

Biofilm's Function in Microbial Ecosystems and its Implications for Human Health

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ABSTRACT

Biofilms are complex structures of microbial communities often including bacteria, fungi, algae, and protozoa, which are enclosed together with their secreted extracellular polymeric matrix. The resulting highly developed architectural structure offers a great survival advantage, allows more efficient metabolic cooperation among the different species, and helps the microorganisms to be less vulnerable to the environment. In human healthcare environments, biofilms represent major problems for people's health, and the costs associated with them are very high. It is estimated that 30% of infections acquired in hospitals are related to biofilms. Most of these infections are caused by biofilms that are constantly contaminating hospital environments. Moreover, biofilms as long-lasting reservoirs for pathogens often lead to chronic infections and induce prolonged localized immune or allergic responses. Also, the host microenvironment influences the formation of these biofilms by determining the microbial distribution and the survival of microbial species. Understanding the complex interactions between biofilm architecture, metabolic synergy, and host features is the key to developing new ecological approaches aimed at sustainably managing pathogenic populations and their harmful effects.

KEYWORDS

Ecosystem, biofilm, antibiofilm strategies, human health

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INTRODUCTION

Biofilms are groups of microorganisms that are physically attached and, in many cases, to living or non-living surfaces. After attachment, these cells produce and surround themselves with a protective substance called the extracellular polymeric substance (EPS). Encased in this EPS network, the bacteria take on a different physiological state. They display a great deal of physiological diversity, are mostly characterized by slow growth rates, and express certain genes that are completely different from those of the rest of the planktonic population. One characteristic of these highly organized communities is quorum sensing, a process allowing bacteria to communicate with each other and, as a result, to change their gene expression in a synchronized way¹⁻³.

Historically, before the advent of advanced molecular techniques, scientists were perplexed by the fact that bacteria in nature were invariably heterogeneous in terms of their physiology, adherent, and resistant to most attempts to grow them in the lab. They discovered that, contrary to the common belief, bacteria were not floating freely; in fact, they were almost entirely attached to solid materials or were part of



particulate complexes that are collectively called “flocs”. In 1988, the core similarity between these various communities was identified by considering them all as biofilms, a simplicity in description that still forms the basis of biofilm studies today⁴⁻⁶. Despite this essential knowledge, today’s hospital protocols still largely fail to recognize the stubbornness of environmental biofilms. It is well-known that most standard disinfection practices are not effective as they target only free bacteria and not the larger, more complex communities supported by the abiotic surfaces. New research has, however, surprisingly revealed some ecological management tools that focus on the management of the biofilm’s habitat rather than chemical eradication. Hence, this review intends to substantially cover the environmental component of biofilm formation and metabolism to bridge the knowledge gap. Through detaching from purely clinical treatments, this paper offers an innovative outline for the embedding of these newfound ecological approaches in long-lasting hospital management.

DEFINITION OF BIOFILMS

Biofilms are complex structures of diverse microbial lineages that live in a self-produced extracellular polymeric matrix or EPS. They usually attach to abiotic or biotic surfaces or can be found in the air, liquid, or liquid, liquid interphase, for instance, in different aquatic environments. Nearly all prokaryotic and eukaryotic microorganisms have the capability of biofilm growth in different manners^{7,8}. Biofilms are the prevailing form of life for microorganisms in almost all surroundings due to the specific physical conditions of the microenvironment they create. The surface, to, volume ratio in biofilm habitats is significantly higher than that of planktonic cells, which results in more physical contact between cells in a biofilm and the presence of extracellular matrix materials that facilitate cell, to, cell communication. Moreover, the solid surfaces and EPS produced in biofilms can lessen environmental pressure and help the exchange of resources such as protons, inorganic and organic liquids, and molecules, thus generating a stable microenvironment for the microorganisms within the biofilms^{9,10}. A fully developed microbial biofilm usually encompasses several layers, such as a layer of microbial cells, the layer of transient extracellular polysaccharides, the EPS matrix, and disoriented areas that may penetrate the biofilm. Cells in a biofilm environment, according to the distinct structural characteristics of biofilms, are under quite stable conditions, thus leading them to produce more virulence factors that are advantageous for the growth of the cells. The switch to biofilm mode makes bacteria extremely resistant to almost all antimicrobial agents of clinical and industrial origin. Besides, biofilms have been identified as a source of direct harm to the health care and food processing industries for a long time and, therefore, have become a major challenge for sanitary control^{11,12}.

FORMATION AND STRUCTURE OF BIOFILMS

The development of a biofilm can essentially be explained by the transition through four different stages. Initially, there is the attachment phase wherein bacterial cells fold down upon a solid substrate, procure, and manufacture a fixation. The next stage is the initial adhesion phase, when the cells attach themselves to the solid substratum in a reversible manner. After that, there is the established adhesion phase where bacteria undergo metabolic activation and attach irreversibly as well as multidirectionally to the receptor of the solid substratum. The last one is the colonial morphology phase, where growth and spatially organized development of bacterial cells bound to the solid substratum take place. The ability of biofilms to characteristically colonize is mainly the reason for the seclusion of microbes in biological systems, and thus, it poses a great challenge in the treatment of chronic infections linked to biofilm formation as well as in the prevention of implant contamination. Moreover, our comprehension of bacterial biofilm growth and development has substantially enhanced our awareness of the microbial community organization as well as the biochemical and physical interactions of the biofilm cells¹³⁻¹⁵.

ECOLOGICAL FUNCTION

Biofilms are one of the main contributors to the survival of organisms in almost every ecological system where microorganisms exist and proliferate. They accomplish a significant part of their indispensable function through intimate association and interaction between the different members of the biofilm

community, which is done by a process of synergistic cooperation. This cooperation is due to the production of extracellular polymeric substances (EPS), which not only assist the whole community in various environmental challenges and stresses but also play a major role in the protection of the community. After a concise and enlightening explanation regarding the biofilm development process, the discussion moves to the multitudinous and diverse roles that biofilms have, as confirmed by extensive ecological studies, which incorporate the wide variety of natural habitats^{16,17}. In addition, human activities and interventions have been a major factor in the development of biofilms through various means, such as the global distribution and the purposeful use of medical devices, and the intentional injection of fresh nutrient sources into both aquatic and terrestrial ecosystems. An ecological view of the issue can be a great help in the successful control or prevention of unwanted biofilm formation. Thus, it could be done by various antimicrobial treatments, or by understanding better the possible long-term effects of the disposal of waste products that may have an impact on biofilm dynamics and resilience¹⁸⁻²⁰.

CLINICAL IMPACT

Biofilms are the main culprits behind recurrent and chronic infections that can be internally or externally present in the human body. The adhesive features of the biofilm are what bring about chronic and recurrent infections, while the biofilm is associated with a considerable number of infectious processes. Being in a biofilm state allows microbes to survive against the host's defense and, at the same time, helps in lowering microbial susceptibility to antimicrobial agents. The biofilm mode has the power to diminish infection resolution, which makes the biofilm an interfering factor in the treatment of infections^{21,22}. Along with the rise of human life expectancy, which is also accompanied by the increasing number of immunocompromised patients, new and effective anti-infectious strategies are highly demanded. Among the many innovative approaches, one is to formulate strategies that would lead to the disruption of biofilms, thus paving new ways for the control of bacterial and fungal infections. For this reason, knowing about the disruption of established biofilms is only a developing phase. Present-day review aims at discussing various propositions of the ways to disrupt bacterial and some fungi/yeast biofilms. Apart from that, the significance of the disruption in infection control is being focused on. The deeper understanding of biofilm disruption is supposed to be a factor that will eventually lead to a decrease in infectious processes^{23,24}. medical treatments such as urinary catheters, artificial heart valves, contact lenses, implanted devices, and even the self, limiting respiratory tract infections become more susceptible to infection. Infectious diseases involving bacterial biofilms are typically very stubborn to treatment and hardly ever respond to the conventional treatment methods. In fact, chronic wounds are the common result of infection and biofilm formation. Microbes in the biofilm mode of life can be up to 1, 000 times less susceptible to antimicrobial agents. It has been suggested that bacteria that exhibit 1% metabolic activity are 1,000 times less susceptible to antibiotics than bacteria that are in the process of replication^{25,26}. Besides that, the radial gradient of nutrients through the biofilm may influence the antibiotic dose needed for killing. These killing microbes were found to have the ability to either turn on genetic circuits that lead to tolerance of antimicrobial agents or to the enzyme that is responsible for cutting the, lactam ring into an inactive form. It follows that even antibiotics that can stop the growth of metabolically active cells in a biofilm are not able to reach the whole biofilm²⁷⁻²⁹.

CONTROL STRATEGIES

Considering the extremely harmful clinical effects of biofilms, their formation and development should be very tightly controlled. In the past, one of the biggest public health issues has been the use of toxic, chemical-controlled methods to get rid of biofilms, and on top of that, they have been largely ineffective³⁰. The main reason for this failure is that such methods have a very limited way of acting for example, going after the initial attachment or hardly killing bacteria once the biofilm is completely mature, and so, new antibiofilm therapies are being developed along the lines of ecological management that harness non-hazardous natural products and alternative technologies for different stages of the biofilm lifecycle.

Biological and biochemical methods are the main areas of change in this transition. Natural biocides and plant extracts are seen to be viable control measures³¹⁻³³. For example, HQ-decorated amino acids can greatly disrupt both quorum-sensing communication and AI-controlled biofilm formation in *Bacillus subtilis* without holding back the entire bacterial growth. In addition, cross-linking enzymes provide a novel approach for tearing down the basic structure of the biofilm. Lysostaphin is one of the enzymes that exerts antibacterial activity against Gram-positive bacteria by degrading the peptidoglycan part of the bacterial cell wall. Likewise, dispersin B cleaves poly-N-acetylglucosamine, which is a major component of the *Staphylococcus epidermidis* extracellular matrix³⁴⁻³⁶. Other very interesting enzymatic works include the application of amylase, DNase, proteinase K, pellicin, and lactonase to break down polymeric substances even at mature stages. Along with these biochemical tools, various physical and biological treatment methods might also be considered before and after biofilm formation. These other technologies refer to thermal treatments (heating), intense pulsed light, microwaves, electrolysis with conductive diamond electrochemical cells, ultrasound, and food-grade high-voltage pulsed electric fields. In addition, the controlled adsorption of particular bacteriophages, target molecules, or charged particles can be a very effective antibiofilm technology³⁷⁻³⁹. In the end, combined strategies seem to be the single most promising avenue for handling biofilms. The likelihood of resistance is drastically reduced by combining inhibitors that target the structural parts of biofilms with those that affect the non-structural development (for example, through covalent inhibition of adhesion factors). New, host-targeted, early-stage preventions and nano-engineered formulations will play a major role in the clinical future of biofilm-associated infectious disease therapies. One of the main ways to break the deadlock in biofilm control is to do away with the myth that these communal living systems are too formidable to be defeated; besides that, it calls for strong multi- and interdisciplinary collaborations between Chemistry, Nanotechnology, Materials Science, Biotechnology, and Applied Microbiology.

FUTURE DIRECTIONS AND RESEARCH CHALLENGES

In sum, it is crucial to mention that we now comprehend biofilms in such a way that the different scientific papers about this topic are a constant source of knowledge. One thing that stands out is that a large number of methods have been designed with the sole purpose of eliminating or minimizing biofilm formation or its long-term survival. Anyway, to come up with strategies to stimulate or develop beneficial biofilms, it will take an even loftier understanding of the positive cases and the ways of changing them⁴⁰. Most microbiome-centered works have only considered energy and resource flows, while our metabolic models are mainly for planktonic organisms, i.e., single cells in a free state. None of the metabolic models properly describes biofilms. Although there are numerous well-established methods to cultivate biofilms in laboratory cultures, to invent drug screens targeting biofilms, and even to create model biofilms with certain architectural features, the growth and behavior of biofilms in natural environments are still inconceivable^{41,42}. First and foremost, we require additional genetic and physiological descriptions of biofilm-forming organisms. Comprehending the biofilm framework is important; however, even after 20 years of intensive research, the current state of the art is still very far from it. By analyzing the research areas that have had the greatest impact on human health, we can observe a variety of instruments that allow the efficient study of extremely rare internal populations. Restrained by ethical issues, we are not allowed to conduct the most helpful experiments in the biofilm context, which would mean investigating intricate populations of cells that are structurally organized in three spatial dimensions and have systemic characteristics over time, such as growth, movement, and taxonomic diversity. As we have to settle for studying simpler and oftentimes unrepresentative models, such as laboratory cultures and natural communities, we should not expect them to provide us with everything that would be useful. To sum up, although these models are attractive and promising, it is important to remember that they are models and simplifications of the problem that we really want to understand. We ought to comprehend biofilms in complex natural environments, simultaneously exploring and expanding the genetic diversity that governs their behavior^{43,44}.

CONCLUSION

To effectively tackle biofilm-related medical complications, there should be less dependence on antibiotics and more focus on a multi-pronged strategy targeting primary bacterial adhesion. Since a single solution cannot tackle the natural diversity of microbial colonization, future studies should aim at a comprehensive understanding of bacterium-material interactions throughout the biofilm life cycle. The harmony that limits the growth of pathogens can be sustained by combining innovative antimicrobial surfaces with proper ecological management. Ultimately, the only feasible way to handle the increasing problem of multidrug-resistant biofilms in clinical settings is a well-thought-out mix of early-stage prevention and optimized antibiotic use.

SIGNIFICANCE STATEMENT

While the influence of environmental parameters on biofilm ontogeny is recognized, the specific mechanisms by which these factors modulate molecular signaling pathways remain poorly defined. This article proposes a conceptual framework that integrates surface topography and nutrient flux with downstream molecular signaling and resultant ecological outcomes. By re-evaluating the classical five-stage biofilm lifecycle through the lens of environmental stressors, we elucidate how these variables dictate the efficacy of antibiofilm interventions, including phytochemical-based inhibitors. This synthesis provides a theoretical foundation for transitioning from broad-spectrum clinical protocols toward niche-targeted, sustainable control strategies that exploit site-specific environmental vulnerabilities.

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