
Preface

Many advances in modern neuroscience are enabled by the availability of chemical tools that allow sensitive, precise, and quantitative measurements of, and control over, biological processes. These powerful reagents are widely used for investigating the nervous system at levels of detail ranging from ion channel structure to neural network dynamics. Recent advances in photochemistry, microscopy, and protein engineering have triggered a surge in the development and application of these interdisciplinary techniques. *Chemical Neurobiology: Methods and Protocols* is intended to assist with the design, characterization, and validation of new chemical tools for neurobiology by providing detailed protocols of procedures and assays deemed essential for their successful development and implementation.

The methods covered are divided into three parts: chemical probes of membrane protein structure and function, photochemical control of protein and cellular function, and chemical probes for imaging in the nervous system. The first part addresses several emerging approaches to neurochemical pharmacology, which not only shed light on ligand–receptor interactions but also provide insight into the delicate relationships between protein structure and function. These protocols cover the use of unnatural amino acids and covalent peptide-toxins to study ion channel structure and function, a novel high-throughput genetic screen that yields insight into small molecule–ion channel interactions, and the application of a functional calcium imaging assay to probe the unique pharmacological properties of bivalent GPCR ligands with heteromeric receptors. As modern neuroscience relies heavily on optical methodology, the remainder of the book is devoted to protocols that will guide the characterization of photochemical reagents that enable researchers to control and detect molecular and cellular signaling. In the context of photopharmacology, the protocols presented will guide the quantification of key properties of caged neurotransmitters such as quantum yield and photolysis kinetics, the wavelength sensitivity and mechanistic pharmacology of photoswitchable ligands for ion channels, and principles underlying the design and implementation of photoreactive ligands for neurotransmitter receptors. On the topic of sensors, this book includes assays for determining the affinity and fluorescence properties of small molecule ion sensors, the sensitivity and optimal optical parameters for imaging membrane potential with voltage-sensitive dyes, pharmacological characterization and optical implementation of fluorescent ligands for neurotransmitter receptors, the use of quantum dots for measuring vesicular release of neurotransmitters, and the innovative application of directed evolution to create protein-based probes for neurotransmitters that can be monitored *in vivo* by MRI.

Instructing by example, each protocol includes background on the biological problems addressable by the tool or technique and considerations critical to the initial design process. Importantly, each protocol is written in a format that can be readily extended to related systems in order to facilitate the development of new chemical tools.

The topics covered should be of value to scientists at many levels, including students aiming to expand their perspective, laboratory researchers seeking technical guidance, and established investigators looking for creative solutions to their research problems in molecular, cellular, and systems neuroscience.

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