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PREFACE

Transmembrane receptors (TMRs) or G protein-coupled receptors (GPCRs) represent by far the largest family of plasma membrane receptors, comprising approximately 10% of the human genome. They regulate virtually all known physiological processes in mammals including the senses of smell, taste, and vision. Indicative of their central importance in current clinical therapeutics is the very large number of drugs that target these receptors, either directly or indirectly. It is, therefore, not surprising that there is great interest in the mechanisms by which these receptors signal and are regulated.

Over the past 15 years two simple paradigms, developed largely based on studies of the β_2 -adrenergic receptor, the β_2 -adrenergic receptor, and rhodopsin, have guided understanding and experimentation in this field. The first is that the TMRs signal by activating heterotrimeric G proteins. The second is that signaling is "short-circuited" or desensitized by a feedback process involving phosphorylation of activated receptors by G protein-coupled receptor kinases (GRKs) followed by binding of arrestin proteins. However, over the past few years it has become clear that these simple paradigms explain only some of the behavior of the receptors. For example, the arrestins are now recognized to be multifunctional adapter proteins, which mediate not only desensitization of the receptors, but their endocytosis and signaling to a growing list of pathways such as MAP kinase, receptor internalization, and Akt. Moreover, a variety of signaling molecules have been demonstrated to interact with the receptors, either directly or indirectly, and these interactions are functionally significant. Many of these interactions are highly sensitive to the conformation of the receptor, that is, they are of higher affinity for the agonist-activated versus the nonactivated form of the receptor.

As the list of receptors interacting and regulating interacting proteins has expanded, there has been increasing interest in techniques that can be used to identify and characterize these interactions, as well as to discover new ones. This volume presents an introduction to a wide variety of optical, biochemical, immunological, and biophysical approaches that