PREFACE

Cellular engineering can be simply defined as the application of engineering tools and concepts to the study and manipulation of living cells. Cellular engineering, and bioengineering in general, is necessarily interdisciplinary, combining tools and ideas from the fields of biology, engineering, applied mathematics, physics, and chemistry. Research engineers and scientists converge on cellular engineering from several different directions: cell and molecular biologists looking for new ways to quantify and model their results, engineers from traditional disciplines (chemical, electrical, mechanical) with an interest in tackling biomedically important problems, and, of course, bioengineers specializing in cell and tissue engineering applications. To gain a mechanistic rather than "black box" understanding of cellular behavior, it is necessary to concern oneself with the phenomena that occur one length scale below that of single cells — the domain of atoms, molecules, and supramolecular assemblies. Further, to motivate the study of cellular behavior and connect it to clinical outcomes, it is also necessary to concern oneself with the next higher length scale, that of cell aggregates and tissues. Thus, cellular engineering is inherently multiscale, but focuses on the behavior of single cells. In this book we further refine the list of topics to a specific, but very important aspect of cellular engineering, the cell surface, where the fundamental biological processes of adhesion and signal transduction occur.

The term *biomolecular interface* has recently been used to describe the intersection of biological science and materials science [A. L. Plant, et al., *Langmuir* 19: 1449–1450 (2003)].

This subdiscipline of cellular engineering – involving the study of soft organic matter, the chemistry and physics of self-assembly, and the application of such knowledge toward new medical therapies and research – is by its nature highly interdisciplinary. Recent work on biological interfaces has revealed important new applications based on spatially controlled molecular layers, determination of the forces involved in biomolecular assemblies that provide the structural integrity and motility of cells, and new ways to assay for effects of protein conformation on outside-in and inside-out biochemical signaling. Advances in microfabrication technologies allow us to exploit the physical milieu of microscale flows to encapsulate and transport single cells within immiscible droplets, or carry out enzymatic reactions at pinned fluid interfaces. Polymer-supported lipid bilayer membranes preserve the lateral mobility of transmembrane proteins, enabling electrophoretic fractionation of protein mixtures or precise modeling of the biological effects of receptor clustering. Many of these studies have been carried out in basic science laboratories isolated from researchers and practitioners in engineering; here we work to bring together this knowledge and find new ways to integrate recent findings and approaches into the growing field of cellular engineering.

This book aims to bring together in one place the important results, concepts, and opinions of how cells interact with biomolecular surfaces. Of particular interest are the interaction and adhesion of cells with each other and with surfaces in complex mechanical environments such as the cardiovascular system. The behavior covered ranges from atomic to molecular, cellular, and multicellular length scales. A variety of experimental and theoretical approaches are used by the authors to study the dynamic interactions between cells: from advanced optical microscopy methods, to transfected cell systems, animal models, and computer simulations. Novel biomolecular surfaces are described that have been engineered either to control or to measure cell function. One recurring theme is that of inflammation and cellular immune response; remarkable progress has been made in recent years on this challenging problem, where the participating cells rapidly upregulate and downregulate their adhesion molecule expression in response to molecular cues, and demonstrate an exquisite balance between chemical adhesion and well-defined fluid shear forces. Those working in the fields of inflammation and vascular biology will be particularly interested in the chapters devoted to these topics, but these chapters also represent model problems demonstrating how engineering concepts and tools may be effectively applied to complex systems in biomedicine.

Principles of Cellular Engineering is organized into four parts. Part I is concerned with the firm adhesion of anchorage-dependent cells to substrates. Chapters are devoted to measurement of the forces that cells actively exert on their substrates (Chapter 1), mechanotransduction and the mechanical coupling between the luminal and basal cell surfaces (Chapter 2), and a spinning disk assay developed to quantify the strength of integrin–ligand adhesive bonds (Chapter 3). Chapter 4 presents evidence in support of the tensegrity, "prestress" model for the cell cytoskeleton. Part II focuses on three important aspects of the cell surface: the relationship between compression of the cell interface and receptor–ligand bond formation (Chapter 5), the lateral mobility of cell surface adhesion receptors (Chapter 6), and the cell glycocalyx layer and its influence on adhesive interactions with other cells (Chapter 7). Part III focuses on artificial systems designed to mimic the biomolecular interface of living cells. Specific examples include molecular dynamics simulations of protein adsorption to ceramic biomaterials (Chapter 8), supported lipid bilayers as models of the cell membrane (Chapter 9), and the use of functionalized glass micropipettes to model cell interactions in the capillary bed (Chapter 10). The final part of the book is dedicated to the roles that fluid shear forces play in the adhesion between reactive surfaces and circulating cells, specifically, the effects of complex hemodynamics (Chapter 11), pairwise interactions between multiple suspended cells (Chapter 12), and the unique physics of platelet-shaped cells (Chapter 13). I thank all of the contributing authors for lending their valuable time and expertise, the editors at Academic Press (in particular, Luna Han) who helped in the planning and production of this book, and my wife Cindy for her support and scientific insights. Finally, I express my thanks to the readers of this book, and the hope that they may find ideas or inspiration in this exciting field of cellular engineering.

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