MICROBIAL BIOFILMS
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The study of biofilm biology has exploded in the past 5 years. However, there is no single source that covers the basic information underlying the research in this field. *Microbial Biofilms* was written to do just that; the book covers broad topics in biofilm biology, including development, antibiotic resistance, architecture, and the role of these communities in disease and industry. Biofilms are an important and growing area of research, and *Microbial Biofilms* was written to be a single text serving as an introduction to this field. Its scope includes both bacteria and fungi, so it will be of general appeal to microbial biologists. This volume would also serve as an excellent primer to the field for nonexperts interested in learning about biofilms, as a possible textbook for courses on biofilm biology, or as a helpful source for graduate students writing qualifying exams in this area.

This is the first book to comprehensively cover a broad variety of aspects of microbial biofilms. It is written at a time when the field is rapidly expanding, and it will serve as an excellent historical marker and snapshot of the start of a new and important field of microbial research. We have also included a historical perspective of the field written by Dr. William Costerton, one of the pioneers in this field, and a chapter on future perspectives of biofilm research has been contributed by Roberto Kolter, one of the key players who kicked off the molecular genetic revolution in biofilm research. *Microbial Biofilms* thus combines cutting edge research with a historical perspective of the field.

We thank all the authors who contributed their time, effort, and expertise to this project.

MAHMOUD GHANNOUM
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INTRODUCTION TO BIOFILMS: CONCEPTUAL THEMES

George A. O’Toole and Mahmoud Ghannoum

It is a wonderful time to work on microbial biofilms. There has been an explosion of studies examining the molecular genetic basis of biofilm formation by bacteria and fungi. The wealth of recent genetic, biochemical, and microscopic data makes this an ideal time to step back and reflect on themes in this rapidly growing field. One of the prime motivations for this book is to summarize where we stand today (the fall of 2003) in terms of our understanding of the molecular genetic basis of microbial biofilm development and biofilm-associated properties. This book is by no means an all-inclusive work—to make it so would require reviewing a literature going back at least 70 years or more (Henrici, 1933). Many scientists have contributed to laying the foundation for the work presented in this volume, and to these pioneers we are grateful.

The earliest studies of biofilms were observations of environmental microbes adhering to a wide range of surfaces. These surfaces included everything from river rocks to medical devices to hulls of ships (reviewed in Costerton et al., 1987, 1995). Microbial ecologists and engineers used a variety of approaches to examine adhered bacteria and model their behavior. The physical properties of the surfaces to which bacteria adhere, including roughness, hydrophobicity and hydrophilicity, and conditioning films, were an early important focus of study in the field, and they defined the experimental approaches utilized. As electron microscopic techniques advanced and were applied, a picture of microbial biofilms and their structure began to emerge. The field was revolutionized by the application of confocal scanning laser microscopy, coupled with fluorescent markers, which allowed visualization of the live, hydrated biofilm (Lawrence et al., 1991). The confocal scanning laser microscopy studies gave us the first three-dimensional view of an undisturbed biofilm, and this methodology remains key to this day.

Despite the advances in understanding the formation and properties of biofilms, a very simple question still plagues the field: What is a biofilm? Biofilms can be broadly defined as communities of microbes associated with a surface, typically encased in an extracellular

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matrix (Costerton et al., 1987, 1994). This definition has been expanded to include surfaces as far ranging as steel pipes, soils, medical implants, and epithelial cells. A definition that once generally applied to a solid-liquid interface has grown to include air-water interfaces, or no obvious interface at all, as in bacterial aggregates in suspension. At this point, however, it is not clear to what extent biofilms at these different interfaces share metabolic or physiological traits. For example, is a macro-colony of *Pseudomonas aeruginosa* on a glass slide substantially similar to or different from a colony of this same organism attached to an epithelial cell or residing in a mucus plug in the lung of a patient with cystic fibrosis? Currently, there is no answer to such a question. The definition of a biofilm can be based on a set of descriptive properties (structure, presence of a matrix, etc.) or be functionally defined (the ability to form a ring in a microtiter plate or display increased antimicrobial resistance). Even for a given organism in a defined model system, such as *P. aeruginosa* growing in a flow cell, recent studies have shown that flow rate of the medium or the carbon source provided can drastically alter the structure and function of these communities (Stoodley et al., 1999, 2001; Klausen et al., 2003), and genetic studies indicate that some organisms may have multiple genetic pathways that are utilized to form a biofilm (O’Toole and Kolter, 1998). The properties of the surface to which these organisms adhere can profoundly impact the structure and composition of the community, as in *Candida albicans* biofilms (Chandra et al., 2001). Throughout this book, different definitions will be presented to define a biofilm, but as of today there is no “right” answer to this question, and we are not sure there ever will (or should) be. Despite the difficulties in defining a biofilm, and the diversity of pathways utilized to make a biofilm documented for bacteria and fungi, the past decade has revealed common phenotypes (developmental stages, antibiotic and biocide resistance, etc.) conserved among biofilms formed by organisms spanning the three domains of life (Davey and O’Toole, 2000; O’Toole et al., 2000; Chandra et al., 2001; Reysenbach and Shock, 2002; Mukherjee et al., 2003). Thus, examination of the commonalities among very different biofilms will likely teach us much.

The roots of biofilm research are firmly anchored in the realm of addressing and trying to overcome practical problems, that is, of understanding which bacteria adhere to what surfaces, why these bacteria adhere, and how they resist elimination by treatment with a variety of antimicrobial agents. This theme of practicality continues today—we are simply using a new set of tools to address these questions. A common thread holding together much of the work contained in this volume is the melding of basic and applied research. Questions that began as practical problems became the subject of basic studies in hopes of better understanding the observed phenomena. Current work in the field strives to understand community physiology, metabolism and ecology, structure/function relationships, the role of genetic exchange, and mechanisms of biofilm development and resistance. The results of this ongoing basic research will no doubt serve as the foundation for the next push to develop strategies to eliminate, modulate, and stimulate biofilm development.

The oral microbes served as one of the first well-defined and well-studied biofilm model systems that were subjected to molecular analysis. This model system nicely exemplifies how the study of biofilms (such as dental plaque) can translate into research with applications in human health. From studies by Kolenbrander, Palmer, and many others emerged the idea that microbes in biofilms are able to physically interact and to do so in very specific ways (Kolenbrander et al., 2002). Later work by several groups studying quorum-sensing systems provided evidence that microbes in a biofilm communicate with extracellular molecules and may behave as a coordinated group (Parsek and Greenberg, 2000; Kolenbrander et al., 2002). These themes of cell-to-cell contact and communication are still the
core of a great deal of work [and controversy (Kjelleberg and Molin, 2002)] presented in the following chapters.

We hope this book will serve as a mile marker for a field that still is quite new in terms of applying molecular genetic approaches. Many avenues remain ripe for exploration. The ideas represented in the chapters of this book are ones that currently serve to drive the field forward. However, we do hope we are around to do this again in 15 to 20 years and to look back to see what we’ve learned and reflect on how far we have come in our understanding of biofilms.

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