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BIOFILM CONTROL STRATEGIES IN MEDICAL AND INDUSTRIAL SETTINGS, PLUS SYNTHETIC BIOLOGY FOR NOVEL BIOMATERIALS, BRIDGE MICRO AND MACRO APPLICATION

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Biofilm control strategies in medical and industrial settings, plus synthetic biology for novel biomaterials, bridge micro and macro application

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Abstract:

Biofilms are microbial communities (bacteria) that exist encased within a layer of extracellular polymeric material. To date, biofilms present significant challenges to both the medical and industrial sectors because of their ability to resist the effects of antibacterial methods and mechanical removal. In addition, biofilms have also been found to provide benefits in certain processes, such as fermentation and the treatment of water. This manuscript reviews the various strategies for controlling biofilms in both medical and industrial applications, specifically addressing surface modification, disruption of the biofilm via enzymatic degradation, disruption of quorum sensing, and the potentials offered by bacteriophage therapies. Specific examples of these strategies are provided within the context of traditional medical applications (coated catheters and wound dressings) and within the context of industrial applications (clean-in-place systems, biocides, anti-fouling coatings for food processing, oil pipelines and marine structures). By utilizing synthetic biology, we provide an overview of engineered microbial consortia (including the use of genetic circuitry in Escherichia coli and Pseudomonas aeruginosa to create on-demand quorum-quenching enzymes (E.g., AiiA lactonases), as well as CRISPR-edited strains to produce pH-responsive anti-adhesive nanofilms and derivatives of dispersin B, which can be delivered through hydrogels or biomarker-responsive surface coatings) that link micro-scale cellular phenomena involving quorum sensing networks and biofilm matrix production to macro-scale functionality through the use of hierarchical three-dimensional (3D) bioprinting techniques and self-assembling lattices. These innovations appear to produce a 70-99% reduction in biofilms, a substantial increase in the scalability and efficiency of fermentation processes, and a greatly improved environmental profile compared to traditional biocides. Therefore, while numerous regulatory and stability barriers exist, synthetic biology represents a new era of adaptive biomaterials that may reduce infection rates by 50%, limit multibillion-dollar industrial losses, and jumpstart sustainable bio-economies by 2035.

Keywords: Biofilms, Industrial- medical applications, Anti- adhesive films, AiiA lactonase, Matrix dispersal CRISPR strains, QS Quenching.

Introduction:

Bacteria create biofilms on material surfaces in a matter of hours. Biofilms are often viewed as problematic materials in areas such as biomedical engineering and the food industry, but they are useful materials in other areas such as fermentation, water treatment, and civil engineering. Biofilm behavior is determined by their genome and the extracellular environment, such as pH, shear stress, and matrices topography, stiffness, wettability, and charges during biofilm formation. The surface properties of biofilms also have feedback effects on biofilm formation at various stages. Because of the advent of new technology such as synthetic biology and genome editing, there have been many studies on functionalizing biofilms for particular applications. [1]

Surface-associated communities of bacteria called biofilms are thought to be the most common form of bacterial existence in the environment. The study of biofilm formation and development is also of interest in the medical field due to the prevalence of biofilms in medical implant infections, chronic wounds, and cystic fibrosis respiratory tracts. In the medical field, biofilm communities are known to have increased virulence, antibiotic resistance, and resistance to the host immune system. These properties are thought to be linked to the biofilm community structure, which not only impacts material transport, such as nutrient/antibiotic penetration, but also is related to variations in metabolism and gene expression among the cells in the community. Some bacteria start biofilm formation without adhering to the surface through the aggregation of planktonic cells. The attachment of pre-formed aggregates to a solid surface leads to the formation of a true biofilm. The formation of an extracellular

matrix of DNA, carbohydrates, protein, and lipids helps to consolidate the attached bacterial colony, making it easier to trap nutrients and protect it from sanitation and even manual removal. [2]

For examples, colonization of Pseudomonas aeruginosa in the cystic fibrosis (CF) lung and sputum. Specimens include preserved tissues of CF patients who died because of chronic P. aeruginosa lung infection before the introduction of intensive antibiotic treatment, lungs explanted from 3 intensively treated chronically P. aeruginosa infected CF patients, and routine sputum from 77 chronically P. aeruginosa infected CF patients. All specimens were analyzed microscopically with hematoxylin-eosin (HE), Gram, and alcian-blue stain, PNA FISH, and immunofluorescence for alginate.

Analysis of the preserved tissues showed that before the introduction of intensive antibiotic treatment, P. aeruginosa infection and damage of the CF lung were associated with the presence of mucoid (alginate) bacteria in structures aggregating and surrounded by severe polymorphonuclear-leukocyte (PMN) inflammation in the respiratory part. Non-mucoid bacteria were not found in this study, and rarely in the conductive part. However, in the lungs explanted, the P. aeruginosa colonies were also mucoid but in contrast to the autopsies, they were very rare in the respiratory part but abundant in the sputum of the conductive part, which also contained abundances of PMNs. Non-mucoid and planktonic P. aeruginosa were also found in this study. In conclusion, the current intensive antibiotic treatment of chronic P. aeruginosa infections, at the Copenhagen CF Centre, appears to control but not eliminate the bacteria in the conductive zone, while the healthy respiratory zone seems to be protected from massive biofilm infections for a long period of time. This strongly suggests that the conductive zone acts as a bacterial reservoir where the bacteria are present in mucoid biofilms in the mucus, protected from antibiotics and host defenses [3].

And In industry, Diverse microorganisms are able to grow on food matrixes and along food industry infrastructures. This growth may give rise to biofilms. This review summarizes, on the one hand, the current knowledge regarding the main bacterial species responsible for initial colonization, maturation and dispersal of food industry biofilms, as well as their associated health issues in dairy products, ready-to-eat foods and other food matrixes. These human pathogens include Bacillus cereus (which secretes toxins that can cause diarrhea and vomiting symptoms), Escherichia coli (which may include enterotoxigenic and even enterohemorrhagic strains), Listeria monocytogenes (a ubiquitous species in soil and water that can lead to abortion in pregnant women and other serious complications in children and the elderly), Salmonella enterica (which, when contaminating a food pipeline biofilm, may induce massive outbreaks and even death in children and elderly), and Staphylococcus aureus (known for its numerous enteric toxins). On the other hand, the present available approaches for biofilm prevention and disruption in food factories are described, including steel surface modifications (such as nanoparticles with different metal oxides, nanocomposites, antimicrobial polymers, hydrogels or liposomes), cell-signaling inhibition strategies (such as lactic and citric acids), chemical treatments (such as ozone, quaternary ammonium compounds, NaOCl and other sanitizers), enzymatic disruption strategies (such as cellulases, proteases, glycosidases and DNAses), non-thermal plasma treatments, bacteriophage approaches (such as P100), bacteriocins (such as nisin), biosurfactants (such as lichenysin or surfactin), and plant essential oils (such as citral- or carvacrol-containing oils) [4].

Biofilms can develop rapidly in food industry environments. The first two steps are the conditioning of the material's surface and the reversible binding of the cells to that surface. Then, the binding becomes irreversible and the formation of microcolonies starts. Finally, the three-dimensional structure of the biofilm is established, and a complex ecosystem is ready for dispersal [5,6]. Of particular significance to the food industry is that some biofilm-forming bacteria in the food factory environment are human pathogens. These human pathogens are able to form biofilm on different artificial substrates in the food industry environment, such as stainless steel, polyethylene, wood, glass, polypropylene, rubber, etc.

Biofilm-related effects (pathogenicity, corrosion of metal surfaces, changes in organoleptic properties due to the secretion of lipases or proteases) are of utmost significance in some industries, such as dairy factories, where many processes and equipment (raw milk tanks, pipelines, butter centrifuges, cheese tanks, pasteurizers, and packing tools) serve as surface substrates for biofilm formation at different temperatures and with different biofilm-forming bacteria. For example, these biofilms may consist of the psychrotrophic Pseudomonas spp. and the thermophilic Geobacillus stearothermophilus. Fresh fish products may be affected by biofilm formation by pathogenic bacteria (Aeromonas hydrophila, L. monocytogenes, S. enterica or Vibrio spp.), leading to serious health and economic problems [7].

Moreover, the bacterial species that form biofilms can have genomic differences regarding important genes related to biofilm properties, resulting in totally different biofilms depending on the conditions. This, together with the great diversity of the environments affected and the different bacterial species that colonize them, makes the elimination of biofilms in the food industry even more difficult.

Food-borne diseases caused by bacterial biofilms on food matrices or in food factory equipment can occur through intoxications or infections. Toxins, for example, can be produced by biofilm present in food processing factories. From there, they can reach a food matrix, which can cause individual or multiple (in the case of an outbreak) intoxications.

In both cases, the presence of biofilms in a food factory represents a risk to human health. The level of risk depends on the bacterial species that form this living tridimensional structure. The most important sites for biofilm formation depend on the type of factory, but they can include water, milk, and other liquid pipelines; pasteurizer plates; reverse osmosis membranes; tables; employee gloves; animal carcasses; contact surfaces; storage silos for raw materials and additives; dispensing tubing; packing material, among others. [4,8].

Biofilm Control strategies in Medical Settings

Biofilms are a major concern in a hospital setting due to their antibiotic resistance and immune system evasion, leading to chronic infections caused by the use of indwelling devices such as catheters and implants. Control methods focus on the adhesion, maturation, and dispersal life cycles. Main methods include surface modifications to resist bacterial adhesion, including hydrophilic polymers, superhydrophobic surfaces, and heparin-coated surfaces, which rely on physicochemical property changes to resist colonization. Enzymatic methods use matrix-degrading enzymes like dispersin B, endolysins, nucleases, and proteases to degrade the extracellular polymeric substance (EPS) matrix. Quorum sensing (QS) inhibitors, including lactonases, acylases, and AHL analogs like bergamottin, target cell-cell communication necessary for biofilm development. Novel approaches combine nanomaterials like silver nanoparticles and chitosan carriers for ROS-mediated degradation, in addition to photocatalytic surfaces and bacteriophage hydrogels for targeted, biocompatible destruction. These diverse approaches improve device lifespan and infection rate reduction, with current research focusing on multifunctional coatings [9]

Biofilm Control Strategies in Industrial Settings

Biofilms result in large economic costs to various sectors due to corrosion, contamination, and decreased efficiency. In the food and beverage industry, biofilms cause product spoilage and bacterial contamination on processing equipment, and methods for controlling them involve sanitizers such as quaternary ammonium compounds and peracids, along with clean-in-place (CIP) systems using enzymatic cleaners specific to EPS. Physical approaches, such as ultrasonic cavitation, remove biofilms from pipes, while silver nanoparticle coatings prevent biofilm formation. The oil and gas industry experiences microbiologically influenced corrosion (MIC) due to sulfate-reducing bacteria; approaches include biocide treatment (tetrakis hydroxymethyl phosphonium sulfate) and cathodic protection, along with QS inhibitors to reduce sessile bacteria in pipelines. [10]

In water treatment plants, such as cooling towers and desalination plants, biofilms contribute to biofouling and the growth of Legionella. Control measures combine chlorination, ozonation, and biofilters with designed bacteriophages or D-amino acids to distribute mature biofilms. Membrane-based systems use anti-adhesive materials such as zwitterionic polymers. The marine sector fights biofouling on ship hulls using silicone foul-release paints and electrolytic systems producing hypochlorite, which reduces drag and fuel consumption. Pharmaceutical production deals with biofilms in fermenters using strict sterilization and rhamnolipid surfactants for non-toxic dispersal. [9]

Integration of Synthetic Biology for Novel Biomaterials

The field of synthetic biology calls for designed microbial communities that produce customized anti-biofilm biomaterials. Genetic circuits in Escherichia coli or Pseudomonas aeruginosa code for QS quenching enzymes (AiiA lactonases) on-demand, delivered in hydrogels for controlled release on industrial surfaces. CRISPR-edited strains biosynthesize self-assembling peptides that create anti-adhesive nanofilms, pH or shear stress responsive

for food processing pipelines or oil platforms. These biomaterials have inducible promoters that connect nitrate sensors (for water treatment plants) to biofilm-dissolving gene expression, providing precise delivery. [11,12]

The power production (cooling systems) and pulp/paper processing sectors use analogous strategies: designed Bacillus subtilis produces dispersin B derivatives, formulated in coatings that detect biofilm biomarkers. This synthetic biology tool provides adaptive, green materials that outcompete conventional biocides, amenable to large-scale production through fermentation. Comparative effectiveness in various industries is provided below. [11]

Table 1. Synthetic biology strategies table [12]

Strategy	Genetic tool	Enzymes/product	Delivery method	Settings	Biofilm reduction
QS Quenching	E. coli/ P. aeruginosa	AiiA laconases	Hydrogels/ coatings	Medical devices, industrial pipelines	80-95% (AI-2/AHL inhibition)
Matrix dispersal	Bacillus subtilis engineered	Dispersin B derivatives	Responsive biomaterials	Power cooling, pulp/paper	70-92% biomass loss
Anti- adhesive films	CRISPR-edited strains	Self-assembling peptides	Nanofilms (pH/nitrate triggered)	Food processing, oil platforms	75-99% adhesion block

Bridging Micro to Macro Scales

Synthetic biology biomaterials range from microscale biofilm processes (QS communication, EPS production) to macroscale applications by designing hierarchical architectures that scale up cellular phenomena to device-sized functionality. At the microscale, genetic designs govern single-cell adhesion and matrix secretion; macroscale integration is achieved through 3D bioprinting partnerships in scaffold fabrication, where QS inhibition in small regions spreads over meters-wide areas, such as industrial bioreactors [12]. Synthetic biology biomaterials link hierarchical microscale cellular phenomena—QS networks, EPS biosynthesis, and motility—to macroscale engineered systems, transducing molecular information into structural responses. Microscale designs (e.g., LuxI/R systems) control single-cell phenomena; macroscale integration through microbial self-assembly or 3D printing assembles centimeter-to-meter-sized structures, such as lattice biofilms that disperse through self-propagated enzymatic waves. Further readings illustrate quorum signal amplification in Pseudomonas microbial partnerships, scaling QS inhibition from μm-sized points to cm-wide surfaces, and materiobiology integration for adaptive biomaterials [13,14].

Applications of Biofilm Control and Synbio Biomaterials

Biofilm control methods in synthetic biology-enhanced applications range from medical to industrial, scaling micro-scale cellular processes to macroscopic systems. In the medical field, QS inhibitors in coated catheters and implants, like AiiA-expressing hydrogels, reduce infections by 50%, prolonging the life of devices and lowering costs. Nanoparticles synergized with phages target chronic wounds, accelerating healing in diabetic patients. [15]

In industrial applications, food pipelines utilize Bacillus consortia to control Listeria, while oil rigs utilize nitrate-sensitive P. putida to control MIC, resulting in billions of dollars saved. Water filtration membranes with CRISPR nanofilms increase permeability by 50%, and ship hulls receive self-healing coatings, reducing fuel consumption by 25%.

Micro-macro scaling uses LuxR genetic switches in 3D scaffolds, increasing bioreactor productivity by 35% and developing self-cleaning filters. Future AI-optimized systems will reduce infections by 50% and provide sustainable infrastructure by 2035. [16]

Discussion

Strategies for controlling biofilms in a medical and industrial context have proven their effectiveness but are limited by scalability and the potential for resistance development. Medical strategies such as QS inhibition and

enzymatic biofilm dispersal show a 40-60% reduction in infections for implants, but planktonic regrowth remains. Industrial applications, ranging from CIP sanitizers in food industries to biocides in oil pipelines, counteract $2-5 billion losses annually but have environmental implications. Synthetic biology calls for revolutionary biomaterials, such as AiiA-hydrogels and CRISPR nanofilms, which provide adaptive and eco-friendly solutions with 3-5 log reductions. Micro-macro bridging through genetic circuits enables the scaling of cellular responses to system-level performance, as seen in self-healing marine coatings that improve efficiency by 25-35%. Comparison among the strategies shows the superiority of synthetic biology: existing strategies provide temporary control, while consortia-based strategies provide predictive and biomarker-responsive deployment. Obstacles include regulatory issues for GMOs and stability issues, requiring hybrid materiobiology.

Conclusion

The integration of synthetic biology in biofilm management is an application of microscale phenomena to macroscale technology, which will transform the lifetime of medical devices and the sustainability of industrial processes. A holistic approach of surface engineering, phage therapy, and synbio biomaterials will be more effective than current one-time approaches, promising a 50% reduction in infections and significant cost reductions by 2035. Future AI-driven evolution will provide robust and self-adjusting materials that will mitigate climate-enhanced microbial challenges and underpin a $3 trillion bioeconomy.

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