Preface

It is now well established that a number of bacteria communicate through diffusible signals that may induce and/or regulate a coordinated response by the individual organisms that make up a given population or biofilm. For many of these organisms, it has been suggested that intercellular signaling functions to report population density or to coordinate a response from all cells in a microbial community. Therefore, cell-to-cell communication has been referred to as auto-induction or quorum sensing. The response of bacteria to quorum sensing signals is quite varied and includes, for example, the induction of bioluminescence, the regulation of virulence gene expression, the formation of biofilms, or the induction of horizontal transfer of genetic material. It is also becoming increasingly apparent that some bacteria may communicate via contact-dependent signaling mechanisms, and that the response to direct cell-to-cell contact influences complex behaviors that may contribute to multicellular development or the adaptation to growth in complex biofilms. In the past five to ten years, increased interest and research in the mechanisms of bacterial cell-to-cell communication has revealed surprising complexity both in the signaling processes themselves and in the breadth of the response of recipient cells to the signal molecules. For example, a variety of chemical species, e.g. acyl-homoserine lactones, oligopeptides, furan derivatives (i.e. AI-2), quinolones, butyrolactones, and unsaturated fatty acids are known or have been suggested to function as diffusible signals. Furthermore, some organisms, most notably *Pseudomonas aeruginosa* and species of *Vibrio*, have been shown to produce and respond to multiple diffusible signal molecules. In many cases, the cellular proteins that are required to synthesize and respond to these diffusible signal molecules have been identified; high-resolution crystal structures have been determined for several of these polypeptides. In addition, the response of several organisms to quorum sensing signals

has been investigated by using microarray technologies; at least in the case of *P. aeruginosa*, the expression of hundreds of genes is influenced by intercellular signaling. Recent research is also beginning to determine how different signaling pathways are integrated in a given bacterial cell, and how these cell-to-cell signaling mechanisms are linked to the processes that control stationary-phase growth in bacteria.

In contrast to the autoinduction or quorum sensing mechanisms described above, contact-dependent signaling in organisms such as *Myxococcus xanthus* or *Porphyromonas gingivalis* may be initiated by non-diffusible signals such as cell-surface polypeptides. The C-signal of *M. xanthus* is probably the best-characterized cell-surface signal and it plays an essential role in the starvation-induced development of spore-filled fruiting bodies by this organism. Organisms that colonize the human oral cavity may also respond to non-diffusible cell surface signals as well as to diffusible signals. These mechanisms may facilitate the colonization process or adaptation of cell to growth in a multispecies biofilm. Thus, the capacity to respond to non-diffusible cell surface signals may be beneficial for cells that exist in a complex multicellular community, or for cells that must adapt to life in an open-flow environment that might limit the accumulation of a diffusible signal.

In general, the greatly increased interest in bacterial cell-to-cell communication that has occurred in recent years has resulted in a much clearer picture of the signaling mechanisms utilized by bacteria and how organisms integrate various input signals to generate a specific coordinated response as a community. This in turn, has led to efforts to exploit these communication pathways as targets for the development of new antimicrobial therapies. Indeed, chemicals that jam or inhibit bacterial signaling have the potential to be highly effective anti-biofilm agents that may overcome the inherent resistance of biofilm-mediated diseases to treatment with antibiotics.

Our foremost objective in compiling this book is to summarize the rapid advances that have been made, and are continuing to be made, in the field of intercellular communication among bacteria. Owing to the broad scope of new information that is available in this field, we have chosen to target this book on the biomedical community and to focus primarily on the mechanisms of cell-to-cell communication in bacteria of medical importance. A recurring theme throughout many of the chapters is the role that cell-to-cell communication plays in regulating virulence and the development of biofilms by these organisms. The contributors to this volume are leading researchers in the field; each chapter reviews the most recent

findings, controversies, and important new information in the author's field of expertise. Our goal is to provide the reader with a comprehensive overview of the various mechanisms and outcomes of bacterial cell-to-cell communication and an appreciation of how these signaling processes may be relevant to the development of microbial communities and to host–pathogen interactions during infection.

We thank the authors for their contributions and for their efforts and cooperation during the assembly of this book. We also thank Katrina Halliday of Cambridge University Press for her assistance in nurturing this project to fruition.