Preface

The emergence of biotechnologies to foster discoveries in genomics, proteomics, and other branches of molecular biosciences has provided the potential for greater precision in medical care, from diagnostics to therapies. However, their successful application to patients has been slow for multiple reasons. The complexity of regulatory frameworks that clinical laboratory tests must adhere to and the sheer complexity of the protein and macromolecules identified as diagnostic and/or prognostic biomarkers in experimental systems account for some of these barriers. Understanding the environments in which these proteins may be assayed will be crucial, particularly where precision medicine is concerned. Thus, the concept of human extravascular fluids and bodily secretions, or more broadly *interstitial fluids*, is something we have grappled with for some time with increasing application in biotechnology.

Conceptually, interstitial fluids may not be as foreign as they first appear. For example, both urine and saliva are interstitial fluids commonly assayed in clinical laboratory tests. While assays for urine (a plasma ultrafiltration) and saliva (derived from glandular secretion and plasma proteins) are simple and quite basic, our further understanding of their makeup and relationship to disease in expanding biosignatures will have commercial importance in therapeutics and diagnostics. Their dynamic properties, currently viewed as static processes, are surprising. With 60% of serum albumin in the extravascular space, the dynamic movement of fluid between the intravascular and extravascular space, exchanging one entire plasma volume every 9 hours, brings to light a context in which understanding biomarkers and biomarker signatures will be needed. Similarly, understanding the dynamics of extravascular spaces derived from sources other than plasma, such as cerebral spinal fluid, will bring to light how biomarkers for specific diseases (e.g., multiple myeloma) can be created with diagnostic/therapeutic value.

This book has been organized into broad biologically relevant categories in the context of interstitial fluids. In the first half of the book, we cover the fundamental concepts of interstitial fluid. We begin by defining its composition and function (Chapter 1), then discuss the extracellular matrices, which are responsible for regulating the composition of interstitial fluids (Chapter 2). We then focus our attention on the biochemistry of the large carbohydrate heteropolymer hyaluronan, as it is a major constituent of the interstitial space and is critically important in understanding synovial fluid (Chapter 3). Lastly, we discuss the factors that regulate proteolysis in the interstitial space, including the possible effects of extracellular matrix components such as collagen and hyaluronan (Chapter 4).

The coagulation system has been studied extensively in terms of diagnostics, primarily by assaying vascular spaces. However, a disconnect with this approach has always been that many of the components exist in the interstitial spaces, notably tissue factor, matrix metalloproteinases, serine protease inhibitors, and coagulation factors. The second part of this book investigates the fibrinolytic system (Chapter 5), kallikreins (Chapter 6), matrix metalloproteinases (Chapter 7), coagulation factors (Chapter 8), and protease inhibitors (e.g., serpins; Chapter 9) in the interstitial space.

With increasing recognition that the interstitial environment is where many of the primary reactions of the coagulation system are playing out in the pathogenesis of disease, future assays will depend on understanding how each of these major systems contributes to the interstitial environment.

By covering a unique array of topics with a broad application to biomedical workers, including physicians and scientists in industrial and academic pursuits of biotechnology, we hope this book expands the understanding of those creating greater precision in medical care. We extend our gratitude to the many scientists that we called upon that have made substantial contributions to the literature. We hope you find our synthesis of their work a useful and valuable resource.