enteroviruses.

Jonathan D. Mase

Sanjana Kandagiri is an undergraduate student at Virginia Tech, where she is pursuing a BS in Chemistry. She performs undergraduate research under the supervision of Michael Schulz in the Department of Chemistry. Her academic pursuits span analytical chemistry, chemical physics, paleontology, and scientific graphic design.

Sanjana Kandagiri

Elizabeth Nowak is an Infectious Diseases physician at Carilion Clinic in Roanoke, Virginia, and an Assistant Professor at Virginia Tech Carilion School of Medicine. She completed residency training in Internal Medicine and Pediatrics at MetroHealth Medical Center in Cleveland, Ohio, followed by an Infectious Diseases Fellowship at Carilion Clinic. Her research bridges basic science, translational investigation, and public health, with a focus on biofilm-associated infections and antimicrobial resistance.

Elizabeth S. Nowak

Michael D. Schulz is an associate professor in the Department of Chemistry at Virginia Tech. He received his PhD in 2014 in organic and polymer chemistry and an MS in pharmaceutical science at the University of Florida under the supervision of Ken Wagener. After conducting research at the Max Planck Institute for Polymer Research as a Fulbright Scholar, he was a postdoctoral scholar in the group of Robert Grubbs at Caltech. He began his independent career at Virginia Tech in 2017. His diverse research interests span both fundamental and applied polymer chemistry including metal-chelating materials, antiviral and antibacterial polymers, and polymer sequestrants.

Michael D. Schulz

resist clearance and seed chronic infections. In wounds, biofilms promote persistent inflammation and treatment failure; for example, most diabetic foot ulcers that progress to lower-limb amputation are biofilm-infected, with serious impacts on morbidity and short-term survival.[13,14] Similarly, catheter-associated urinary tract infections (CAUTIs)—driven by biofilm formation that begins within days of catheter insertion—are among the most common hospital-acquired infections (HAIs). Annually, CAUTIs afflict hundreds of thousands of U.S. patients and contribute to thousands of deaths.[15] In fact, CAUTIs account for 30–40% of all HAIs, globally.[16] Current clinical strategies are largely reactive, relying on device removal, and prolonged antibiotic regimens. Unfortunately, these approaches are often ineffective, contribute to antimicrobial resistance, and disrupt the patient's microbiome. Preventing biofilm formation altogether represents an urgent yet unmet need in the medical field.

This review highlights emerging polymer-based strategies designed to prevent or disrupt biofilm formation on medical devices. First, we outline the biology of biofilm formation and the structural features that make these microbial communities so recalcitrant to treatment. We then discuss how polymer design has been leveraged to develop two main classes of antibiofilm materials: active polymers, which kill bacterial cells directly, and passive polymers, which create antifouling barriers that block bacterial adhesion (Fig. 1). By examining these approaches, we aim to clarify both the challenges and the opportunities for translating polymeric antibiofilm technologies into clinical practice.

Biofilm formation

Bacterial biofilms contribute to the spread of infectious diseases and are frequently implicated in persistent chronic infections.[17,18] Biofilm formation proceeds through several distinct stages (Fig. 2).[3,19,20] Initially, free-roaming (planktonic) bacteria attach to a surface. This early attachment is followed by microcolony development, during which cells proliferate and secrete extracellular polymeric substances (EPS)—a matrix primarily composed of polysaccharides, proteins, and nucleic acids—to which additional bacteria can adhere.[21] As the biofilm matures, cells embedded within the EPS can detach and revert to the planktonic state, enabling dispersal and the seeding of new biofilms.[19,20] The EPS functions as both a physical and chemical barrier, impeding antibiotic penetration

and shielding resident bacteria from host immune defenses.[22,23] This protective environment contributes to the persistence and pathogenicity of device-associated infections.[24–26]

Bacterial biofilms are a major contributor to HAIs, which substantially increase patient morbidity and mortality.[27] Device-associated infections are responsible for 25.6% of HAIs,[28] and are commonly associated with biofilm-forming pathogens, which can be endogenous bacteria or exogenous bacteria introduced during device insertion.[27,29–32] Additionally, an estimated 80% of chronic and surgical site infections are attributable to biofilm-forming organisms.[33] These biofilm-associated infections are most frequently associated with *Staphylococcus aureus* (*S. aureus*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Escherichia coli* (*E. coli*), *Staphylococcus epidermidis* (*S. epidermidis)*, and *Enterococcus faecalis* (*E. faecalis*), all of which originate from either the patient's microbiota or hospital-acquired sources.[33,34]

Strategies to control biofilms generally focus on preventing their formation or eradicating established communities. Both approaches are hindered by the widespread emergence of antibiotic resistance.[35] Most clinically used antibiotics are derived from microbial natural products and act by targeting essential cellular processes.[36,37] However, these agents typically act on a single target, and many have already been compromised by resistance. This problem is further exacerbated by antibiotic pollution from hospitals, agriculture, aquaculture, and industry, which causes bacteria to be exposed to sub-minimum inhibitory concentrations (sub-MIC) of antibiotics. This low-level exposure drives the selection and dissemination of resistance genes.[38–44]

The distinct physiology of biofilms further limits antibiotic efficacy by restricting diffusion of drugs through the matrix and reducing metabolic activity such that metabolism-targeting drugs become less effective.[45–48] The development of new antibiotics is slow, costly, and high risk; research into just one antibiotic can span 10–14 years and require a company to invest roughly $1 billion.[49,50] However, only a few drug candidates ever enter clinical use.[51] Most new agents are structural analogues of existing drugs rather than scaffolds with novel mechanisms, and high-throughput screening has likewise failed to substantially expand the scope of novel small-molecule antibiotics.[52] These limitations have prompted growing interest in polymers as alternative antimicrobial materials, due to their structural versatility and ability to act as antibacterial or antifouling agents, or as coatings that integrate multiple antimicrobial mechanisms.

Antimicrobial coatings

Medical devices represent a persistent point of vulnerability for infection, as their surfaces readily serve as substrates for bacterial adhesion and subsequent biofilm formation. Biofilms are especially problematic because they display an intrinsic resistance to conventional antibiotic therapies, rendering many infections difficult to eradicate once established.[53] To address this challenge, polymeric coatings have emerged as a
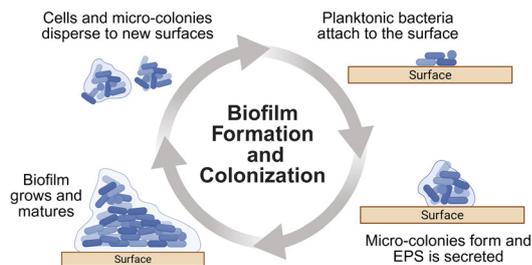

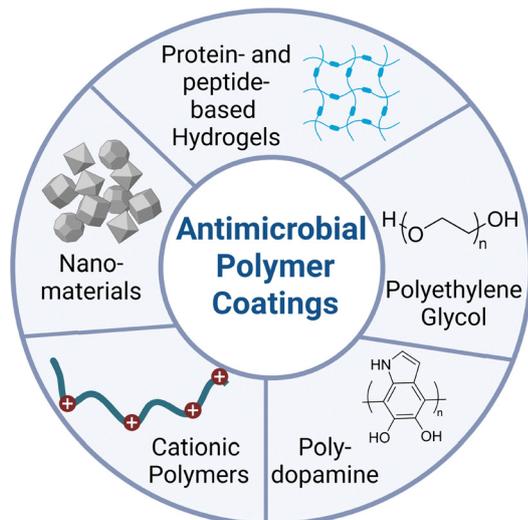Fig. 2 Steps of biofilm formation and colonization of surfaces.

Fig. 3 Overview of different types of antimicrobial polymer coatings.

particularly attractive strategy. These materials can act at the earliest stage of infection, primarily by preventing the adhesion of planktonic bacteria to device surfaces. Hydrogels, thin films, and related polymeric constructs not only provide a protective barrier between the device and its biological environment but can also be engineered to incorporate bioactive agents that actively interfere with microbial colonization (Fig. 3).[54] In doing so, coatings on indwelling medical hardware offer a route to reducing infection risk by inhibiting bacteria before a mature biofilm can form.

Protein- and peptide-containing hydrogels. Hydrogels are hydrated polymeric networks that form a soft, water-rich interface.[55] By establishing a tightly bound hydration layer, these materials create a barrier that prevents protein adsorption and bacterial attachment.[56] Aside from these advantageous antifouling behaviours, many hydrogels are also moldable, biodegradable, or capable of encapsulating antimicrobial agents.[57] Hydrogel coatings have been used for various biomedical applications ranging from wound dressings to coatings for indwelling medical hardware, such as catheters or orthopedic implants.[58–60] One promising strategy is to incorporate antimicrobial proteins into hydrogel matrices. These proteins can maintain high antibacterial efficacy, while also lowering the likelihood of resistance development.[60] For example, Pavlukhina et al. developed a layer-by-layer approach in which an enzyme, dispersin B, was loaded into glutaraldehyde-crosslinked polyallylamine.[60] In this study, the authors increased enzyme content with increased hydrogel layers, resulting in non-eluting enzymatic antibiofilm coatings capable of multi-day antimicrobial activity. The success of such a multilayer hydrogel–protein system highlights a broader opportunity for the field: designing non-leaching, surface-active coatings that maintain long-term antimicrobial performance without continuous drug release.

Relatedly, antimicrobial peptides (AMPs) are short, low-molecular-weight biopolymers (typically 12–50 amino acids long) that can be integrated into hydrogel networks as active antimicrobial components.[61] Unlike passive antifouling coatings, AMP-containing hydrogels can exert direct antimicrobial activity.[62] Their ability to disrupt bacterial membranes while inducing minimal resistance has made AMPs attractive candidates for biomedical applications.[62–64] Moreover, many AMPs are also capable of self-assembly, enabling the creation of peptide-only hydrogel coatings that resist colonization while mimicking aspects of native extracellular environments. Finally, AMPs' intrinsic properties—low immunogenicity, high structural versatility, and biodegradability—further facilitate their application in coatings for medical devices.[65,66]

Recent efforts have focused on developing synthetic peptide mimics with tunable functionality.[67–72] For example, Kumar and coworkers reported an antibacterial hydrogel using naphthyl anthranilamide (NaA)-capped peptide mimics. These short peptide sequences, synthesized via ring-opening polymerization (ROP) of isatoic anhydride followed by the incorporation of cationic substituents, yielded a library of amphiphilic peptide analogues that could form nanofibrous networks. This library consisted of ultra-short NaA-capped peptides with varied cationic group, anthranilamide-core substituent, or counter ion. The authors observed that peptide mimics containing primary ammonium groups were the most effective antibacterials.[73] Continuous nanofiber release was observed when testing against S. aureus, allowing antibacterial efficacy to last over nine days. The authors noted that the choice of cationic group significantly influenced the hydrophobicity–hydrophilicity balance of the overall material.[73] This study demonstrates the potential of peptide mimics as dynamic antimicrobial coatings.

Polyethylene glycol. The antifouling potential of polyethylene glycol (PEG) was first explored in the 1980s and early 1990s. These early studies focused on blood-contacting biomaterials, where the strong hydration and charge neutrality of PEG were shown to greatly reduce protein adsorption and cell or platelet adhesion.[74–76] Since then, PEG-based hydrogels have been extensively studied as antifouling materials. For example, Hult and co-workers developed photocured thiol–ene hydrogel coatings from PEG to investigate how PEG chain length, terminal vinyl groups, and thiol crosslinkers influenced degradation and antifouling behaviour.[77] Coating degradation is a critical parameter because the adherence and biofilm formation of microbes results in accelerated surface degradation and corrosion, as well as increased surface roughening.[77] Increasing PEG chain length improved protein and microbial resistance, but it also accelerated the hydrogel's degradation.[77]

Although PEG effectively delays microbial adhesion, its protection is fundamentally passive. To expand its utility, PEG has frequently been combined with antimicrobial agents to provide both passive and active inhibition.[27,78–82] For example, Bernthal and coworkers developed a "smart" antimicrobial implant coating using branched PEG-poly(propylene sulfide) that encapsulates and releases antibiotics (vancomycin and tigecycline).[83] In a murine implant model, this coating significantly reduced bacterial load in both the

implant and adjacent tissue, with tigecycline outperforming vancomycin.

Similarly, Sileika and colleagues engineered a PEG–silver nanoparticle (AgNP) coating on polydopamine-coated polycarbonate substrates.[84] In this system, PEG slowed the release of AgNPs, extending their activity from 6 to $\geq$10 days while simultaneously enhancing bactericidal performance against *E. coli*, *P. aeruginosa*, and *S. epidermidis*. PEG grafting also improved antifouling by reducing bacterial attachment relative to the AgNPs or polydopamine alone. AgNPs and their incorporation into coatings have been well investigated for their broad-spectrum antimicrobial effects,[85–90] largely driven by enzymes (particularly sulfhydryl-containing enzymes) interacting with silver, which blocks enzymatic processes and causes membrane destabilization.[86] Together, these studies illustrate PEG's dual role as a passive antifouling barrier and as a versatile scaffold for incorporating antimicrobial agents.

However, PEG coatings have several drawbacks. First, they are insufficient once biofilms have become established, underscoring the need for more active approaches. Second, PEG's long-term clinical use is problematic due to the emergence of patients who express anti-PEG antibodies.[91,92] Efforts have been made to design PEG-alternatives that maintain PEG's desirable properties (*e.g.*, inertness, hydrophilicity) while avoiding such negative biological side effects: polyglycerols, poly(2-oxazolines), and poly(acrylamides) are some of many options.[93,94]

Furthermore, many PEG-alternatives have been investigated as antifouling coatings, and some coatings even display antibacterial activity.[95] For example, recent studies have looked at sulfoxide-containing polymers for their antifouling properties in nanoparticle drug delivery,[96,97] and sulfoxides are further known to possess antibacterial properties when incorporated into a PEG backbone, highlighting their potential in antibiofilm applications.[98] As the field continues to investigate novel PEG-alternatives, those that display antibacterial activity may find further utility as biofilm inhibitors. Interested readers can consult several recent review articles for more expansive discussions on this growing field.[99–102]

Polydopamine. The clinical translation of antibacterial coatings is often limited by interfacial incompatibilities that hinder adhesion across diverse substrates (*e.g.*, medical devices).[84] Inspired by the adhesive proteins secreted by mussels, surface-initiated polymerization of dopamine has emerged as a versatile strategy to address this limitation. Dopamine spontaneously oxidizes to form polydopamine, producing thin, conformal films that adhere strongly to virtually any substrate and can subsequently be functionalized with antimicrobial agents to inhibit bacterial colonization and biofilm development.[84,103] Although polydopamine has been reported to exert some intrinsic antibacterial effects, particularly against *S. aureus*, *E. coli*, and *P. aeruginosa*, its most common role is as an adhesive interface for immobilizing antimicrobial agents to a surface.[104–106] In this capacity, polydopamine provides a robust platform for the incorporation of antibiotics, metals, or polymeric antimicrobials into coatings

Table 1 Examples of polydopamine facilitating attachment of antimicrobial agents to various surfaces

Antimicrobial agent	Polydopamine-coated surface	Ref.
H$_2$O$_2$-generating catechol	Polypropylene	107
Silver nanoparticles (AgNPs)	Silicone	108
	Polycarbonate	84
	Polymer-ceramic composite	109
	Titanium	110 and 111
Sulfobetaine	Silicone	112
ε-polylysine/gum arabic layer-by-layer assembly	Anodized titanium	113
Lipopeptide	Polyurethane	114
Nitric oxide	Glass	115
	Titanium^a	116
	Iron oxide Nanoparticles	105
	Silicone^a	117
	Selenium Nanoparticles^b	118
Cu^{2+}	Titanium	119
Vancomycin	Titanium	120
Curcumin	Titanium	121

^{a} Nitric oxide was generated *in situ* assisted by copper. ^{b} Nitric oxide was generated *in situ* assisted by selenium.

that can be applied to indwelling medical hardware to reduce HAIs (Table 1).

For example, Schulz and co-workers developed an antibiofilm catheter coating using a polydopamine-antibiotic (gentamicin) composite (PD-Gent).[106] The authors found that when synthesizing these coatings with dopamine concentrations >1.0 mg mL^{-1}, the composite was unable to inhibit the growth of planktonic *P. aeruginosa* and biofilm formation. However, when these coatings were synthesized with less dopamine (0.25–1.0 mg mL^{-1}), PD-Gent was consistently effective against bacterial colonies, despite containing less gentamicin. This change in bactericidal activity was attributed to polydopamine aggregates present at higher polydopamine concentrations that likely prevented antibiotic–bacteria interactions. The PD-Gent coating remained effective when changing the underlying substrate (polystyrene, polyvinyl chloride, or silicone) or the antibiotic (tobramycin, amikacin), demonstrating the versatility of this approach. Finally, the authors evaluated their coating's effectiveness by simulating bacteriuria flow through coated commercial foley urinary catheters. After 24 hours the PD-Gent–coated catheters generated a 3-fold reduction in biofilm formation compared to the uncoated catheters.

Nanomaterials. Nanomaterials have attracted considerable attention as antibacterial and antibiofilm materials, building on the extensive research into their use as medical therapeutics and diagnostics.[122] Beyond roles in imaging, many nanomaterials exhibit intrinsic antibacterial activity, or can be engineered to disrupt biofilms. For example, metallic nanoparticles can generate heat through magnetic hyperthermia (*e.g.*, using iron oxide nanoparticles), act as carriers for antibiofilm agents, or directly exert bactericidal effects through metal–microbe interactions (*e.g.*, gold and silver nanoparticles).[123–129] These properties can be further enhanced by incorporating nanoparticles into polymer matrices, yielding a hybrid system that integrates the mechanical stability and processability of

polymers with the antimicrobial and cytotoxic activity of metallic nanoparticles.[130] Such polymer–nanoparticle composites have been investigated as antibiofilm coatings for catheters, which remain prone to persistent biofilm-associated infections.[123–129,131]

Polymer–nanoparticle composites are particularly attractive due to their tuneable physiochemical properties (*i.e.*, particle size, morphology, metal identity, and polymeric surface coating), which can be adjusted to modulate stability and antimicrobial activity.[132–137] For example, Rahaman *et al.* synthesized copper nanoparticles stabilized with poly(vinyl pyrrolidone) (PVP) or poly(vinyl alcohol) (PVA), demonstrating the advantages of polymer coatings in nanoparticle stabilization and antibiofilm performance.[138] Both formulations significantly reduced the growth of planktonic bacterial cells (with slightly greater inhibition against *S. aureus*) and diminished exopolysaccharide production, suggesting that polymer coatings can not only stabilize copper nanoparticles against aggregation and oxidation, but also enhance overall antibiofilm performance.
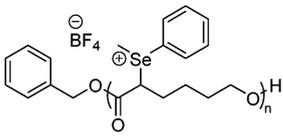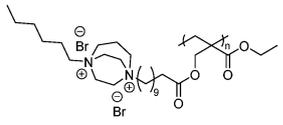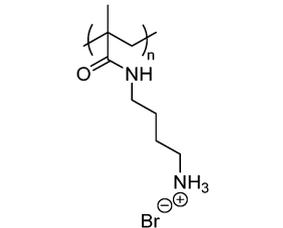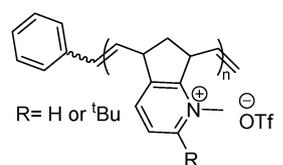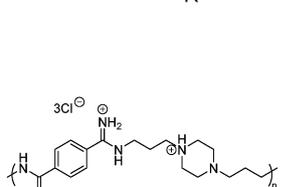
Beyond metallic systems, non-metallic polymer-based nanomaterials have been increasingly explored for antibiofilm applications. These systems include nanoemulsions,[139,140] nanogels,[141,142] and polymeric nanoparticles that frequently incorporate biological or synthetic components such as cell membranes,[143,144] lipids,[145,146] natural polymers,[147–149] or synthetic polymer matricies.[142,150,151] Usually, the nanomaterial's primary function is to facilitate the targeted delivery of antimicrobial agents within the biofilm matrix. For example, Anjum *et al.* synthesized poly(lactic-*co*-glycolic acid) (PLGA) nanoparticles loaded with xylitol and functionalized with concanavalin A for treating *S. aureus* and *P. aeruginosa* biofilm infections.[152] Free xylitol poorly penetrates the biofilm matrix; however, when delivered *via* PLGA nanoparticles, the authors observed improved penetration and biofilm inhibition. In fact, the xylitol-loaded nanoparticles successfully permeated *S. aureus* biofilm, *P. aeruginosa* biofilm, and a polymicrobial biofilm with both bacterial species after 30 minutes. Live/dead viability assays corroborated these findings, revealing markedly greater biofilm eradication by xylitol-loaded nanoparticles compared to free xylitol. The authors attributed this enhanced activity to the improved transport of the nanoparticles through the biofilm matrix, enabling localized drug release. This study highlights the promising ability for nanoparticles to overcome the physical and chemical barriers that impede conventional drug delivery.

Overall, nanomaterials provide a powerful toolkit for antibiofilm intervention by enhancing targeting and penetration. Nevertheless, several translational challenges remain. Many nanomaterial synthesis strategies are complex and difficult to scale up, and the toxicity profiles of these materials must be evaluated in a case-specific manner. Additionally, most advances remain confined to the laboratory scale at present. Bridging the gap between lab and clinic will require the development of reproducible, scalable synthetic methodologies, comprehensive long-term toxicity studies, and rigorous clinical evaluations to fully realize the therapeutic potential of nanomaterials.

Cationic polymers

Cationic polymers are one of the most widely explored classes of antimicrobial materials because they can bypass conventional mechanisms of antibiotic resistance.[153] Their activity typically relies on two synergistic features: a cationic moiety that promotes electrostatic adsorption to the negatively charged cell membrane of the bacteria, and hydrophobic groups that insert into the lipid bilayer to destabilize the membrane and cause cell lysis.[154] Common cationic functionalities include quaternary ammonium (QAC), imidazolium, guanidinium, pyridinium, triazolium, and phosphonium groups, which can be introduced directly into polymer backbones or pendant side chains, or formulated as ionic liquids (Table 2).[155,156] By varying charge density and hydrophobicity–hydrophilicity balance, these polymers can be tailored to optimize antimicrobial potency while maintaining biocompatibility. A wide range of structural motifs have been explored to exploit this charge–hydrophobicity balance, which highlights how variations in cationic group and backbone architecture influence antibacterial efficacy and cytocompatibility (Table 2).

Table 2 Representative examples of cationic polymers showing antibacterial efficacy

Polymer backbone	Strain	MIC µg mL^{-1}	Ref.
	E. coli and *S. aureus.*	1	157
	E. coli and *S. aureus.*	62.5	158
	E. coli	18	159
	MRSA	50	160
	E. coli	25–50	
	B. subtills	4	161
	S. aureus	4	
	E. coli	2–4	
	E. faecalis	2	
	E. faecium	4	
	K. pneumoniae	2–4	
	A. baumannii	2	
	P. aeruginosa	4	
	M. smegmatis	2.5	
	M. tuberculosis	25	
	E. cloacae	2–4	
	MRSA	2	

Recently, selenium-based cationic polymers have garnered significant interest due to their promising antimicrobial performance.[162–165] For example, Zhu and coworkers developed a degradable family of selenium-containing polyesters *via* ring-opening polymerization of selenide-functionalized ε-caprolactone monomers, followed by methylation to yield polyselenonium salts.[157] In this study, four variants with side chains of differing hydrophobicity—C_3, C_5, C_{10}, and phenyl—were prepared, with degrees of polymerization between 12 and 13. All four polymers exhibited potent antibacterial activity against *E. coli* and *S. aureus* while maintaining good mammalian cell viability at biocidal concentrations. Among them, the phenyl-substituted polyselenonium salt displayed the lowest MIC (1 μg mL^{-1}) and minimum bactericidal concentration (MBC) (2 μg mL^{-1}), along with superior biocompatibility (before and after degradation) compared to its alkyl-substituted counterparts. Hydrophobicity was identified as a key determinant of efficacy: moderate hydrophobicity (C_5 or phenyl) enhanced bacterial killing, whereas excessively long alkyl chains (C_{10}) reduced solubility and biocompatibility (Fig. 4).

In this report, mechanistic studies using zeta potential and quartz crystal microbalance revealed that cationic selenium species first adsorb electrostatically onto the bacterial surface, shifting cell surface potentials from –43.6 mV to –7.4 mV (*E. coli*) and –34.3 mV to –3.79 mV (*S. aureus*). Subsequent insertion of hydrophobic groups into the lipid bilayer caused membrane disruption, collapse, and cytoplasmic leakage. Importantly, cytotoxicity assays showed >80–90% fibroblast viability at antibacterial concentrations, and biocompatibility further improved upon polymer degradation. These results suggest that phenyl-substituted polyselenonium salts offer an optimal balance of hydrophobicity, antimicrobial potency, and safety, making them promising candidates for antibacterial coatings.[157]

Finally, there has been recent interest in developing polyurethane-based cationic biofilm inhibitors, as polyurethanes are already frequently used when fabricating medical devices.[166–169] For example, work from the Joy lab has featured polyurethanes with fixed charge-to-hydrophobicity ratios (60:40) that incorporate amino acid mimetics: arginine or lysine mimetics for cationic functionality and alanine or phenylalanine mimetics for hydrophobic character. Though the charged polyurethanes generally exhibited poor activity against planktonic bacteria (MICs >250 μg mL^{-1} were predominately observed), the materials consistently inhibited biofilm colony growths of *E. coli*, *P. aeruginosa*, and *S. aureus* at significantly lower concentrations (MICs <8 μg mL^{-1}). This stark difference in activity can be explained, in part, by the fact that the materials derive their activity not from typical bactericidal mechanisms (*e.g.*, cell membrane rupturing) but instead from disrupting key processes in biofilm development. Primarily the polymers prevented colony formation by altering the bacteria's cell surface charge and by reducing bacteria swarming motility, or the bacteria's ability to migrate across surfaces.[167]

Antibiofilm glycopolymers

Cell surfaces are coated with a dense layer of glycosylated biomolecules, collectively known as the glycocalyx. These surface glycans mediate diverse molecular recognition events, and many bacteria display lectins that specifically bind to host glycans, enabling adhesion and initiating biofilm formation.[170] These interactions between sugar-binding sites and cell-surface glycans are crucial biological events that have often been exploited to develop biomimetic molecules.[171,172] Drawing inspiration from these natural recognition processes, synthetic glycopolymers—polymers bearing pendant carbohydrate moieties—have been developed to mimic the glycocalyx and modulate cell–microbe interactions.

Across Gram-negative and Gram-positive species, bacteria typically develop resistance against conventional antibiotics through five mechanisms: enzymatic drug degradation, target modification, altered porin expression, efflux pump activity, and biofilm formation.[173,174] However, bacteria are unable to circumvent interactions with glycopolymers through such mechanisms. By targeting highly conserved bacterial structures such as fimbriae, glycopolymers use an inhibition mechanism with a lower risk for resistance development.[175–177]

Glycopolymers leverage the principle of multivalency, wherein multiple carbohydrate units along the polymer backbone simultaneously engage multiple bacterial lectins (Fig. 5). These interactions are facilitated through cooperative binding, with affinities far exceeding those of individual monovalent interactions.[178] For example, single carbohydrate–protein interactions typically exhibit dissociation constants (K_d) in the millimolar range. Multivalent analogues can enhance binding
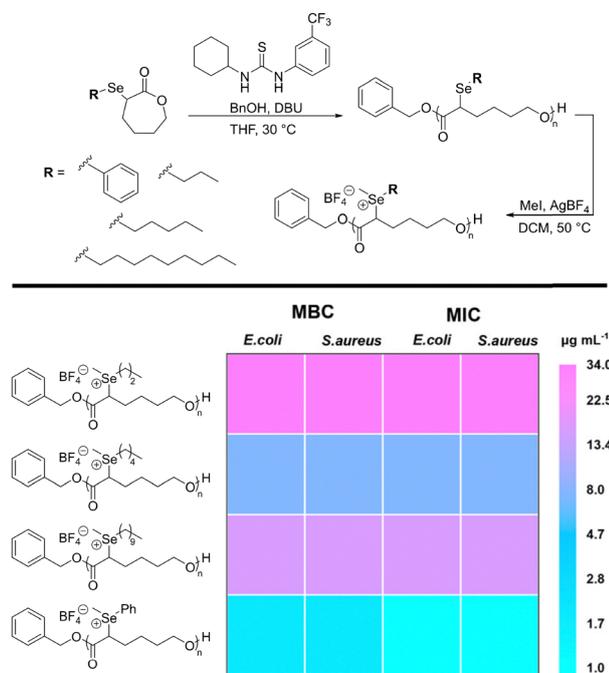

Fig. 4 Heatmap of MBCs and MICs for polyselenoniums. Reproduced from ref. 157 with permission from the American Chemical Society, copyright 2022.
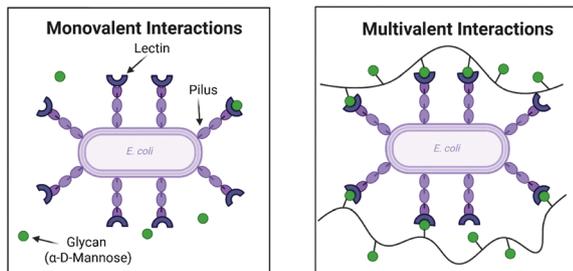
Fig. 5 Monovalent (glycan) vs. multivalent (glycopolymer) interactions with bacteria lectins.

by several orders of magnitude, reaching micromolar to nanomolar affinities.[179–181]

Antibacterial glycopolymers typically incorporate additional antimicrobial motifs, such as cationic side chains, to couple competitive binding with direct bactericidal activity (see Table 3 for a summary of these materials). However, unfunctionalized glycopolymers can also inhibit bacteria. By presenting sugars in a multivalent manner, glycopolymers can outcompete native glycans for bacterial lectins and inhibit growth. For example, Schulz and coworkers demonstrated this strategy using glycopolymers prepared via ring-opening metathesis polymerization. Polymers with mannose side-chains selectively inhibited E. coli growth, consistent with the high affinity of Type 1 fimbriae for α-D-mannose residues.[85] Typically, Type 1 fimbriae on the E. coli pathogen selectively recognize terminal α-D-mannose residues on host polysaccharides to mediate adhesion and initiate biofilm formation.[182] This study demonstrates the ability of unfunctionalized glycopolymers to inhibit bacterial growth without the addition of conventional antibacterial moieties.

In this review we discuss only materials developed to inhibit or disrupt biofilm formation. For further information on antibacterial glycopolymers more broadly, we direct readers to several excellent reviews of the field.[183–185] Here, we divide antibiofilm glycomaterials into three categories: unfunctionalized glycopolymers, cationic glycopolymers, and glycosylated nanomaterials (Fig. 6).

Unfunctionalized glycopolymers. Unfunctionalized glycopolymers represent a distinct class of antibiofilm materials wherein the material's activity arises exclusively from the presence of pendant saccharides. Rather than relying on an intrinsic bactericidal mechanism, these polymers act through a passive mechanism: multivalent sugars along the polymer backbone engage bacterial adhesins and disrupt the early
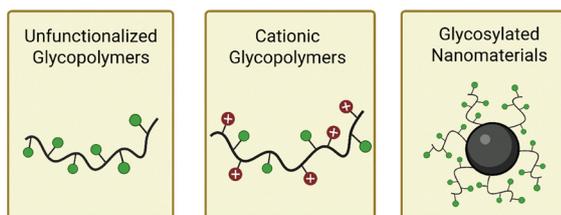

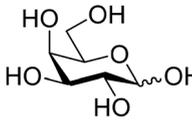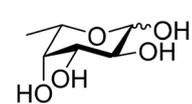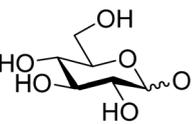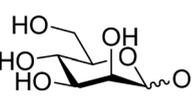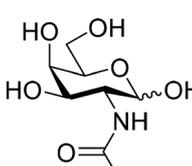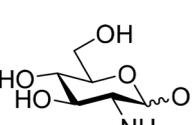**Fig. 6** Major classes of glycomaterials that are designed to inhibit biofilm formation.

stages of surface colonization. Importantly, this inhibition occurs without compromising bacterial viability. This antibacterial activity echoes the natural role of the mucin glycoproteins in mucus, where sugar-mediated interactions suppress adhesion and slow biofilm development. While the nonbiocidal nature of these materials may limit applications requiring direct bactericidal action, it also presents opportunities in designing antifouling materials for cases where preserving the native microbial balance is desirable.[175–177,186–191] Such passive strategies highlight the potential of glycopolymers to modulate host–pathogen interactions while minimizing selective pressure for resistance, and the passive inhibition paradigm has motivated efforts to translate unfunctionalized glycopolymers into practical antibiofilm materials.[192–196]

Several studies have drawn inspiration from natural, mucin-mediated suppression of bacterial colonization. For example, Werlang et al. developed silk-based glycopolymers functionalized with a series of different monosaccharides: N-acetyl glucosamine (GlcNAc), N-acetyl galactosamine (GalNAc), N-acetyl neuraminic acid (Neu5Ac), galactosamine (GalN), and glucosamine (GlcN) (Fig. 7).[177] The authors then evaluated each polymer's ability to inhibit Streptococcus mutans (S. mutans) biofilm formation.[177] Only glycopolymers that contained GalNAc or Neu5Ac demonstrated biofilm reduction compared to media controls. The authors also compared the polymers' antibiofilm efficacy against that of native mucus. Native mucus (containing highly glycosylated serine, threonine, and proline domains) reduced biofilm formation by 70%, compared to GalNAc- and Neu5Ac-functionalized polymers, which showed a 98% and 40% reduction, respectively. Mechanistic studies revealed distinct modes of action. Neu5Ac-containing polymers decreased planktonic viability of S. mutans, while GalNAc-containing polymers suppressed biofilm formation by directly interfering with bacterial adhesion without affecting cell viability. On the other hand, GlcNAc-containing polymers induced biofilm growth. These findings illustrate how changing the glycan identity can generate distinct pro- or antibiofilm pathways.

Glycopolymers have also been explored as synthetic mimics of host–bacteria interactions, leveraging sugar–lectin binding events to block bacterial adhesion and subsequent biofilm formation. In P. aeruginosa, the LecB lectin recognizes L-fucose and D-mannose residues on host cell surfaces. Inspired by these interactions, Hartmann and coworkers, synthesized α-L-fucose–functionalized polyamide oligomers (1.9–3.0 kDa) that outcompeted host glycans in binding LecB. These synthetic glycopolymers effectively disrupted bacterial adhesion and suppressed biofilm production by 15–20%, illustrating the potential of targeted lectin–ligand interactions as a design principle for antifouling materials.[197] However, no clear trend in antibiofilm activity emerged from changing the fucose content, even though LecB-binding assays confirmed that polymers with a higher fucose density displayed stronger interactions between polymer and lectin, consistent with multivalent binding principles. These results suggest that P. aeruginosa biofilm development is governed by processes more

Table 3 Examples of glycopolymers showing antibiofilm efficacy against different bacterial strains. Abbreviations: Photothermal therapy (PTT), photodynamic therapy (PDT), quaternary ammonium compound (QAC), gold nanorods (AuNRs), nanoparticle (NP)

Glycan	α/β	Active moiety	Polymer backbone	Strain	Ref.
D-galactose	β	N/A	Dendritic peptide	P. aeruginosa	194
	β	QAC	Chitosan	P. aeruginosa	200
	β	PDT/QAC	Polyacrylate	P. aeruginosa, E. coli, S. aureus, and B. amyloliquefaciens	203
	β	CuS NP/ Photothermal therapy (PTT)	Polymethacrylate	P. aeruginosa, S. aureus	207
	β	Gold nanorods (AuNRs)	Polymethacrylate	P. aeruginosa	211
	β	AgNP	Polyacrylamide	S. mutans, E. coli, S. aureus, P. aeruginosa	212
	β	Tobramycin	Polyacrylamide	P. aeruginosa	225
	β	Spiropyran (PTT)	Polyacrylate	P. aeruginosa	214
	β	Guanidine (cationic)/BODIPY (PDT)	Polymethacrylate	S. mutans	226
	β	BODIPY (PDT)	Polymethacrylate	P. aeruginosa	227
	β	Graphene oxide NP	PEG linker	P. aeruginosa	217
L-fucose	α	QAC	Chitosan	P. aeruginosa	200
	α/β	AuNRs	Polymethacrylate	P. aeruginosa	211
	β	Graphene oxide NP	PEG linker	P. aeruginosa	217
	α/β	AuNRs	Polymethacrylate	P. aeruginosa	175
	α	N/A	Oligo(amido amine)	P. aeruginosa	228
D-glucose	α	Graphene oxide NP	PEG linker	P. aeruginosa	217
	N/A	Lysine (cationic)	Block co-beta peptide	A. aureus, MRSA, S. aureus, S. agalactiae, S. pyogenes, S. pneumonia, E. faecalis	229 230
D-mannose	α	Tobramycin	Polyacrylamide	P. aeruginosa	213
	α	Cu/AgNP	Pentaerythritol dendrimer core	E. coli	208
N-acetyl galactosamine	β	N/A	Silk fibroin	S. mutans	177
D-glucosamine	α/β	AgNP/QAC	Polyacrylamide	P. aeruginosa, E. coli, S. aureus, and B. amyloliquefaciens	210

complex than LecB–carbohydrate recognition alone, underscoring the limitations of purely passive glycopolymer strategies.

Though unfunctionalized glycopolymers demonstrate that glycan presentation alone can weaken bacterial adhesion and biofilm formation, these materials' activity remains highly specific to the glycan–pathogen pairs they mimic. This specificity limits their utility as broad-spectrum antifouling agents. This limitation is potentially addressed by designing active glycopolymers that combine adhesion-blocking motifs with bactericidal or disruptive functionalities. Such dual-acting materials may offer more robust and generalizable antibiofilm performance, bridging the gap between passive mimics of mucin and fully synthetic antimicrobial polymers. Nevertheless, unfunctionalized glycomaterials have provided the glycopolymer community with key fundamental insights into polymer-bacteria interactions.

Cationic glycopolymers. Cationic polymers have emerged as a widely adopted framework for designing antibacterial
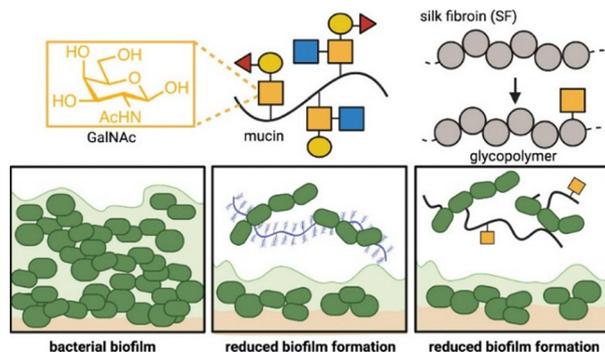
Fig. 7 Silk-based glycopolymers to treat oral pathogenic *S. mutans* and commensal *S. sanguinis*. Reproduced from ref. 177 with permission from the American Chemical Society, copyright 2024.

materials, due to their capacity to disrupt bacterial membranes and maintain efficacy against drug-resistant strains. The incorporation of carbohydrate functionalities extends the utility of cationic polymers by guiding bacterial targeting, tempering cytotoxic side effects, and introducing synergistic modes of action.[198,199] These attributes position cationic glycopolymers as a promising class of active antibiofilm agents that move beyond passive adhesion blockers toward more aggressive, multifunctional strategies.[200]

Zhang *et al.* highlighted the advantages of combining carbohydrates with cationic motifs by synthesizing block copolymers of glucose and lysine prepared *via* cationic ROP.[201] β-Lactam-based monomers were used that enabled the formation of well-defined polymer blocks (Fig. 8). The initial antibacterial assays revealed that the lysine homopolymer was broadly active against most Gram-positive bacteria but was also highly cytotoxic and hemolytic. In contrast, a glucose:lysine block copolymer with a 7 : 13 ratio retained a comparable potency against *S. aureus*, while eliminating the hemolytic side effects. This
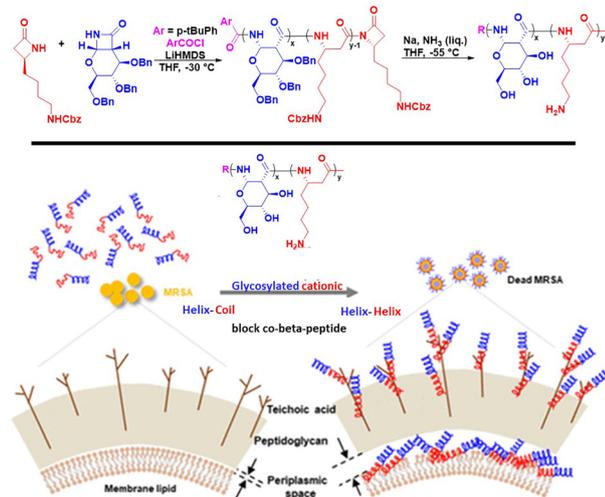
modular strategy illustrates how glycan units can be incorporated within the polymer backbone, creating a framework to balance antibacterial potency with biocompatibility.[201] This copolymer also displayed potency against community- and hospital-acquired methicillin-resistant *S. aureus* (MRSA) strains, including those resistant to vancomycin and daptomycin (Fig. 8). In addition to dispersing and eradicating MRSA biofilms with a 99.9% reduction (substantially outperforming vancomycin), the copolymer provided complete protection *in vivo*. All mice challenged with a lethal dose of MRSA survived when treated with the copolymer, compared to only a 67% survival rate for those treated with vancomycin. These results underscore the advantages of carbohydrate incorporation into cationic polymers, which enhances selectivity and antibiofilm performance while mitigating cytotoxicity. Subsequent mechanistic studies investigated this synergy. It was found that the cationic block intercalated into the bacterial cell envelope, imparting bactericidal activity, while the carbohydrate segment acted as an antifouling domain, reducing bacterial adhesion and disrupting biofilm matrix interactions. Together, these two mechanisms suppressed biofilm growth and promoted dispersion, demonstrating that the combination of glycans and cationic functionalities can overcome the toxicity and hemolysis issues that often limit cationic antimicrobial polymers.[202]

Similarly, Dai *et al.* developed cationic glycopolymers that incorporated a photodynamic therapy (PDT) unit to generate reactive oxygen species (ROS) (Fig. 9).[203] The design involved thiazole-derived cations that anchored within bacterial membranes, while the PDT moiety produced ROS to induce bactericidal effects. Galactose units were incorporated to enhance biocompatibility and bacterial specificity. The resulting polymers inhibited biofilm formation and eradicated *S. aureus* and *P. aeruginosa* biofilms, with increasing potency with increasing glycan content. Notably, cytotoxicity assays revealed ~80% cell viability at concentrations greater than 500-fold above the MIC, highlighting the material's large therapeutic window. Collectively, these studies illustrate the value of pairing cationic activity with carbohydrate functionalities to create potent, selective antibiofilm agents. By simultaneously disrupting bacterial membranes, dispersing biofilm matrices, and maintaining host compatibility, cationic glycopolymers address many of the limitations inherent to purely sugar- or cationic-based systems.

Fig. 8 Interaction between the Co-β-peptide and Cell Envelope Components of MRSA. Reproduced from ref. 201 with permission from Springer Nature, copyright 2019.
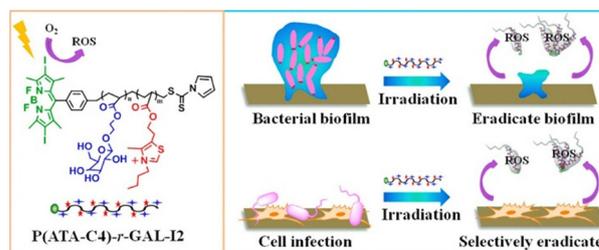

Fig. 9 Cationic glycopolymers with PDT units to generate ROS for combating biofilm formation. Reproduced from ref. 203 with permission from the American Chemical Society, copyright 2018.

However, significant obstacles still limit the translation of cationic glycopolymers into clinical practice. Carbohydrate incorporation often attenuates cytotoxicity of cationic scaffolds in vitro; however, this benefit can fail to manifest in vivo.[204] Additionally, manipulating the material's structural parameters (i.e., charge density, hydrophilicity, molecular weight, and architecture) can strongly influence the in vivo toxicity of cationic polymers.[205] However, these parameters have not been systematically examined for cationic glycopolymers.

Glycosylated nanomaterials. Glyconanotechnology provides a versatile platform for applications spanning drug delivery, diagnostics, and pathogen recognition.[206] Within this broad field, biofilm inhibition and removal represent particularly promising directions. A common strategy integrates biocidal metal nanoparticles with glycopolymer conjugates to create multifunctional nanocomposites that couple antimicrobial potency with carbohydrate-mediated specificity.[207–211] In a recent study, Wei et al. reported glycopolymersome-supported silver nanocomposites designed to combat multidrug-resistant bacteria and disrupt biofilms (Fig. 10).[212] Using reversible addition-fragmentation chain transfer (RAFT)-mediated polymerization-induced self-assembly, galactose-based acrylamide glycomonomers were first polymerized and then chain-extended with a pyridine block. The silver ions that were coordinated to the pyridine segment were subsequently reduced with sodium borohydride to generate AgNPs embedded within the glycopolymersome structure. The resulting nanocomposites exhibited markedly enhanced antibacterial activity compared to either AgNPs or glycopolymers alone.

Against E. coli, the MIC decreased from >62 μg mL^{-1} for AgNPs to 16 μg mL^{-1} for the nanocomposites. Concentration-dependent biofilm inhibition was also observed, with 70–80% inhibition across E. coli, S. aureus, and P. aeruginosa. The strongest efficacy was against P. aeruginosa, which was attributed to galactose–LecA lectin interactions. The cytocompatibility also improved: hemolysis remained below 5% while cell

viability remained above 70% at all concentrations tested, reflecting the protective role of the glycopolymer shell. In vivo evaluation using a rat dentin model with S. mutans showed that these glycosylated nanocomposites fully prevented biofilm formation over 14 days, whereas untreated controls or treatments with AgNPs or glycopolymers alone were ineffective. This work illustrates how encapsulating silver nanoparticles within glycopolymersomes can lower toxicity, enhance antibacterial potency, and improve biofilm inhibition, highlighting the potential of glyconanocomposites as multifunctional, biocompatible antibiofilm platforms.

While metallic nanomaterials have dominated glyconanotechnology research, non-metallic nanostructures conjugated with glycopolymers have also been explored for antibiofilm applications. A prevalent strategy leverages glycosylated nanoassemblies as targeted drug-delivery vehicles to enhance the penetration and efficacy of conventional antibiotics within biofilms.[213]

In parallel, glycopolymer-based nanoparticles have been engineered to deliver PDT agents. In these systems, the glycopolymer shell mediates selective biofilm targeting and penetration, after which irradiation induces the generation of ROS to eradicate resident bacteria while minimizing off-target damage.[214–216] For instance, Tricomi et al. investigated glycopolymer-coated graphene oxide nanomaterials to combat P. aeruginosa biofilms.[217] In this study, L-fucose, D-mannose, and D-galactose were conjugated to graphene oxide surfaces through a green mechanochemical ball-milling process and subsequently evaluated for their antibacterial efficacy. The fucose- and galactose-functionalized derivatives killed more than 99% of P. aeruginosa at half the concentration of unfunctionalized graphene oxide. Similarly, these derivatives significantly reduced biofilm attachment to polystyrene surfaces. Scanning electron microscopy revealed that the glycosylated graphene oxides were able to inhibit bacteria from forming mature biofilm colonies, whereas the control graphene oxide did not. This work reinforces the observation that strategic carbohydrate functionalization can enhance both the potency and biofilm-disrupting capabilities of antimicrobial nanomaterials.

Despite the rapid growth of glycosylated nanomaterials, some debate remains over their associated health risks.[218] Designing non-toxic nanomaterials has proven challenging due to the intrinsic structural complexity and unique behaviors of nanomaterial structures (e.g., aggregation), making standard toxicological measurements potentially insufficient for capturing the material's full biological impact.[219,220] This challenge is particularly relevant for the multifunctional systems discussed here, where surface coatings, ligands, and diverse functional groups can influence interactions with biological environments. Comprehensive and tailored toxicological studies are thus essential to assess the safety, biodistribution, and long-term effects of these emerging antimicrobial platforms.

Concluding thoughts on glycopolymers. Over the last few decades, glycomaterials have emerged as powerful components
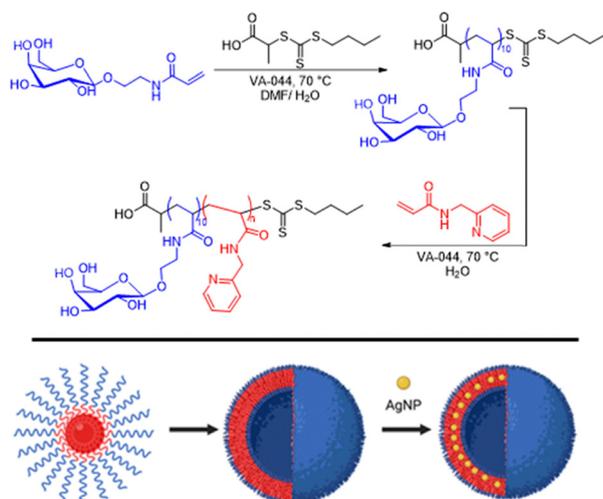

Fig. 10   Illustration of glycopolymersome-supported AgNP composite.[212]

in the design of next-generation antibacterial strategies, particularly in the face of escalating antimicrobial resistance (Table 3). This review focuses on systems targeting biofilms as a central mechanism of resistance, although many of these materials also display direct bactericidal activity. Across diverse platforms, integrating glycopolymers with complementary antimicrobial functionalities consistently yields clear advantages, including reduced cytotoxicity and enhanced antibacterial efficacy. However, significant challenges persist. To date, most reported systems remain confined to the academic lab, with progression toward clinical evaluation still exceedingly rare.

Although not strictly classified as glycopolymers, polysaccharides such as cationic poly(acetyl, arginyl) glucosamine (PAAG) have been extensively studied for their ability to inhibit and disrupt biofilms across multiple bacterial species.[221–224] These systems provide valuable mechanistic insights that may guide the rational design and safety optimization of future glycosylated materials. While polysaccharide-based materials such as PAAG have advanced into clinical trials, no synthetic glycopolymer systems are currently under such evaluation.

Key barriers to translation include the cost and complexity of synthesis, which can impede large-scale production and commercial viability. However, these challenges are not unique to glycomaterials and echo similar challenges that currently successful therapeutic materials also faced during their early development. Moving forward, establishing predictable, cost-effective, and scalable synthetic routes will be essential to enable broader application. Equally important will be the integration of glycopolymers into practical delivery platforms that align with clinical manufacturing and regulatory frameworks. By addressing these challenges, the field will be well-positioned to translate the unique advantages of glycopolymers from the laboratory into real-world antibiofilm intervention therapies.

Clinical perspectives

Antimicrobial resistance is one of the most significant global health challenges of the twenty-first century, projected to contribute to more than 8 million deaths per year by 2050.[231] No major new classes of antibiotics have been discovered since the 1980s, and most antibiotic candidates are based on existing chemical frameworks.[232–235] Importantly, reliance on conventional systemic antimicrobials not only drives drug resistance but also causes unintended off-target effects, ranging from potentially irreversible side effects to profound disruptions in the microbiome, including *Clostridioides difficile* infections.[236,237] For example, it is estimated that nearly one in five emergency room visits in the United States are related to an antibiotic adverse event,[238] and exposure to antimicrobials directly affects the risk of developing drug-resistance genes.[239]

The overall prevalence of medical devices has increased in recent decades, coinciding with advancements in device development and an aging population.[240,241] Devices now exist for almost every organ system, including central venous and urinary catheters, surgical meshes, vascular grafts, shunts, deep brain stimulators, cochlear implants, prosthetic valves, pacemaker-defibrillator systems, left ventricular assist devices, and prosthetic joints. This increase in device use has also led to a rise in associated infections.[240,242] As expected, infections on devices that are difficult to remove surgically are associated with high rates of morbidity and mortality.[240,242] For example, prosthetic-valve endocarditis is associated with over 30% mortality,[242,243] and prosthetic hip infections carry a 21% mortality rate by 5-years, a 4-fold increase from age-based rates.[244] Often, these types of infections require both invasive surgical procedures and prolonged courses of systemic antibiotics, posing a significant burden to patients and the healthcare system.[241–243]

Though some prophylactic techniques have been developed, approaches to biofilm-related infections are largely reactive, focusing on treatment only after an infection has been diagnosed. There is a critical need for biofilm prevention strategies that exist outside of these treatment paradigms. The design of polymers that prevent surface adhesion could offer multiple advantages for implanted devices, including a lower risk of colonization, reduced reliance on systemic antimicrobials, and more selective local targeting of specific pathogens or organ systems. To have a clinical impact, such surfaces would not necessarily need to be bactericidal, since planktonic cells are readily cleared by the immune system or targeted antimicrobials. Such an approach represents a treatment strategy that preserves conventional antimicrobials, combats multidrug-resistant pathogens, and protects the host microbiome.

Conclusion

Throughout this review, we have highlighted recent advances in the design and application of polymeric materials for antibiofilm purposes. Current research demonstrates two major approaches: (i) engineering polymers with intrinsic antibiofilm activity through chemical and structural modification, and (ii) employing polymers as platforms to enhance the delivery or efficacy of established antimicrobial agents.

The diversity of polymer functionalities explored to date—including cationic moieties, nitric oxide donors, metallic and glycosylated systems, photosensitizers, and antibiotic conjugates—underscores the versatility of synthetic polymers in addressing biofilm-associated infections. Subtle changes in polymer parameters such as topology, molecular weight, backbone identity, and functional group chemistry can yield markedly different antibiofilm outcomes. Glycopolymers are a particularly interesting case, where small variations in glycan stereochemistry can switch their effects from inhibitory to promotive, revealing unique biofilm-modulating mechanisms beyond conventional bactericidal action.

Despite this promise, clinical translation of antibacterial polymers remains a major challenge. Synthetic complexity, high production costs, and limited scalability often hinder real-world implementation. Consequently, a growing emphasis has emerged on developing practical, application-driven materials. Moving forward, efforts to develop cost-effective and

scalable fabrication methods must proceed in parallel with the discovery of new antibiofilm materials. Realizing the translational potential of these materials will require integrating polymer design with device engineering, thus ensuring that materials are optimized not only for performance but also for deployment in clinical and commercial settings.

Beyond these translational obstacles, major fundamental questions remain. The mechanisms by which polymers interact with bacterial membranes, EPS networks, and surface adhesins remain only partly understood, and even small changes in polymer structure can produce large effects. Mapping these (often nonlinear) structure–function relationships and integrating them into predictive models is both a major challenge and a major opportunity. A deeper mechanistic foundation will make it possible to move beyond empirical screening toward an increasingly rational and sophisticated design of antibiofilm polymers.

As scientific and translational challenges are addressed in parallel, the field is poised for rapid progress. The convergence of increasingly precise polymer synthesis tools, deeper microbiology insights, and growing clinical need creates an exceptional opportunity. Increasing interactions among historically siloed but scientifically interrelated fields allow us to ask—and answer—questions that were out of reach only a few years ago. As these advances come together, the prospect of creating robust, clinically deployable antibiofilm materials becomes increasingly realistic. The next generation of polymer-based strategies may therefore not only complement existing therapies, but fundamentally change how we prevent and treat biofilm-related infections.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results, software or code have been included, and no new data were generated or analysed as part of this review.

Acknowledgements

References

1 M. Matijašić, T. Meštrović, H. Paljetak, M. Perić, A. Barešić and D. Verbanac, Gut Microbiota beyond Bacteria-Mycobiome, Virome, Archaeome, and Eukaryotic Parasites in IBD, *Int. J. Mol. Sci.*, 2020, **21**, 8.

2 M. Eisenstein, The skin microbiome, *Nature*, 2020, **588**(7838), S209–S209.

3 K. A. Floyd; A. R. Eberly and M. Hadjifrangiskou, 3 - Adhesion of bacteria to surfaces and biofilm formation on medical devices, *In Biofilms and Implantable Medical Devices*, ed Y. Deng; W. Lv, Woodhead Publishing, 2017, pp. 47–95.

4 L. Sedghi, V. DiMassa, A. Harrington, S. V. Lynch and Y. L. Kapila, The oral microbiome: Role of key organisms and complex networks in oral health and disease, *Periodontology*, 2021, **87**(1), 107–131.

5 K. Kriebel, C. Hieke, B. Müller-Hilke, M. Nakata and B. Kreikemeyer, Oral Biofilms from Symbiotic to Pathogenic Interactions and Associated Disease -Connection of Periodontitis and Rheumatic Arthritis by Peptidylarginine Deiminase, *Front. Microbiol.*, 2018, **9**, 53.

6 A. Maddi and F. A. Scannapieco, Oral biofilms, oral and periodontal infections, and systemic disease, *Am. J. Dent.*, 2013, **26**(5), 249–254.

7 S. Kitamoto, H. Nagao-Kitamoto, R. Hein, T. M. Schmidt and N. Kamada, The Bacterial Connection between the Oral Cavity and the Gut Diseases, *J. Dent. Res.*, 2020, **99**(9), 1021–1029.

8 I. Rowland, G. Gibson, A. Heinken, K. Scott, J. Swann, I. Thiele and K. Tuohy, Gut microbiota functions: metabolism of nutrients and other food components, *Eur. J. Nutr.*, 2018, **57**(1), 1–24.

9 N. M. Delzenne, C. Knudsen, M. Beaumont, J. Rodriguez, A. M. Neyrinck and L. B. Bindels, Contribution of the gut microbiota to the regulation of host metabolism and energy balance: a focus on the gut–liver axis, *Proc. Nutr. Soc.*, 2019, **78**(3), 319–328.

10 E. M. Halawa, M. Fadel, M. W. Al-Rabia, A. Behairy, N. A. Nouh, M. Abdo, R. Olga, L. Fericean, A. M. Atwa, M. El-Nablaway and A. Abdeen, Antibiotic action and resistance: updated review of mechanisms, spread, influencing factors, and alternative approaches for combating resistance, *Front. Pharmacol.*, 2024, **14**, 2023.

11 J. L. Del Pozo and R. Patel, The Challenge of Treating Biofilm-associated Bacterial Infections, *Clin. Pharmacol. Ther.*, 2007, **82**(2), 204–209.

12 N. N. Tran, T. Morrisette, S. C. J. Jorgensen, J. M. Orench-Benvenutti and R. Kebriaei, Current therapies and challenges for the treatment of Staphylococcus aureus biofilm-related infections, *Pharmacotherapy*, 2023, **43**(8), 816–832.

13 C. Pouget, C. Dunyach-Remy, A. Pantel, S. Schuldiner, A. Sotto and J. P. Lavigne, Biofilms in Diabetic Foot Ulcers: Significance and Clinical Relevance, *Microorganisms*, 2020, **8**, 10.

14 A. I. Adler, E. J. Boyko, J. H. Ahroni and D. G. Smith, Lower-extremity amputation in diabetes. The independent effects of peripheral vascular disease, sensory neuropathy, and foot ulcers, *Diabetes Care*, 1999, **22**(7), 1029–1035.

15 G. T. Werneburg, Catheter-Associated Urinary Tract Infections: Current Challenges and Future Prospects, *Res. Rep. Urol.*, 2022, **14**, 109–133.

16 K. M. Al-Sayaghi, T. A. H. Alqalah, S. A. Alkubati, S. A. Alshoabi, M. Alsabri, G. G. Alrubaiee, M. A. Almoliky, K. A. Saleh, A. K. Al-Sayaghi, R. A. Elshatarat, Z. T. Saleh, A. M. Saleh and H. R. Abdel-Aziz, Healthcare workers' compliance with the catheter associated urinary tract infection prevention guidelines: an observational study in Yemen, *Antimicrob. Resis. Infection Control*, 2023, **12**(1), 144.

17 V. G. Preda and O. Săndulescu, Communication is the key: biofilms, quorum sensing, formation and prevention, *Discoveries*, 2019, **7**(3), 2359–7232.

18 S. Mendhe, A. Badge, S. Ugemuge and D. Chandi, Impact of Biofilms on Chronic Infections and Medical Challenges, *Cureus*, 2023, **15**(11), e48204.

19 M. A. Rather, K. Gupta and M. Mandal, Microbial biofilm: formation, architecture, antibiotic resistance, and control strategies, *Braz. J. Microbiol.*, 2021, **52**(4), 1701–1718.

20 S. Sharma, J. Mohler, S. D. Mahajan, S. A. Schwartz, L. Bruggemann and R. Aalinkeel, Microbial Biofilm: A Review on Formation, Infection, Antibiotic Resistance, Control Measures, and Innovative Treatment, *Microorganisms*, 2023, **11**, 6.

21 J. Wang, P. Li, N. Wang, J. Wang and D. Xing, Antibacterial features of material surface: strong enough to serve as antibiotics?, *J. Mater. Chem. B*, 2023, **11**(2), 280–302.

22 S. Singh, S. Datta, K. B. Narayanan and K. N. Rajnish, Bacterial exopolysaccharides in biofilms: role in antimicrobial resistance and treatments, *J. Genet. Eng. Biotechnol.*, 2021, **19**(1), 140.

23 J. S. Gunn, L. O. Bakaletz and D. J. Wozniak, What's on the Outside Matters: The Role of the Extracellular Polymeric Substance of Gram-negative Biofilms in Evading Host Immunity and as a Target for Therapeutic Intervention, *J. Biol. Chem.*, 2016, **291**(24), 12538–12546.

24 A. Vertes, V. Hitchins and K. S. Phillips, Analytical Challenges of Microbial Biofilms on Medical Devices, *Anal. Chem.*, 2012, **84**(9), 3858–3866.

25 M. M. Zafer, G. A. Mohamed, S. R. M. Ibrahim, S. Ghosh, C. Bornman and M. A. Elfaky, Biofilm-mediated infections by multidrug-resistant microbes: a comprehensive exploration and forward perspectives, *Arch. Microbiol.*, 2024, **206**(3), 101.

26 D. Lebeaux, J. M. Ghigo and C. Beloin, Biofilm-related infections: bridging the gap between clinical management and fundamental aspects of recalcitrance toward antibiotics, *Microbiol. Mol. Biol. Rev.*, 2014, 1098–5557.

27 D. Mitra, E.-T. Kang and K. G. Neoh, Polymer-Based Coatings with Integrated Antifouling and Bactericidal Properties for Targeted Biomedical Applications, *ACS Appl. Polym. Mater.*, 2021, **3**(5), 2233–2263.

28 S. Magill Shelley, R. Edwards Jonathan, W. Bamberg, G. Beldavs Zintars, G. Dumyati, A. Kainer Marion, R. Lynfield, M. Maloney, L. McAllister-Hollod, J. Nadle, M. Ray Susan, D. L. Thompson, L. E. Wilson and S. K. Fridkin, Multistate Point-Prevalence Survey of Health Care–Associated Infections, *N. Engl. J. Med.*, 2014, **370**(13), 1198–1208.

29 H. Wu, C. Moser, H.-Z. Wang, N. Høiby and Z.-J. Song, Strategies for combating bacterial biofilm infections, *Int. J. Oral Sci.*, 2015, **7**(1), 1–7.

30 Z. Song, L. Borgwardt, N. Høiby, H. Wu, T. S. Sørensen and A. Borgwardt, Prosthesis infections after orthopedic joint replacement: the possible role of bacterial biofilms, *Orthop. Rev.*, 2013, **5**(2), 65–71.

31 A. Silverstein and C. F. Donatucci, Bacterial Biofilms and implantable prosthetic devices, *Int. J. Impotence Res.*, 2003, **15**(S5), S150–S154.

32 H. O. Gbejuade, A. M. Lovering and J. C. Webb, The role of microbial biofilms in prosthetic joint infections, *Acta Orthop.*, 2015, **86**(2), 147–158.

33 A. Hrynyshyn, M. Simões and A. Borges, Biofilms in Surgical Site Infections: Recent Advances and Novel Prevention and Eradication Strategies, *Antibiotics*, 2022, **11**, 1.

34 A. Giacometti, O. Cirioni, A. M. Schimizzi, M. S. Del Prete, F. Barchiesi, M. M. D'Errico, E. Petrelli and G. Scalise, Epidemiology and microbiology of surgical wound infections, *J. Clin. Microbiol.*, 2000, **38**(2), 918–922.

35 E. A. Saverina, N. A. Frolov, O. A. Kamanina, V. A. Arlyapov, A. N. Vereshchagin and V. P. Ananikov, From Antibacterial to Antibiofilm Targeting: An Emerging Paradigm Shift in the Development of Quaternary Ammonium Compounds (QACs), *ACS Infect. Dis.*, 2023, **9**(3), 394–422.

36 M. A. Kohanski, D. J. Dwyer and J. J. Collins, How antibiotics kill bacteria: from targets to networks, *Nat. Rev. Microbiol.*, 2010, **8**(6), 423–435.

37 J. Davies, Are antibiotics naturally antibiotics?, *J. Ind. Microbiol. Biotechnol.*, 2006, **33**(7), 496–499.

38 S. Q. Shah, F. C. Cabello, T. M. L'Abée-Lund, A. Tomova, H. P. Godfrey, A. H. Buschmann and H. Sørum, Antimicrobial resistance and antimicrobial resistance genes in marine bacteria from salmon aquaculture and non-aquaculture sites, *Environ. Microbiol.*, 2014, **16**(5), 1310–1320.

39 D. Hocquet, A. Muller and X. Bertrand, What happens in hospitals does not stay in hospitals: antibiotic-resistant bacteria in hospital wastewater systems, *J. Hosp. Infect.*, 2016, **93**(4), 395–402.

40 J. E. M. Watts, H. J. Schreier, L. Lanska and M. S. Hale, The Rising Tide of Antimicrobial Resistance in Aquaculture: Sources, Sinks and Solutions, *Mar. Drugs*, 2017, **15**(6), 158.

41 A. Pruden, R. Pei, H. Storteboom and K. H. Carlson, Antibiotic Resistance Genes as Emerging Contaminants: Studies in Northern Colorado, *Environ. Sci. Technol.*, 2006, **40**(23), 7445–7450.

42 J. Wang, L. Chu, L. Wojnárovits and E. Takács, Occurrence and fate of antibiotics, antibiotic resistant genes (ARGs) and antibiotic resistant bacteria (ARB) in municipal wastewater treatment plant: An overview, *Sci. Total Environ.*, 2020, **744**, 140997.

43 F. C. Cabello, H. P. Godfrey, A. Tomova, L. Ivanova, H. Dölz, A. Millanao and A. H. Buschmann, Antimicrobial use in aquaculture re-examined: its relevance to antimicrobial resistance and to animal and human health, *Environ. Microbiol.*, 2013, **15**(7), 1917–1942.

44 J. Bengtsson-Palme and D. G. Larsson, Concentrations of antibiotics predicted to select for resistant bacteria: Proposed limits for environmental regulation, *Environ. Int.*, 2016, **86**, 140–149.

45 D. Davies, Understanding biofilm resistance to antibacterial agents, *Nat. Rev. Drug Discovery*, 2003, **2**(2), 114–122.

46 J. W. Costerton, P. S. Stewart and E. P. Greenberg, Bacterial biofilms: a common cause of persistent infections, *Science*, 1999, **284**(5418), 1318–1322.

47 C. Sternberg, B. B. Christensen, T. Johansen, A. Toftgaard Nielsen, J. B. Andersen, M. Givskov and S. Molin, Distribution of bacterial growth activity in flow-chamber biofilms, *Appl. Environ. Microbiol.*, 1999, **65**(9), 4108–4117.

48 P. A. Suci, M. W. Mittelman, F. P. Yu and G. G. Geesey, Investigation of ciprofloxacin penetration into Pseudomonas aeruginosa biofilms, *Antimicrob. Agents Chemother.*, 1994, **38**(9), 2125–2133.

49 N. Gargate, M. Laws and K. M. Rahman, Current economic and regulatory challenges in developing antibiotics for Gram-negative bacteria, *npj Antimicrob. Resist.*, 2025, **3**(1), 50.

50 A new class of antibiotics is cause for cautious celebration — but the economics must be fixed, *Nature*, 2024, **625**(7993), 7.

51 G. S. Burrill, Personalized Medicine or Blockbusterology?, *Cancer*, 2002, **2**(41.3), 5.2.

52 J. F. Barrett, Can biotech deliver new antibiotics?, *Curr. Opin. Microbiol.*, 2005, **8**(5), 498–503.

53 A. Banerjee, P. Chowdhury, K. Bauri, B. Saha and P. De, Inhibition and eradication of bacterial biofilm using polymeric materials, *Biomater. Sci.*, 2023, **11**(1), 11–36.

54 A. Valliammai, A. Selvaraj, P. Mathumitha, C. Aravindraja and S. K. Pandian, Polymeric antibiofilm coating comprising synergistic combination of citral and thymol prevents methicillin-resistant Staphylococcus aureus biofilm formation on titanium, *Mater. Sci. Eng. C*, 2021, **121**, 111863.

55 A. Copling, M. Akantibila, R. Kumaresan, G. Fleischer, D. Cortes, R. S. Tripathi, V. J. Carabetta and S. L. Vega, Recent Advances in Antimicrobial Peptide Hydrogels, *Int. J. Mol. Sci.*, 2023, **24**, 8.

56 M. Wang, Y. Zheng, C. Yin, S. Dai, X. Fan, Y. Jiang, X. Liu, J. Fang, B. Yi, Q. Zhou and T. Wang, Recent Progress in antibacterial hydrogel coatings for targeting biofilm to prevent orthopedic implant-associated infections, *Front. Microbiol.*, 2023, **14**.

57 T. Peng, Q. Shi, M. Chen, W. Yu and T. Yang, Antibacterial-Based Hydrogel Coatings and Their Application in the Biomedical Field-A Review, *J. Funct. Biomater.*, 2023, **14**, 5.

58 D. Pranantyo, C. K. Yeo, Y. Wu, C. Fan, X. Xu, Y. S. Yip, M. I. G. Vos, S. H. Mahadevegowda, P. L. K. Lim, L. Yang, P. T. Hammond, D. I. Leavesley, N. S. Tan and M. B. Chan-Park, Hydrogel dressings with intrinsic antibiofilm and antioxidative dual functionalities accelerate infected diabetic wound healing, *Nat. Commun.*, 2024, **15**(1), 954.

59 D. U. Lee, M. Kayumov, J. Park, S. K. Park, Y. Kang, Y. Ahn, W. Kim, S. H. Yoo, J.-K. Park, B.-G. Kim, Y. S. Oh, I.-S. Jeong and D. Y. Choi, Antibiofilm and antithrombotic hydrogel coating based on superhydrophilic zwitterionic carboxymethyl chitosan for blood-contacting devices, *Bioact. Mater.*, 2024, **34**, 112–124.

60 S. V. Pavlukhina, J. B. Kaplan, L. Xu, W. Chang, X. Yu, S. Madhyastha, N. Yakandawala, A. Mentbayeva, B. Khan and S. A. Sukhishvili, Noneluting Enzymatic Antibiofilm Coatings, *ACS Appl. Mater. Interfaces*, 2012, **4**(9), 4708–4716.

61 I. Negut, B. Bita and A. Groza, Polymeric Coatings and Antimicrobial Peptides as Efficient Systems for Treating Implantable Medical Devices Associated-Infections, *Polymers*, 2022, **14**, 8.

62 N. Raheem and S. K. Straus, Mechanisms of Action for Antimicrobial Peptides With Antibacterial and Antibiofilm Functions, *Front. Microbiol.*, 2019, **10**.

63 B. Zhang, D. Lu and H. Duan, Recent advances in responsive antibacterial materials: design and application scenarios, *Biomater. Sci.*, 2023, **11**(2), 356–379.

64 H. Q. Karp, E. S. Nowak, G. A. Kropp, N. A. Col, M. D. Schulz, N. Sriranganathan and J. Rao, Broad Host Range Peptide Nucleic

Acids Prevent Gram-negative Biofilms Implicated in Catheter-Associated Urinary Tract Infections, *Microorganisms*, 2025, 1948.

65 Z. Guo, Y. Wang, T. Tan, Y. Ji, J. Hu and Y. Zhang, Antimicrobial d-Peptide Hydrogels, *ACS Biomater. Sci. Eng.*, 2021, **7**(4), 1703–1712.

66 M. Yang, R. Xing, G. Shen, C. Yuan and X. Yan, A versatile cyclic dipeptide hydrogelator: Self-assembly and rheology in various physiological conditions, *Colloids Surf., A*, 2019, **572**, 259–265.

67 Z. Jiang, J. Feng, F. Wang, J. Wang, N. Wang, M. Zhang, C.-Y. Hsieh, T. Hou, W. Cui and L. Ma, AI-Guided Design of Antimicrobial Peptide Hydrogels for Precise Treatment of Drug-resistant Bacterial Infections, *Adv. Mater.*, 2025, **37**(20), 2500043.

68 N. A. Obaid, S. Almarzoky Abuhussain, K. K. Mulibari, F. Alshanqiti, S. A. Malibari, S. S. Althobaiti, M. Alansari, E. Muneef, L. Almatrafi, A. Alqarzi, N. Alotaibi, A. M. Mostafa and A. Hagag, Antimicrobial-resistant pathogens related to catheter-associated urinary tract infections in intensive care units: A multi-center retrospective study in the Western region of Saudi Arabia, *Clin. Epidemiol. Global Health*, 2023, **21**, 101291.

69 H. Zhang, Z. Wu, J. Zhou, Z. Wang, C. Yang, P. Wang, M. S. Fareed, Y. He, J. Su, R. Cha and K. Wang, The Antimicrobial, Hemostatic, and Anti-Adhesion Effects of a Peptide Hydrogel Constructed by the All-d-Enantiomer of Antimicrobial Peptide Jelleine-1, *Adv. Healthcare Mater.*, 2023, **12**(29), e2301612.

70 S. Debnath, A. Shome, D. Das and P. K. Das, Hydrogelation Through Self-Assembly of Fmoc-Peptide Functionalized Cationic Amphiphiles: Potent Antibacterial Agent, *J. Phys. Chem. B*, 2010, **114**(13), 4407–4415.

71 A. P. McCloskey, E. R. Draper, B. F. Gilmore and G. Laverty, Ultrashort self-assembling Fmoc-peptide gelators for anti-infective biomaterial applications, *J. Pept. Sci.*, 2017, **23**(2), 131–140.

72 E. R. Cross, S. M. Coulter, S. Pentlavalli and G. Laverty, Unravelling the antimicrobial activity of peptide hydrogel systems: current and future perspectives, *Soft Matter*, 2021, **17**(35), 8001–8021.

73 V. R. Aldilla, R. Chen, R. Kuppusamy, S. Chakraborty, M. D. P. Willcox, D. S. Black, P. Thordarson, A. D. Martin and N. Kumar, Hydrogels with intrinsic antibacterial activity prepared from naphthyl anthranilamide (NaA) capped peptide mimics, *Sci. Rep.*, 2022, **12**(1), 22259.

74 N. P. Desai and J. A. Hubbell, Biological responses to polyethylene oxide modified polyethylene terephthalate surfaces, *J. Biomed. Mater. Res.*, 1991, **25**(7), 829–843.

75 J. Hoffmann, J. Groll, J. Heuts, H. Rong, D. Klee, G. Ziemer, M. Moeller and H. P. Wendel, Blood cell and plasma protein repellent properties of star-PEG-modified surfaces, *J. Biomater. Sci., Polym. Ed.*, 2006, **17**(9), 985–996.

76 W. R. Gombotz, W. Guanghui, T. A. Horbett and A. S. Hoffman, Protein adsorption to poly(ethylene oxide) surfaces, *J. Biomed. Mater. Res.*, 1991, **25**(12), 1547–1562.

77 P. Lundberg, A. Bruin, J. W. Klijnstra, A. M. Nyström, M. Johansson, M. Malkoch and A. Hult, Poly(ethylene glycol)-Based Thiol-ene Hydrogel Coatings—Curing Chemistry, Aqueous Stability, and Potential Marine Antifouling Applications, *ACS Appl. Mater. Interfaces*, 2010, **2**(3), 903–912.

78 X. He, G. Sathishkumar, K. Gopinath, K. Zhang, Z. Lu, C. Li, E.-T. Kang and L. Xu, One-step self-assembly of biogenic Au NPs/PEG-based universal coatings for antifouling and photothermal killing of bacterial pathogens, *Chem. Eng. J.*, 2021, **421**, 130005.

79 M. Charnley, M. Textor and C. Acikgoz, Designed polymer structures with antifouling–antimicrobial properties, *React. Funct. Polym.*, 2011, **71**(3), 329–334.

80 W. Xi, V. Hegde, S. D. Zoller, H. Y. Park, C. M. Hart, T. Kondo, C. D. Hamad, Y. Hu, A. H. Loftin, D. O. Johansen, Z. Burke, S. Clarkson, C. Ishmael, K. Hori, Z. Mamouei, H. Okawa, I. Nishimura, N. M. Bernthal and T. Segura, Point-of-care antimicrobial coating protects orthopaedic implants from bacterial challenge, *Nat. Commun.*, 2021, **12**(1), 5473.

81 Z. Li, X. Yang, H. Liu, X. Yang, Y. Shan, X. Xu, S. Shang and Z. Song, Dual-functional antimicrobial coating based on a quaternary ammonium salt from rosin acid with in vitro and *in vivo* antimicrobial and antifouling properties, *Chem. Eng. J.*, 2019, **374**, 564–575.

82 A. M. C. Maan, A. H. Hofman, W. M. de Vos and M. Kamperman, Recent Developments and Practical Feasibility of Polymer-Based Antifouling Coatings, *Adv. Funct. Mater.*, 2020, **30**(32), 2000936.

83 A. I. Stavrakis, S. Zhu, V. Hegde, A. H. Loftin, A. G. Ashbaugh, J. A. Niska, L. S. Miller, T. Segura and N. M. Bernthal, In Vivo Efficacy of a "Smart" Antimicrobial Implant Coating, *J. Bone Jt. Surg.*, 2016, **98**(14), 1183–1189.

84 T. S. Sileika, H.-D. Kim, P. Maniak and P. B. Messersmith, Antibacterial Performance of Polydopamine-Modified Polymer Surfaces Containing Passive and Active Components, *ACS Appl. Mater. Interfaces*, 2011, **3**(12), 4602–4610.

85 B. A. Hall, O. J. Wadsworth, L. M. Breiner, J. C. Chappell, A. S. Brenner, J. P. McCord, A. N. Lowell and M. D. Schulz, Inherent antibacterial properties of mannose-containing polynorbornene glycomaterials, *Chem. Commun.*, 2025, **61**(23), 4539–4542.

86 J. D. Denstedt and P. A. Cadieux, Eliminating biofilm from ureteral stents: the holy grail, *Curr. Opin. Neurol.*, 2009, **19**, 2.

87 J. S. Kim, E. Kuk, K. N. Yu, J.-H. Kim, S. J. Park, H. J. Lee, S. H. Kim, Y. K. Park, Y. H. Park, C.-Y. Hwang, Y.-K. Kim, Y.-S. Lee, D. H. Jeong and M.-H. Cho, Antimicrobial effects of silver nanoparticles, *Nanomedicine*, 2007, **3**(1), 95–101.

88 T. Maneerung, S. Tokura and R. Rujiravanit, Impregnation of silver nanoparticles into bacterial cellulose for antimicrobial wound dressing, *Carbohydr. Polym.*, 2008, **72**(1), 43–51.

89 M. Rai, A. Yadav and A. Gade, Silver nanoparticles as a new generation of antimicrobials, *Biotechnol. Adv.*, 2009, **27**(1), 76–83.

90 D. R. Monteiro, L. F. Gorup, S. Silva, M. Negri, E. R. de Camargo, R. Oliveira, D. B. Barbosa and M. Henriques, Silver colloidal nanoparticles: antifungal effect against adhered cells and biofilms of Candida albicans and Candida glabrata, *Biofouling*, 2011, **27**(7), 711–719.

91 W.-A. Chen, D.-Y. Chang, B.-M. Chen, Y.-C. Lin, Y. Barenholz and S. R. Roffler, Antibodies against Poly(ethylene glycol) Activate Innate Immune Cells and Induce Hypersensitivity Reactions to PEGylated Nanomedicines, *ACS Nano*, 2023, **17**(6), 5757–5772.

92 A. Bianchi, P. Bottau, E. Calamelli, S. Caimmi, G. Crisafulli, F. Franceschini, L. Liotti, F. Mori, C. Paglialunga, F. Saretta, M. Tosca, F. Cardinale, A. Licari, M. Miraglia Del Giudice and C. Caffarelli, Hypersensitivity to polyethylene glycol in adults and children: An emerging challenge, *Acta Biomed.*, 2021, **92**(S7), e2021519.

93 M. Barz, R. Luxenhofer, R. Zentel and M. J. Vicent, Overcoming the PEG-addiction: well-defined alternatives to PEG, from structure–property relationships to better defined therapeutics, *Polym. Chem.*, 2011, **2**(9), 1900–1918.

94 T. T. Hoang Thi, E. H. Pilkington, D. H. Nguyen, J. S. Lee, K. D. Park and N. P. Truong, The Importance of Poly(ethylene glycol) Alternatives for Overcoming PEG Immunogenicity in Drug Delivery and Bioconjugation, *Polymers*, 2020, 298.

95 H. Yang, Y. Wang, L. Yao, J. Wang and H. Chen, Antifouling Polymer Coatings for Bioactive Surfaces, *Langmuir*, 2025, **41**(10), 6471–6496.

96 R. Qiao, C. Fu, Y. Li, X. Qi, D. Ni, A. Nandakumar, G. Siddiqui, H. Wang, Z. Zhang, T. Wu, J. Zhong, S.-Y. Tang, S. Pan, C. Zhang, M. R. Whittaker, J. W. Engle, D. J. Creek, F. Caruso, P. C. Ke, W. Cai, A. K. Whittaker and T. P. Davis, Sulfoxide-Containing Polymer-Coated Nanoparticles Demonstrate Minimal Protein Fouling and Improved Blood Circulation, *Adv. Sci.*, 2020, **7**(13), 2000406.

97 Y. Zhang, M. Hu, R. Xin, X. Xu, Z. Zhang, H. Peng, R. Cai, C. Chen, A. K. Whittaker and C. Fu, Enhanced Hydrophilicity and Antifouling Performance of PEG with Sulfoxide-Containing Side Chains for Nanomedicine Applications, *Polym. Sci. Technol.*, 2025, **1**(7), 640–650.

98 J. Yook, D. Jeong and J.-C. Lee, Synthesis of Citronellol-Derived Antibacterial Polymers and Effect of Thioether, Sulfoxide, Sulfone, and Ether Functional Groups on Their Bactericidal Activity, *Macromolecules*, 2023, **56**(9), 3406–3420.

99 R. H. Pelton and A. Karami, Simulating Polydisperse Polymer Adsorption onto Porous Substrates, *Langmuir*, 2025, **41**(25), 16625–16633.

100 A. S. Imbia, A. Ounkaew, X. Mao, H. Zeng, Y. Liu and R. Narain, Mussel-Inspired Polymer-Based Coating Technology for

100 Antifouling and Antibacterial Properties, *Langmuir*, 2024, **40**(21), 10957–10965.

101 J. Wang, L. Li, Y. Wu and Y. Liu, Design and Application of Antifouling Bio-Coatings, *Polymers*, 2025, 793.

102 C. Doyle and M. Ahmed, Antifouling Coatings Inspired by Biological Templates, *Macromol. Rapid Commun.*, 2025, **46**(12), 2400932.

103 Y. Fu, L. Yang, J. Zhang, J. Hu, G. Duan, X. Liu, Y. Li and Z. Gu, Polydopamine antibacterial materials, *Mater. Horiz.*, 2021, **8**(6), 1618–1633.

104 L. Su, Y. Yu, Y. Zhao, F. Liang and X. Zhang, Strong Antibacterial Polydopamine Coatings Prepared by a Shaking-assisted Method, *Sci. Rep.*, 2016, **6**(1), 24420.

105 N. N. M. Adnan, Z. Sadrearhami, A. Bagheri, T.-K. Nguyen, E. H. H. Wong, K. K. K. Ho, M. Lim, N. Kumar and C. Boyer, Exploiting the Versatility of Polydopamine-Coated Nanoparticles to Deliver Nitric Oxide and Combat Bacterial Biofilm, *Macromol. Rapid Commun.*, 2018, **39**(13), 1800159.

106 G. A. Kropp, H. Q. Karp, J. Rao, H. S. Muller, N. Sriranganathan, E. S. Nowak and M. D. Schulz, Polydopamine-Antibiotic Composite Coating for Antibiofilm Applications, *Macromol. Biosci.*, 2025, e00501.

107 P. Kord Forooshani, E. Polega, K. Thomson, M. S. A. Bhuiyan, R. Pinnaratip, M. Trought, C. Kendrick, Y. Gao, K. A. Perrine, L. Pan and B. P. Lee, Antibacterial Properties of Mussel-Inspired Polydopamine Coatings Prepared by a Simple Two-Step Shaking-Assisted Method, *Front. Chem.*, 2019, 7, 631.

108 B.-B. Wang, Y.-H. Quan, Z.-M. Xu and Q. Zhao, Preparation of highly effective antibacterial coating with polydopamine/chitosan/silver nanoparticles via simple immersion, *Prog. Org. Coat.*, 2020, **149**, 105967.

109 W. Guo, Y. Wu, B. Li, L. Zhao, S. Feng, Y. Wei, C. Liu, Y. Huang, S. Wang, B. Liu, H. Mai, H. You and Y. Long, Silver-loaded polydopamine coating mediated dual-mode antibacterial and biological response for composite scaffolds, *J. Am. Ceram. Soc.*, 2025, **108**(11), e70066.

110 J. Cui, H. Shu, X. Gu, S. Wu, X. Liu and P. Cao, Enhancing antibacterial performance and stability of implant materials through surface modification with polydopamine/silver nanoparticles, *Colloids Surf., B*, 2025, **245**, 114327.

111 H. Zhang, X. Shen, Z. Fei, X. Fan, L. Ma, H. Wang, C. Tian, B. Zhang, R. Luo, Y. Wang and S. Huang, Ag-Incorporated Polydopamine/Tannic Acid Coating on Titanium With Enhanced Cytocompatible and Antibacterial Properties, *Front. Bioeng. Biotechnol.*, 2022, **10**, 877738.

112 Y.-J. Fan, M. T. Pham and C.-J. Huang, Development of Antimicrobial and Antifouling Universal Coating via Rapid Deposition of Polydopamine and Zwitterionization, *Langmuir*, 2019, **35**(5), 1642–1651.

113 Y. Zhang, F. Wang, Q. Huang, A. B. Patil, J. Hu, L. Fan, Y. Yang, H. Duan, X. Dong and C. Lin, Layer-by-layer immobilizing of polydopamine-assisted ε-polylysine and gum Arabic on titanium: Tailoring of antibacterial and osteogenic properties, *Mater. Sci. Eng. C*, 2020, **110**, 110690.

114 S. Lamba, K. Wang, J. Lu, A. R. J. Phillips, S. Swift and V. Sarojini, Polydopamine-Mediated Antimicrobial Lipopeptide Surface Coating for Medical Devices, *ACS Appl. Bio Mater.*, 2024, **7**(11), 7574–7584.

115 Z. Sadrearhami, F. N. Shafiee, K. K. K. Ho, N. Kumar, M. Krasowska, A. Blencowe, E. H. H. Wong and C. Boyer, Antibiofilm Nitric Oxide-Releasing Polydopamine Coatings, *ACS Appl. Mater. Interfaces*, 2019, **11**(7), 7320–7329.

116 J. Mendhi, S. S. Ramachandra, I. Prasadam, S. Ivanovski, Y. Yang and Y. Xiao, Endogenous nitric oxide-generating surfaces via polydopamine-copper coatings for preventing biofilm dispersal and promoting microbial killing, *Mater. Sci. Eng. C*, 2021, **128**, 112297.

117 L. Zhou, X. Li, K. Wang, F. Shen, L. Zhang, P. Li, T. Shang, J. Wang and N. Huang, Cu(‖)-loaded polydopamine coatings with *in situ* nitric oxide generation function for improved hemocompatibility, *Regen. Biomater.*, 2020, **7**(2), 153–160.

118 S. Geng, Q. Fan, K. Lin, F. Mazur and R. Chandrawati, Polydopamine-Coated Selenium Nanoparticles as a Stable Catalyst for Tunable and Sustained Nitric Oxide Generation, *Small Sci.*, 2025, **5**(8), 2500151.

119 J. Li, B. Jiang, L. Yang, P. Zhang, J. Wu, Y. Yang, Y. Yang, G. Wang, J. Chen, L. Zhang, S. Huang, L. Zhang and E. Zhang, Dual-functional titanium implants via polydopamine-mediated lithium and copper co-incorporation: synergistic enhancement of osseointegration and antibacterial efficacy, *Front. Bioeng. Biotechnol.*, 2025, **13**, 1593545.

120 T. Zhang, W. Zhou, Z. Jia, Q. Wei, D. Fan, J. Yan, C. Yin, Y. Cheng, H. Cai, X. Liu, H. Zhou, X. Yang, Y. Zheng and Z. Liu, Polydopamine-assisted functionalization of heparin and vancomycin onto microarc-oxidized 3D printed porous Ti6Al4V for improved hemocompatibility, osteogenic and anti-infection potencies, *Sci. China Mater.*, 2018, **61**(4), 579–592.

121 M. Chen, W. Yu, Q. Shi, H. Wen, G. Li, Y. Wang, T. Wang, S. Liu and T. Yang, Boosting the Anti-Infection Ability of Titanium Implants by Coating Polydopamine–Curcumin, *Coatings*, 2024, 640.

122 A. A. Ali, R. D. Al Bostami and A. Al-Othman, Nanogel-based composites for bacterial antibiofilm activity: advances, challenges, and prospects, *RSC Adv.*, 2024, **14**(15), 10546–10559.

123 D. L. Bordón, E. Herrera, M. Laura González, L. I. Rossi, M. L. Aimar, A. M. Vázquez and A. M. Granados, Catalytic and biocidal activity of silver and gold nanoparticles obtained by green synthesis using aqueous extracts of glossy privet (Ligustrum lucidum) dry fruits, *J. Mol. Liq.*, 2024, **415**, 126378.

124 R. Aguilar-Garay, L. F. Lara-Ortiz, M. Campos-López, D. E. Gonzalez-Rodriguez, M. M. Gamboa-Lugo, J. A. Mendoza-Pérez, Á. Anzueto-Ríos, D. E. Nicolás-Álvarez and A. Comprehensive, Review of Silver and Gold Nanoparticles as Effective Antibacterial Agents, *Pharmaceuticals*, 2024, **17**(9), 1134.

125 A. Balestri, J. Cardellini and D. Berti, Gold and silver nanoparticles as tools to combat multidrug-resistant pathogens, *Curr. Opin. Colloid Interface Sci.*, 2023, **66**, 101710.

126 P. Singh and I. Mijakovic, Green synthesis and antibacterial applications of gold and silver nanoparticles from Ligustrum vulgare berries, *Sci. Rep.*, 2022, **12**(1), 7902.

127 M.-H. Moosavy, M. de la Guardia, A. Mokhtarzadeh, S. A. Khatibi, N. Hosseinzadeh and N. Hajipour, Green synthesis, characterization, and biological evaluation of gold and silver nanoparticles using Mentha spicata essential oil, *Sci. Rep.*, 2023, **13**(1), 7230.

128 N. Abed and P. Couvreur, Nanocarriers for antibiotics: A promising solution to treat intracellular bacterial infections, *Int. J. Antimicrob. Agents*, 2014, **43**(6), 485–496.

129 P. J. Weldrick, M. J. Hardman and V. N. Paunov, Smart active antibiotic nanocarriers with protease surface functionality can overcome biofilms of resistant bacteria, *Mater. Chem. Front.*, 2021, **5**(2), 961–972.

130 G. Prozorova, A. Emel'Yanov, A. Ivanova, T. Semenova, T. Y. Fadeeva, A. Nevezhina, S. Korzhova and A. Pozdnyakov, A novel water-soluble polymer nanocomposite containing ultra-small Fe3O4 nanoparticles with strong antibacterial and antibiofilm activity, *Nanoscale*, 2025, **17**(3), 1458–1472.

131 H. Yazdani-Ahmadabadi, K. Yu, S. Khoddami, D. F. Felix, H. H. Yeh, H. D. Luo, I. Moskalev, Q. Wang, R. Wang, D. Grecov, L. Fazli, D. Lange and J. N. Kizhakkedathu, Robust Nanoparticle-Derived Lubricious Antibiofilm Coating for Difficult-to-Coat Medical Devices with Intricate Geometry, *ACS Nanosci. Au*, 2023, **3**(1), 67–83.

132 V. C. Ibarra, L. O. Vargas-Sanchez, A. Rodríguez-Moreno, N. V. Zavala-Alonso, M. Loredo-Tobias, M. E. García-Arreola and R. Manisekaran, Antibiofilm property of poly(methyl)methacrylate and silver nanocomposite on a mixed population of oral bacteria, *Next Nanotechnol.*, 2025, **8**, 100230.

133 A. S. Takamiya, D. R. Monteiro, L. F. Gorup, E. A. Silva, E. R. de Camargo, J. E. Gomes-Filho, S. H. P. de Oliveira and D. B. Barbosa, Biocompatible silver nanoparticles incorporated in acrylic resin for dental application inhibit Candida albicans biofilm, *Mater. Sci. Eng. C*, 2021, **118**, 111341.

134 L. L. Hamid, R. S. Zakir, N. M. Abdel Rahman, R. H. Idrahim and S. M. Abdel Rahman, Construction and Characterization of Polyethylene Glycol/Sodium Alginate Hydrogel Loaded With Zirconia Nanoparticles: Potential Antibacterial and Antibiofilm Agent to Inhibit Dental Caries In Vitro and *In Vivo*, *Microsc. Res. Tech.*, 2025, **88**(8), 2268–2284.

135 W. Q. Hong, W.-H. Lee, S. H. Musa, N. A. Kamaruzaman and C.-Y. Loo, Evaluation of hydrogel loading with curcumin and silver nanoparticles: biocompatibilities and anti-biofilm activities, *Biometals*, 2025, **38**(2), 663–682.

136 M. Solomon, A. M. Holban, B. Bălăceanu-Gurău, L. M. Ditu, A. Alberts, A. M. Grumezescu, L. S. Manolescu and M. M. Mihai, Silver Nanoparticles Functionalized with Polymeric Substances to Reduce the Growth of Planktonic and Biofilm Opportunistic Pathogens, *Int. J. Mol. Sci.*, 2025, 3930.

137 Z. Chegini, M. Azizi, M. Safaiee, F. Kalhori, R. Zare Shahraki, J. Hemmati, S. M. Hosseini, A. Teimoori, A. Shariati and M. R. Arabestani, Wound healing properties and antibiofilm activity of hydrogel matrix containing nitric oxide, silver nanoparticles, and ciprofloxacin against Pseudomonas aeruginosa burn wound infection, *Sci. Rep.*, 2025, **15**(1), 26508.

138 I. Rahaman, N. Srivastava, D. Thakur, A. Jamwal and L. Kumar, Enhanced Antibiofilm Activity of Copper Nanoparticles Stabilized With Polyvinyl Pyrrolidone and Polyvinyl Alcohol Against Pseudomonas aeruginosa and Staphylococcus aureus, *J. Biomed. Mater. Res., Part B*, 2025, **113**(8), e35633.

139 K. Razdan, V. S. Gondil, S. Chhibber, K. K. Singh and V. R. Sinha, Levofloxacin loaded clove essential oil nanoscale emulsion as an efficient system against Pseudomonas aeruginosa biofilm, *J. Drug Delivery Sci. Technol.*, 2022, **68**, 103039.

140 M. E. El-Naggar, A. M. Abdelgawad, R. Abdel-Sattar, A. A. Gibriel and B. A. Hemdan, Potential antimicrobial and antibiofilm efficacy of essential oil nanoemulsion loaded polycaprolactone nanofibrous dermal patches, *Eur. Polym. J.*, 2023, **184**, 111782.

141 T. Du, Z. Xiao, G. Zhang, L. Wei, J. Cao, Z. Zhang, X. Li, Z. Song, W. Wang, J. Liu, X. Du and S. Wang, An injectable multifunctional hydrogel for eradication of bacterial biofilms and wound healing, *Acta Biomater.*, 2023, **161**, 112–133.

142 L. Yang, F. Teles, W. Gong, S. A. Dua, L. Martin and M. H. Schoenfisch, Antibacterial action of nitric oxide-releasing hyperbranched polymers against ex vivo dental biofilms, *Dent. Mater.*, 2020, **36**(5), 635–644.

143 L. Weng, L. Wu, R. Guo, J. Ye, W. Liang, W. Wu, L. Chen and D. Yang, Lactobacillus cell envelope-coated nanoparticles for antibiotic delivery against cariogenic biofilm and dental caries, *J. Nanobiotechnol.*, 2022, **20**(1), 356.

144 X. Pang, X. Liu, Y. Cheng, C. Zhang, E. Ren, C. Liu, Y. Zhang, J. Zhu, X. Chen and G. Liu, Sono-Immunotherapeutic Nanocapturer to Combat Multidrug-Resistant Bacterial Infections, *Adv. Mater.*, 2019, **31**(35), 1902530.

145 Z. Zhou, F. Hu, S. Hu, M. Kong, C. Feng, Y. Liu, X. Cheng, Q. Ji and X. Chen, pH-Activated nanoparticles with targeting for the treatment of oral plaque biofilm, *J. Mater. Chem. B*, 2018, **6**(4), 586–592.

146 M. Kluzek, Y. Oppenheimer-Shaanan, T. Dadosh, M. I. Morandi, O. Avinoam, C. Raanan, M. Goldsmith, R. Goldberg and J. Klein, Designer Liposomic Nanocarriers Are Effective Biofilm Eradicators, *ACS Nano*, 2022, **16**(10), 15792–15804.

147 J. Cao, Y. Zhao, Y. Liu, S. Tian, C. Zheng, C. Liu, Y. Zhai, Y. An, H. J. Busscher, L. Shi and Y. Liu, Phosphorylcholine-Based Polymer Encapsulated Chitosan Nanoparticles Enhance the Penetration of Antimicrobials in a Staphylococcal Biofilm, *ACS Macro Lett.*, 2019, **8**(6), 651–657.

148 P. Wang, Y. Zeng, J. Liu, L. Wang, M. Yang and J. Zhou, Antimicrobial and anti-biofilm effects of dihydroartemisinin-loaded chitosan nanoparticles against methicillin-resistant Staphylococcus aureus, *Microb. Pathog.*, 2025, **199**, 107208.

149 Y. Tan, S. Ma, M. Leonhard, D. Moser, G. M. Haselmann, J. Wang, D. Eder and B. Schneider-Stickler, Enhancing antibiofilm activity with functional chitosan nanoparticles targeting biofilm cells and biofilm matrix, *Carbohydr. Polym.*, 2018, **200**, 35–42.

150 Z. Huang, T. Zhou, Y. Yuan, S. Natalie Kłodzińska, T. Zheng, C. Sternberg, H. Mørck Nielsen, Y. Sun and F. Wan, Synthesis of carbon quantum dot-poly lactic-*co*-glycolic acid hybrid nanoparticles for chemo-photothermal therapy against bacterial biofilms, *J. Colloid Interface Sci.*, 2020, **577**, 66–74.

151 J. Li, G. Pan, G. V. Zyryanov, Y. Peng, G. Zhang, L. Ma, S. Li, P. Chen and Z. Wang, Positively Charged Semiconductor Conjugated Polymer Nanomaterials with Photothermal Activity for Antibacterial and Antibiofilm Activities In Vitro and *In Vivo*, *ACS Appl. Mater. Interfaces*, 2023, **15**(34), 40864–40876.

152 A. Anjum, P.-Y. Chung and S.-F. Ng, PLGA/xylitol nanoparticles enhance antibiofilm activity via penetration into biofilm extracellular polymeric substances, *RSC Adv.*, 2019, **9**(25), 14198–14208.

153 H. Qiu, Z. Si, Y. Luo, P. Feng, X. Wu, W. Hou, Y. Zhu, M. B. Chan-Park, L. Xu and D. Huang, The Mechanisms and the Applications of Antibacterial Polymers in Surface Modification on Medical Devices, *Front. Bioeng. Biotechnol.*, 2020, **8**, 910.

154 Y. Yang, Z. Cai, Z. Huang, X. Tang and X. Zhang, Antimicrobial cationic polymers: from structural design to functional control, *Polym. J.*, 2018, **50**(1), 33–44.

155 M. Abdollahi, A. Baharian, M. Mohamadhoseini, M. Hassanpour, P. Makvandi, M. Habibizadeh, B. Jafari, R. Nouri, Z. Mohamadnia and N. Nikfarjam, Advances in ionic liquid-based antimicrobial wound healing platforms, *J. Mater. Chem. B*, 2024, **12**(38), 9478–9507.

156 N. Nikfarjam, M. Ghomi, T. Agarwal, M. Hassanpour, E. Sharifi, D. Khorsandi, M. Ali Khan, F. Rossi, A. Rossetti, E. Nazarzadeh Zare, N. Rabiee, D. Afshar, M. Vosough, T. Kumar Maiti, V. Mattoli, E. Lichtfouse, F. R. Tay and P. Makvandi, Antimicrobial Ionic Liquid-Based Materials for Biomedical Applications, *Adv. Funct. Mater.*, 2021, **31**(42), 2104148.

157 Y. Li, X. Ma, J. Zhang, X. Pan, N. Li, G. Chen and J. Zhu, Degradable Selenium-Containing Polymers for Low Cytotoxic Antibacterial Materials, *ACS Macro Lett.*, 2022, **11**(12), 1349–1354.

158 B. Dizman, M. O. Elasri and L. J. Mathias, Synthesis and antimicrobial activities of new water-soluble bis-quaternary ammonium methacrylate polymers, *J. Appl. Polym. Sci.*, 2004, **94**(2), 635–642.

159 P. Salas-Ambrosio, S. Vexler, R. P S, I. A. Chen and H. D. Maynard, Caffeine and Cationic Copolymers with Antimicrobial Properties, *ACS Bio Med Chem Au*, 2023, **3**(2), 189–200.

160 S. N. Hancock, N. Yuntawattana, E. Diep, A. Maity, A. Tran, J. D. Schiffman and Q. Michaudel, Ring-opening metathesis polymerization of N-methylpyridinium-fused norbornenes to access antibacterial main-chain cationic polymers, *Proc. Natl. Acad. Sci. U. S. A.*, 2023, **120**(51), e2311396120.

161 S. Bai, J. Wang, K. Yang, C. Zhou, Y. Xu, J. Song, Y. Gu, Z. Chen, M. Wang, C. Shoen, B. Andrade, M. Cynamon, K. Zhou, H. Wang, Q. Cai, E. Oldfield, S. C. Zimmerman, Y. Bai and X. Feng, A polymeric approach toward resistance-resistant antimicrobial agent with dual-selective mechanisms of action, *Sci. Adva.*, 2021, **7**(5), eabc9917.

162 A. R. Egorov, A. A. Artemjev, V. A. Kozyrev, D. N. Sikaona, V. V. Rubanik, V. V. Rubanik Jr, I. S. Kritchenkov, N. Z. Yagafarov, O. M. Khubiev, T. A. Tereshina, E. K. Kultyshkina, B. Medjbour, V. N. Khrustalev and A. S. Kritchenkov, Synthesis of Selenium-Containing Chitosan Derivatives and Their Antibacterial Activity, *Appl. Biochem. Microbiol.*, 2022, **58**(2), 132–135.

163 A. Dai, W. Wang, X. Heng, W. Shu, S. Lu, Y. Xu, D. Wang, X. Pan, N. Li, G. Chen and J. Zhu, High-Efficiency Bactericidal and Biofilm Elimination Ability of the Biodegradable Alternating Sequence Main-Chain Polyselenium Salt, *ACS Appl. Polym. Mater.*, 2024, **6**(9), 4975–4984.

164 Q. Wang, L.-M. Barnes, K. I. Maslakov, C. A. Howell, M. J. Illsley, P. Dyer and I. N. Savina, In situ synthesis of silver or selenium nanoparticles on cationized cellulose fabrics for antimicrobial application, *Mater. Sci. Eng. C*, 2021, **121**, 111859.

165 T. Huang, J. A. Holden, E. C. Reynolds, D. E. Heath, N. M. O'Brien-Simpson and A. J. O'Connor, Multifunctional Antimicrobial Polypeptide-Selenium Nanoparticles Combat Drug-Resistant Bacteria, *ACS Appl. Mater. Interfaces*, 2020, **12**(50), 55696–55709.

166 C. Peng, A. Vishwakarma, Z. Li, T. Miyoshi, H. A. Barton and A. Joy, Modification of a conventional polyurethane composition provides significant anti-biofilm activity against Escherichia coli, *Polym. Chem.*, 2018, **9**(23), 3195–3198.

167 A. Vishwakarma, F. Dang, A. Ferrell, H. A. Barton and A. Joy, Peptidomimetic Polyurethanes Inhibit Bacterial Biofilm Formation and Disrupt Surface Established Biofilms, *J. Am. Chem. Soc.*, 2021, **143**(25), 9440–9449.

168 R. Gharibi and S. Agarwal, Polyurethanes from Hydrophobic Elastic Materials to Hydrogels with Potent Nonleaching Biocidal and Antibiofilm Activity, *ACS Appl. Polym. Mater.*, 2021, **3**(9), 4695–4707.

169 R. F. Menger, J. J. Beck, T. Borch and C. S. Henry, Colorimetric Paper-Based Analytical Device for Perfluorooctanesulfonate Detection. ACS ES&T, *Water*, 2022, **2**(4), 565–572.

170 A. L. Lewis; J. J. Kohler and M. Aebi, Microbial Lectins: Hemagglutinins, Adhesins, and Toxins, in *Essentials of Glycobiology [Internet]*, ed. A. Varki, R. D. Cummings, J. D. Esko, P. Stanley, G. W. Hart and M. Aebi, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 2022.

171 J. J. Lundquist and E. J. Toone, The Cluster Glycoside Effect, *Chem. Rev.*, 2002, **102**(2), 555–578.

172 Y. C. Lee and R. T. Lee, Carbohydrate-Protein Interactions: Basis of Glycobiology, *Acc. Chem. Res.*, 1995, **28**(8), 321–327.

173 E. van Duijkeren, A.-K. Schink, C. Roberts Marilyn, Y. Wang and S. Schwarz, Mechanisms of Bacterial Resistance to Antimicrobial Agents, *Microbiol. Spectrum*, 2018, **6**(2), DOI: 10.1128/microbiolspec.arba-0019-2017.

174 E. M. Halawa, M. Fadel, M. W. Al-Rabia, A. Behairy, N. A. Nouh, M. Abdo, R. Olga, L. Ferican, A. M. Atwa, M. El-Nablaway and A. Abdeen, Antibiotic action and resistance: updated review of mechanisms, spread, influencing factors, and alternative approaches for combating resistance, *Front. Pharmacol.*, 2023, **14**, 1305294.

175 X. He, X. Sheng, X. Yao, Y. Wang, L. Zhang, H. Wang and L. Yuan, The anti-biofilm effect of α-amylase/glycopolymer-decorated gold nanorods, *Colloids Surf., B*, 2025, **246**, 114393.

176 X. Chen, B. Wu, H. A. Perera and M. Yan, Synthesis of Glycopolymer Micelles for Antibiotic Delivery, *Molecules*, 2023, **28**, 10.

177 C. A. Werlang, J. K. Sahoo, G. Cárcarmo-Oyarce, C. Stevens, D. Uzun, R. Putnik, O. Hasturk, J. Choi, D. L. Kaplan and K. Ribbeck, Selective Biofilm Inhibition through Mucin-Inspired Engineering of Silk Glycopolymers, *J. Am. Chem. Soc.*, 2024, **146**(50), 34661–34668.

178 L. L. Kiessling; T. Young; T. D. Gruber and K. H. Mortell, *Multivalency in Protein–Carbohydrate Recognition*, Springer Berlin Heidelberg, 2008, pp. 2483–2523.

179 H. M. Branderhorst, R. Ruijtenbeek, R. M. J. Liskamp and R. J. Pieters, Multivalent Carbohydrate Recognition on a Glycodendrimer-Functionalized Flow-Through Chip, *ChemBioChem*, 2008, **9**(11), 1836–1844.

180 M. R. Thalji, A. A. Ibrahim, K. F. Chong, A. V. Soldatov and G. A. M. Ali, Glycopolymer-Based Materials: Synthesis, Properties, and Biosensing Applications, *Top Curr. Chem.*, 2022, **380**(5), 45.

181 R. Mei, X. Heng, X. Liu and G. Chen, Glycopolymers for Antibacterial and Antiviral Applications, *Molecules*, 2023, **28**, 3.

182 D. J. Wurpel, S. A. Beatson, M. Totsika, N. K. Petty and M. A. Schembri, Chaperone-Usher Fimbriae of Escherichia coli, *PLoS One*, 2013, **8**(1), e52835.

183 R. Mei, X. Heng, X. Liu and G. Chen, Glycopolymers for Antibacterial and Antiviral Applications, *Molecules*, 2023, 985.

184 Y. Miura, Y. Hoshino and H. Seto, Glycopolymer Nanobiotechnology, *Chem. Rev.*, 2016, **116**(4), 1673–1692.

185 U. I. M. Gerling-Driessen, M. Hoffmann, S. Schmidt, N. L. Snyder and L. Hartmann, Glycopolymers against pathogen infection, *Chem. Soc. Rev.*, 2023, **52**(8), 2617–2642.

186 C. A. Werlang, W. G. Chen, K. Aoki, K. M. Wheeler, C. Tymm, C. J. Mileti, A. C. Burgos, K. Kim, M. Tiemeyer and K. Ribbeck, Mucin O-glycans suppress quorum-sensing pathways and genetic transformation in Streptococcus mutans, *Nat. Microbiol.*, 2021, **6**(5), 574–583.

187 B. X. Wang, K. M. Wheeler, K. C. Cady, S. Lehoux, R. D. Cummings, M. T. Laub and K. Ribbeck, Mucin Glycans Signal through the Sensor Kinase RetS to Inhibit Virulence-Associated Traits in Pseudomonas aeruginosa, *Curr. Biol.*, 2021, **31**(1), 90–102.e7.

188 L. Kavanaugh Nicole, Q. Zhang Angela, J. Nobile Clarissa, D. Johnson Alexander and K. Ribbeck, Mucins Suppress Virulence Traits of Candida albicans, *mBio*, 2014, **5**(6), e01911-14, DOI: 10.1128/mbio.01911-14.

189 M. Caldara, R. S. Friedlander, N. L. Kavanaugh, J. Aizenberg, K. R. Foster and K. Ribbeck, Mucin biopolymers prevent bacterial aggregation by retaining cells in the free-swimming state, *Curr. Biol.*, 2012, **22**(24), 2325–2330.

190 E. S. Frenkel and K. Ribbeck, Salivary mucins protect surfaces from colonization by cariogenic bacteria, *Appl. Environ. Microbiol.*, 2015, **81**(1), 332–338.

191 C. A. Werlang, W. G. Chen, K. Aoki, K. M. Wheeler, C. Tymm, C. J. Mileti, A. C. Burgos, K. Kim, M. Tiemeyer and K. Ribbeck, Mucin O-glycans suppress quorum-sensing pathways and genetic transformation in Streptococcus mutans, *Nat. Microbiol.*, 2021, **6**(5), 574–583.

192 C. Ligeour, O. Vidal, L. Dupin, F. Casoni, E. Gillon, A. Meyer, S. Vidal, G. Vergoten, J.-M. Lacroix, E. Souteyrand, A. Imberty, J.-J. Vasseur, Y. Chevolot and F. Morvan, Mannose-centered aromatic galactoclusters inhibit the biofilm formation of Pseudomonas aeruginosa, *Org. Biomol. Chem.*, 2015, **13**(31), 8433–8444.

193 E. M. V. Johansson, S. A. Crusz, E. Kolomiets, L. Buts, R. U. Kadam, M. Cacciarini, K.-M. Bartels, S. P. Diggle, M. Cámara, P. Williams, R. Loris, C. Nativi, F. Rosenau, K.-E. Jaeger, T. Darbre and J.-L. Reymond, Inhibition and Dispersion of Pseudomonas aeruginosa Biofilms by Glycopeptide Dendrimers Targeting the Fucose-Specific Lectin LecB, *Chem. Biol.*, 2008, **15**(12), 1249–1257.

194 R. U. Kadam, M. Bergmann, M. Hurley, D. Garg, M. Cacciarini, M. A. Swiderska, C. Nativi, M. Sattler, A. R. Smyth, P. Williams, M. Cámara, A. Stocker, T. Darbre and J. L. Reymond, A glycopeptide dendrimer inhibitor of the galactose-specific lectin LecA and of Pseudomonas aeruginosa biofilms, *Angew. Chem., Int. Ed.*, 2011, **50**(45), 10631–10635.

195 E. Kolomiets, E. M. V. Johansson, O. Renaudet, T. Darbre and J.-L. Reymond, Neoglycopeptide Dendrimer Libraries as a Source of Lectin Binding Ligands, *Org. Lett.*, 2007, **9**(8), 1465–1468.

196 E. L. Dane, A. E. Ballok, G. A. O'Toole and M. W. Grinstaff, Synthesis of bioinspired carbohydrate amphiphiles that promote and inhibit biofilms, *Chem. Sci.*, 2014, **5**(2), 551–557.

197 K. S. Bücher, N. Babic, T. Freichel, F. Kovacic and L. Hartmann, Monodisperse Sequence-Controlled α-l-Fucosylated Glycooligomers and Their Multivalent Inhibitory Effects on LecB, *Macromol. Biosci.*, 2018, **18**(12), 1800337.

198 M. Liu, J. Li and B. Li, Mannose-Modified Polyethylenimine: A Specific and Effective Antibacterial Agent against Escherichia coli, *Langmuir*, 2018, **34**(4), 1574–1580.

199 M. Alvarez-Paino, A. Muñoz-Bonilla, F. López-Fabal, J. L. Gómez-Garcés, J. P. A. Heuts and M. Fernández-García, Effect of glycounits on the antimicrobial properties and toxicity behavior of polymers based on quaternized DMAEMA, *Biomacromolecules*, 2015, **16**(1), 295–303.

200 P. Sahariah, F. Papi, K. L. Merz, O. E. Sigurjonsson, R. L. Meyer and C. Nativi, Chitosan–saccharide conjugates for eradication of Pseudomonas aeruginosa biofilms, *RSC Appl. Polym.*, 2024, **2**(3), 461–472.

201 K. Zhang, Y. Du, Z. Si, Y. Liu, M. E. Turvey, C. Raju, D. Keogh, L. Ruan, S. L. Jothy, S. Reghu, K. Marimuthu, P. P. De, O. T. Ng, J. R. Mediavilla, B. N. Kreiswirth, Y. R. Chi, J. Ren, K. C. Tam, X.-W. Liu, H. Duan, Y. Zhu, Y. Mu, P. T. Hammond, G. C. Bazan, K. Pethe and M. B. Chan-Park, Enantiomeric glycosylated cationic block co-beta-peptides eradicate Staphylococcus aureus biofilms and antibiotic-tolerant persisters, *Nat. Commun.*, 2019, **10**(1), 4792.

202 K. Zhang, C. Raju, W. Zhong, K. Pethe, A. Gründling and M. B. Chan-Park, Cationic Glycosylated Block Co-β-peptide Acts on the Cell Wall of Gram-positive Bacteria as Anti-biofilm Agents, *ACS Appl. Bio Mater.*, 2021, **4**(5), 3749–3761.

203 X. Dai, X. Chen, Y. Zhao, Y. Yu, X. Wei, X. Zhang, C. Li and A. Water-Soluble Galactose-Decorated, Cationic Photodynamic Therapy Agent Based on BODIPY to Selectively Eliminate Biofilm, *Biomacromolecules*, 2018, **19**(1), 141–149.

204 R. Toy, P. Pradhan, V. Ramesh, N. C. Di Paolo, B. Lash, J. Liu, E. L. Blanchard, C. J. Pinelli, P. J. Santangelo, D. M. Shayakhmetov and K. Roy, Modification of primary amines to higher order amines reduces *in vivo* hematological and immunotoxicity of cationic nanocarriers through TLR4 and complement pathways, *Biomaterials*, 2019, **225**, 119512.

205 A. M. Weiss, M. A. Lopez, I. I. Rawe, B. W. Manna, S. Chen, Q. Mulder, E. J. Rowan and S. J. Esser-Kahn, A. P., Understanding How Cationic Polymers' Properties Inform Toxic or Immunogenic Responses via Parametric Analysis, *Macromolecules*, 2023, **56**(18), 7286–7299.

206 D. Kamath and S. H. Bossmann, Advances in glyconanotechnology based biomedical applications, *J. Cancer Biol.*, 2025, **6**(1), 4–9.

207 X. Wei, Y. Gao, Y. Hu, Y. Zhang and X. Zhang, A light-activated nanotherapeutic with broad-spectrum bacterial recognition to

eliminate drug-resistant pathogens, *J. Mater. Chem. B*, 2021, **9**(5), 1364–1369.

208 A. El Riz, A. Tchoumi Neree, L. Mousavifar, R. Roy, Y. Chorfi and M. A. Mateescu, Metallo-Glycodendrimeric Materials against Enterotoxigenic Escherichia coli, *Microorganisms*, 2024, 966.

209 X. He, X. Sheng, X. Yao, Y. Wang, L. Zhang, H. Wang and L. Yuan, The anti-biofilm effect of α-amylase/glycopolymer-decorated gold nanorods, *Colloids Surf., B*, 2025, **246**, 114393.

210 Q. Guo, Y. Zhao, X. Dai, T. Zhang, Y. Yu, X. Zhang and C. Li, Functional Silver Nanocomposites as Broad-Spectrum Antimicrobial and Biofilm-Disrupting Agents, *ACS Appl. Mater. Interfaces*, 2017, **9**(20), 16834–16847.

211 Y. Zhao, Q. Guo, X. Dai, X. Wei, Y. Yu, X. Chen, C. Li, Z. Cao, X. Zhang and A. Biomimetic Non-Antibiotic, Approach to Eradicate Drug-Resistant Infections, *Adv. Mater.*, 2019, **31**(7), 1806024.

212 H. Wei, C. Yang, F. Bi, B. Li, R. Xie, D. Yu, S. Fang, Z. Hua, Q. Wang and G. Yang, Structure-Controllable and Mass-Produced Glycopolymersomes as a Template of the Carbohydrate@Ag Nanobiohybrid with Inherent Antibacteria and Biofilm Eradication, *Biomacromolecules*, 2024, **25**(1), 315–327.

213 D. Boffoli, F. Bellato, G. Avancini, P. Gurnani, G. Yilmaz, M. Romero, S. Robertson, F. Moret, F. Sandrelli, P. Caliceti, S. Salmaso, M. Cámara, G. Mantovani and F. Mastrotto, Tobramycin-loaded complexes to prevent and disrupt Pseudomonas aeruginosa biofilms, *Drug Delivery Transl. Res.*, 2022, **12**(8), 1788–1810.

214 Z. Ma, J. Li, Y. Bai, Y. Zhang, H. Sun and X. Zhang, A bacterial infection-microenvironment activated nanoplatform based on spiropyran-conjugated glycoclusters for imaging and eliminating of the biofilm, *Chem. Eng. J.*, 2020, **399**, 125787.

215 W. Wang, Y. Hu, Z. Chen, L. Yu, S. Huang, Y. Zhang, J. Li, Y. Xue, A. Li, Y. Wang, Z. Wu and X. Zhang, Guanidine and Galactose Decorated Nanophotosensitizer with Oxygen Self-Sufficient Capability for the Localized Ablation of Oral Biofilm, *Adv. Funct. Mater.*, 2023, **33**(37), 2300474.

216 Y. Zhao, Z. Lu, X. Dai, X. Wei, Y. Yu, X. Chen, X. Zhang and C. Li, Glycomimetic-Conjugated Photosensitizer for Specific Pseudomonas aeruginosa Recognition and Targeted Photodynamic Therapy, *Bioconjugate Chem.*, 2018, **29**(9), 3222–3230.

217 J. Tricomi, M. Cacaci, G. Biagiotti, L. Caselli, L. Niccoli, R. Torelli, A. Gabbani, M. Di Vito, F. Pineider, M. Severi, M. Sanguinetti, E. Menna, M. Lelli, D. Berti, S. Cicchi, F. Bugli and B. Richichi, Ball milled glyco-graphene oxide conjugates markedly disrupted Pseudomonas aeruginosa biofilms, *Nanoscale*, 2022, **14**(28), 10190–10199.

218 S. Medici, M. Peana, A. Pelucelli and M. A. Zoroddu, An updated overview on metal nanoparticles toxicity, *Semin. Cancer Biol.*, 2021, **76**, 17–26.

219 Z. Ferdous and A. Nemmar, Health Impact of Silver Nanoparticles: A Review of the Biodistribution and Toxicity Following Various Routes of Exposure, *Int. J. Mol. Sci.*, 2020, 2375.

220 R. Kumar, A. Kumar, S. Bhardwaj, M. Sikarwar, S. Sriwastaw, G. Sharma and M. Gupta, Nanotoxicity unveiled: Evaluating exposure risks and assessing the impact of nanoparticles on human health, *J. Trace Element Miner.*, 2025, **13**, 100252.

221 P. Narayanaswamy Vidya, P. Duncan Andrew, J. LiPuma John, P. Wiesmann William, M. Baker Shenda and M. Townsend Stacy, In Vitro Activity of a Novel Glycopolymer against Biofilms of Burkholderia cepacia Complex Cystic Fibrosis Clinical Isolates, *Antimicrob. Agents Chemother.*, 2019, **63**(6), e00498-19, DOI: 10.1128/aac.00498-19.

222 V. P. Narayanaswamy, S. M. Townsend, A. J. Loughran, W. Wiesmann and S. Baker, Polycationic Glycopolymer Demonstrates Activity Against Persisters and Biofilms of Non-tuberculosis Mycobacteria Cystic Fibrosis Clinical Isolates in vitro, *Front. Microbiol.*, 2022, **13**, 821820.

223 B. A. Garcia, M. S. McDaniel, A. J. Loughran, J. D. Johns, V. Narayanaswamy, C. Fernandez Petty, S. E. Birket, S. M. Baker, R. Barnaby, B. A. Stanton, J. B. Foote, S. M. Rowe and W. E. Swords, Poly(acetyl, arginyl) glucosamine disrupts Pseudomonas aeruginosa biofilms and enhances bacterial clearance in a rat lung infection model, *Microbiology*, 2022, **168**, 1.

224 V. P. Narayanaswamy, L. L. Keagy, K. Duris, W. Wiesmann, A. J. Loughran, S. M. Townsend and S. Baker, Novel Glycopolymer

225 D. Boffoli, F. Bellato, G. Avancini, P. Gurnani, G. Yilmaz, M. Romero, S. Robertson, F. Moret, F. Sandrelli, P. Caliceti, S. Salmaso, M. Cámara, G. Mantovani and F. Mastrotto, Tobramycin-loaded complexes to prevent and disrupt Pseudomonas aeruginosa biofilms, *Drug Delivery Transl. Res.*, 2022, **12**(8), 1788–1810.

226 W. Wang, Y. Hu, Z. Chen, L. Yu, S. Huang, Y. Zhang, J. Li, Y. Xue, A. Li, Y. Wang, Z. Wu and X. Zhang, Guanidine and Galactose Decorated Nanophotosensitizer with Oxygen Self-Sufficient Capability for the Localized Ablation of Oral Biofilm, *Adv. Funct. Mater.*, 2023, 33.

227 Y. Zhao, Z. Lu, X. Dai, X. Wei, Y. Yu, X. Chen, X. Zhang and C. Li, Glycomimetic-Conjugated Photosensitizer for Specific Pseudomonas aeruginosa Recognition and Targeted Photodynamic Therapy, *Bioconjugate Chem.*, 2018, **29**(9), 3222–3230.

228 K. S. Bücher, N. Babic, T. Freichel, F. Kovacic and L. Hartmann, Monodisperse Sequence-Controlled α-l-Fucosylated Glycooligomers and Their Multivalent Inhibitory Effects on LecB, *Macromol. Biosci.*, 2018, **18**(12), e1800337.

229 K. Zhang, Y. Du, Z. Si, Y. Liu, M. E. Turvey, C. Raju, D. Keogh, L. Ruan, S. L. Jothy, S. Reghu, K. Marimuthu, P. P. De, O. T. Ng, J. R. Mediavilla, B. N. Kreiswirth, Y. R. Chi, J. Ren, K. C. Tam, X. W. Liu, H. Duan, Y. Zhu, Y. Mu, P. T. Hammond, G. C. Bazan, K. Pethe and M. B. Chan-Park, Enantiomeric glycosylated cationic block co-beta-peptides eradicate Staphylococcus aureus biofilms and antibiotic-tolerant persisters, *Nat. Commun.*, 2019, **10**(1), 4792.

230 K. Zhang, C. Raju, W. Zhong, K. Pethe, A. Gründling and M. B. Chan-Park, Cationic Glycosylated Block Co-β-peptide Acts on the Cell Wall of Gram-positive Bacteria as Anti-biofilm Agents, *ACS Appl. Bio Mater.*, 2021, **4**(5), 3749–3761.

231 M. Naghavi, S. E. Vollset, K. S. Ikuta, L. R. Swetschinski, A. P. Gray, E. E. Wool, G. Robles Aguilar, T. Mestrovic, G. Smith, C. Han, R. L. Hsu, J. Chalek, D. T. Araki, E. Chung, C. Raggi, A. Gershberg Hayoon, N. Davis Weaver, P. A. Lindstedt, A. E. Smith, U. Altay, N. V. Bhattacharjee, K. Giannakis, F. Fell, B. McManigal, N. Ekapirat, J. A. Mendes, T. Runghien, O. Srimokla, A. Abdelkader, S. Abd-Elsalam, R. G. Aboagye, H. Abolhassani, H. Abualruz, U. Abubakar, H. J. Abukhadijah, S. Aburuz, A. Abu-Zaid, S. Achalapong, I. Y. Addo, V. Adekanmbi, T. E. Adeyeoluwa, Q. E. S. Adnani, L. A. Adzigbli, M. S. Afzal, S. Afzal, A. Agodi, A. J. Ahlstrom, A. Ahmad, S. Ahmad, T. Ahmad, A. Ahmadi, A. Ahmed, H. Ahmed, I. Ahmed, M. Ahmed, S. Ahmed, S. A. Ahmed, M. A. Akkaif, S. Al Awaidy, Y. Al Thaher, S. O. Alalalmeh, M. T. AlBataineh, W. A. Aldhaleei, A. A. S. Al-Gheethi, N. B. Alhaji, A. Ali, L. Ali, S. S. Ali, W. Ali, K. Allel, S. Al-Marwani, A. Alrawashdeh, A. Altaf, A. B. Al-Tammemi, J. A. Al-Tawfiq, K. H. Alzoubi, W. A. Al-Zyoud, B. Amos, J. H. Amuasi, R. Ancuceanu, J. R. Andrews, A. Anil, I. A. Anuoluwa, S. Anvari, A. E. Anyasodor, G. L. C. Apostol, J. Arabloo, M. Arafat, A. Y. Aravkin, D. Areda, A. Aremu, A. A. Artamonov, E. A. Ashley, M. O. Asika, S. S. Athari, M. M. W. Atout, T. Awoke, S. Azadnajafabad, J. M. Azam, S. Aziz, A. Y. Azzam, M. Babaei, F.-X. Babin, M. Badar, A. A. Baig, M. Bajcetic, S. Baker, M. Bardhan, H. J. Barqawi, Z. Basharat, A. Basiru, M. Bastard, S. Basu, N. S. Bayleyegn, M. A. Belete, O. O. Bello, A. Beloukas, J. A. Berkley, A. S. Bhagavathula, S. Bhaskar, S. S. Bhuyan, J. A. Bielicki, N. I. Briko, C. S. Brown, A. J. Browne, D. Buonsenso, Y. Bustanji, C. G. Carvalheiro, C. A. Castañeda-Orjuela, M. Cenderadewi, J. Chadwick, S. Chakraborty, R. M. Chandika, S. Chandy, V. Chansamouth, V. K. Chattu, A. A. Chaudhary, P. R. Ching, H. Chopra, F. R. Chowdhury, D.-T. Chu, M. Chutiyami, N. Cruz-Martins, A. G. da Silva, O. Dadras, X. Dai, S. D. Darcho, S. Das, F. P. De la Hoz, D. M. Dekker, D. Diaz, B. F. R. Dickson, S. G. Djorie, M. Dodangeh, S. Dohare, K. G. Dokova, O. P. Doshi, R. K. Dowou, H. L. Dsouza, S. J. Dunachie, A. M. Dziedzic, T. Eckmanns, A. Ed-Dra, A. Eftekharimehrabad, T. C. Ekundayo, I. El Sayed, M. Elhadi, W. El-Huneidi, C. Elias, S. J. Ellis, R. Elsheikh, I. Elsohaby, C. Eltaha, B. Eshrati, M. Eslami, D. W. Eyre, A. O. Fadaka, A. F. Fagbamigbe, A. Fahim, A. Fakhri-Demeshghieh, F. O. Fasina, M. M. Fasina, A. Fatehizadeh, N. A. Feasey, A. Feizkhah, G. Fekadu, F. Fischer, I. Fitriana, K. M. Forrest, C. Fortuna Rodrigues, J. E. Fuller, M. A. Gadanya, M. Gajdács, A. P. Gandhi, E. E. Garcia-Gallo, D. O. Garrett, R. K. Gautam, M. W. Gebregergis, M. Gebrehiwot, T. G. Gebremeskel, C. Geffers, L. Georgalis, R. M. Ghazy,

M. Golechha, D. Golinelli, M. Gordon, S. Gulati, R. D. Gupta, S. Gupta, V. K. Gupta, A. D. Habteyohannes, S. Haller, H. Harapan, M. L. Harrison, A. I. Hasaballah, I. Hasan, R. S. Hasan, H. Hasani, A. H. Haselbeck, M. S. Hasnain, I. I. Hassan, S. Hassan, M. S. Hassan Zadeh Tabatabaei, K. Hayat, J. He, O. E. Hegazi, M. Heidari, K. Hezam, R. Holla, M. Holm, H. Hopkins, M. M. Hossain, M. Hosseinzadeh, S. Hostiuc, N. R. Hussein, L. D. Huy, E. D. Ibáñez-Prada, A. Ikiroma, I. M. Ilic, S. M. S. Islam, F. Ismail, N. E. Ismail, C. D. Iwu, C. J. Iwu-Jaja, A. Jafarzadeh, F. Jaiteh, R. Jalilzadeh Yengejeh, R. D. G. Jamora, J. Javidnia, T. Jawaid, A. W. J. Jenney, H. J. Jeon, M. Jokar, N. Jomehzadeh, T. Joo, N. Joseph, Z. Kamal, K. K. Kanmodi, R. S. Kantar, J. A. Kapisi, I. M. Karaye, Y. S. Khader, H. Khajuria, N. Khalid, F. Khamesipour, A. Khan, M. J. Khan, M. T. Khan, V. Khanal, F. F. Khidri, J. Khubchandani, S. Khusuwan, M. S. Kim, A. Kisa, V. A. Korshunov, F. Krapp, R. Krumkamp, M. Kuddus, M. Kulimbet, D. Kumar, E. A. P. Kumaran, A. Kuttikkattu, H. H. Kyu, I. Landires, B. K. Lawal, T. T. T. Le, I. M. Lederer, M. Lee, S. W. Lee, A. Lepape, T. L. Lerango, V. S. Ligade, C. Lim, S. S. Lim, L. W. Limenh, C. Liu, X. Liu, X. Liu, M. J. Loftus, M. H. I. Amin, K. L. Maass, S. B. Maharaj, M. A. Mahmoud, P. Maikanti-Charalampous, O. M. Makram, K. Malhotra, A. A. Malik, A. Malik, F. Marks, B. A. Martinez-Guerra, M. Martorell, H. Masoumi-Asl, A. G. Mathioudakis, J. May, T. A. McHugh, J. Meiring, H. N. Meles, A. Melese, E. B. Melese, G. Minervini, N. S. Mohamed, S. Mohammed, S. Mohan, A. H. Mokdad, L. Monasta, A. Moodi Ghalibaf, C. E. Moore, Y. Moradi, E. Mossialos, V. Mougin, G. D. Mukoro, F. Mulita, B. Muller-Pebody, E. Murillo-Zamora, S. Musa, P. Musicha, L. A. Musila, S. Muthupandian, A. J. Nagarajan, P. Naghavi, F. Nainu, T. S. Nair, H. H. R. Najmuldeen, Z. S. Natto, J. Nauman, B. P. Nayak, G. T. Nchanji, P. Ndishimye, I. Negoi, R. I. Negoi, S. A. Nejadghaderi, Q. P. Nguyen, E. A. Noman, D. C. Nwakanma, S. O'Brien, T. J. Ochoa, I. A. Odetokun, O. A. Ogundijo, T. R. Ojo-Akosile, S. R. Okeke, O. C. Okonji, A. T. Olagunju, A. Olivas-Martinez, A. A. Olorukooba, P. Olwoch, K. I. Onyedibe, E. Ortiz-Brizuela, O. Osuolale, P. Ounchanum, O. T. Oyeyemi, M. P. A. Padukudru, R. R. Parikh, J. Patel, S. Patil, S. Pawar, A. Y. Peleg, P. Peprah, J. Perdigão, C. Perrone, I.-R. Petcu, K. Phommasone, Z. Z. Piracha, D. Poddighe, A. J. Pollard, R. Poluru, A. Ponce-De-Leon, J. Puvvula, F. N. Qamar, N. H. Qasim, C. D. Rafai, P. Raghav, L. Rahbarnia, F. Rahim, V. Rahimi-Movaghar, M. Rahman, M. A. Rahman, H. Ramadan, S. K. Ramasamy, P. S. Ramesh, P. W. Ramteke, R. K. Rana, U. Rani, M.-M. Rashidi, D. Rathish, S. Rattanavong, S. Rawaf, E. M. M. Redwan, L. F. Reyes, T. Roberts, J. V. Robotham, V. D. Rosenthal, A. G. Ross, N. Roy, K. E. Rudd, C. J. Sabet, B. A. Saddik, M. R. Saeb, U. Saeed, S. Saeedi Moghaddam, W. Saengchan, M. Safaei, A. Saghazadeh, N. Saheb Sharif-Askari, A. Sahebkar, S. S. Sahoo, M. Sahu, M. Saki, N. Salam, Z. Saleem, M. A. Saleh, Y. L. Samodra, A. M. Samy, A. Saravanan, M. Satpathy, A. E. Schumacher, M. Sedighi, S. Seekaew, M. Shafie, P. A. Shah, S. Shahid, M. J. Shahwan, M. Shakoor, N. Shalev, M. A. Shamim, M. A. Shamshirgaran, A. Shamsi, A. Sharifan, R. P. Shastry, M. Shetty, A. Shittu, S. Shrestha, E. E. Siddig, T. Sideroglou, J. Sifuentes-Osornio, L. M. L. R. Silva, E. A. F. Simões, A. J. H. Simpson, A. Singh, S. Singh, R. Sinto, S. S. M. Soliman, S. Soraneh, N. Stoesser, T. Z. Stoeva, C. K. Swain, L. Szarpak, S. Tabatabai, S. S. T Y, Z. M.-A. Taha, K.-K. Tan, N. Tasak, N. Y. Tat, A. Thaiprakong, P. Thangaraju, C. C. Tigoi, K. Tiwari, M. R. Tovani-Palone, T. H. Tran, M. Tumurkhuu, P. Turner, A. J. Udoakang, A. Udoh, N. Ullah, S. Ullah, A. G. Vaithinathan, M. Valenti, T. Vos, H. T. L. Vu, Y. Waheed, A. S. Walker, J. L. Walson, T. Wangrangsimakul, K. G. Weerakoon, H. F. L. Wertheim, P. C. M. Williams, A. A. Wolde, T. M. Wozniak, Z. Wu, M. K. K. Yadav, S. Yaghoubi, Z. S. Yahaya, A. Yarahmadi, S. Yezli, Y. E. Yismaw, D. K. Yon, C.-W. Yuan, H. Yusuf, F. Zakham, G. Zamagni, H. Zhang, Z.-J. Zhang, M. Zielińska, A. Zumla, S. e H. H. Zyoud, S. H. Zyoud, S. I. Hay, A. Stergachis, B. Sartorius, B. S. Cooper, C. Dolecek and C. J. L. Murray, Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050, *Lancet*, 2024, **404**(10459), 1199–1226.

232 C. R. MacNair, S. T. Rutherford and M.-W. Tan, Alternative therapeutic strategies to treat antibiotic-resistant pathogens, *Nat. Rev. Microbiol.*, 2024, **22**(5), 262–275.

233 B. Plackett, Why big pharma has abandoned antibiotics, *Nature*, 2020, **586**(7830), S50–S52.

234 G. A. Durand, D. Raoult and G. Dubourg, Antibiotic discovery: history, methods and perspectives, *Int. J. Antimicrob. Agents*, 2019, **53**(4), 371–382.

235 R. I. Aminov, A brief history of the antibiotic era: lessons learned and challenges for the future, *Front. Microbiol.*, 2010, **1**, 134.

236 Centers for Diseases Control and Prevention, *Antibiotic Resistance Threats in the United States, 2019*, U.S. Department of Health and Human Services, Atlanta, GA, 2019.

237 P. Feuerstadt, N. Theriault and G. Tillotson, The burden of CDI in the United States: a multifactorial challenge, *BMC Infect. Dis.*, 2023, **23**(1), 132.

238 N. Shehab, P. R. Patel, A. Srinivasan and D. S. Budnitz, Emergency department visits for antibiotic-associated adverse events, *Clin. Infect. Dis.*, 2008, **47**(6), 735–743.

239 J. Curran, J. Lo, V. Leung, K. Brown, K. L. Schwartz, N. Daneman, G. Garber, J. H. C. Wu and B. J. Langford, Estimating daily antibiotic harms: an umbrella review with individual study meta-analysis, *Clin. Microbiol. Infect.*, 2022, **28**(4), 479–490.

240 J. S. VanEpps and J. G. Younger, Implantable Device-Related Infection, *Shock*, 2016, **46**(6), 597–608.

241 M. Kuder, A. Gelman and J. M. Zenilman, Prevalence of Implanted Medical Devices in Medicine Inpatients, *J. Patient Saf.*, 2018, **14**(3), 153–156.

242 R. O. Darouiche, Treatment of infections associated with surgical implants, *N. Engl. J. Med.*, 2004, **350**(14), 1422–1429.

243 A. Ramos-Martínez, F. Domínguez, P. Muñoz, M. Marín, Á. Pedraz, M. C. Fariñas, V. Tascón, A. De Alarcón, R. Rodríguez-García, J. M. Miró, J. Goikoetxea, G. Ojeda-Burgos, F. Escrihuela-Vidal and J. Calderón-Parra, Clinical presentation, microbiology, and prognostic factors of prosthetic valve endocarditis. Lessons learned from a large prospective registry, *PLoS One*, 2023, **18**(9), e0290998.

244 R. Patel, Periprosthetic Joint Infection, *N. Engl. J. Med.*, 2023, **388**(3), 251–262.