Preface

Tools for observing and controlling specific molecular or physiological pathways in intact cells and tissues are opening up new frontiers in the understanding and engineering of complex biological systems and even pointing the way toward novel kinds of therapy and prosthetic for treating human disease. One of the most popular strategies is to utilize what has come to be known as an "optogenetic" strategy—namely, to create a genetically encoded optical reporter of biological activity, or a light-driven actuator of biological signaling, and then to express the gene that encodes for this molecule in a specific cell or set of cells, often within an intact tissue or organism. Then, the investigator uses light to perform the readout of the biological system state by monitoring cells expressing optical reporters, say using a microscope, or to alter the biological system via illuminating it so that cells expressing the light-driven actuator are selectively altered.

The use of genetically encoded reagents insures ease of use, as well as the ability to target specific cells, even within intact tissues or organisms, thanks to the wealth of transgenic and gene-delivery mechanisms available for use in a variety of organisms utilized in modern biological science and preclinical medicine. The use of light insures high temporal fidelity of the observation or of the perturbation, and also supports spatial targeting of the observation or perturbation to defined cells or targets in the brain or body. In this way, observational or causal information, precisely obtained, about how a given molecularly defined pathway plays a role in cell-, tissue-, and organism-level operation can be obtained.

Over the past few years, the number of groups making, and utilizing, such optogenetic tools, has exploded. Several of the participants in this volume were involved with a Minisymposium at the 2010 Society for Neuroscience Meeting in San Diego, California, chaired by Thomas Knöpfel and Ed Boyden, titled "Towards the Second Generation of Optogenetic Tools." The symposium was standing room only throughout, a testament to the power such tools are having on neuroscience, a field in which there is a great desire to observe and see what is happening in a diversity of cells which are in turn assembled into very complex three-dimensional circuit formations within the brain. After the symposium was over, we decided that perhaps a book that was basically an extension of being the proceedings of such an event could be of great interest.

This book focuses on some recent inventions in the space of optogenetic tools, accompanied by critical evaluations of how they differ from past innovations in this space. The first half of this volume is made up of chapters that are organized around the kinds of tools being invented. Chapter 1, by Dugué and colleagues, gives an overview of the space of optogenetics, followed by Chapters 2 and 3 by Lin and by Boyden and colleagues, respectively, which deals with molecules that can be expressed in neurons to make them sensitive to being activated or silenced by pulses of light. We then switch directions, for two chapters, focusing on tools for reading out neural activity, using molecules that change fluorescence in response to changes in voltage (Chapter 4 by Knöpfel and colleagues) or calcium (Chapter 5 by Looger and colleagues). We then continue with a chapter on how protein multimerization can be controlled with light, using light-driven proteins from plants that, when illuminated, bind to one another (Chapter 6 by Tucker), thus enabling optical control of gene expression and other signaling functions.

The second half of this volume explores how tools can be used, in a variety of systems. Chapter 7, by Emiliani and colleagues, focuses on strategies for the use of two-photon microscopy to activate optogenetic reagents. In Chapter 8, Scott and colleagues explore the use of optogenetics in zebrafish;

in Chapter 9, Urban and Rossier explore the use of optogenetics in the mammalian cerebral cortex; and in Chapter 10, Zeng and Madisen explore the use of optogenetics in the context of transgenic mice. In Chapter 11, Han explains how to utilize optogenetics in the context of the living nonhuman primate brain, and in Chapter 12, Yellen and colleagues utilize optogenetics to study metabolism.

Our goal is that this volume not only presents current details about optogenetic tools but also the underlying logic of how they work and how they can be applied, as well as practical information about their use.

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