Preface

The small fruit fly, *Drosophila melanogaster*, has for over a century now had a large impact on biological and biomedical research. From the description of the rules of heredity to the elucidation of signals necessary for development, *Drosophila* research has greatly contributed to—and often lead to—the emergence of important paradigms in our understanding of development, physiology, behavior, and disease. The use of *Drosophila* as a model system for the genetic control of almost every biological process one can think of has meant that we now have a detailed understanding of the genetic logic underlying this animal's development, as well as of the cellular organization of most of its tissues and organs. It is therefore rather surprising that our knowledge of the fly brain has lagged significantly behind our understanding of other aspects of its development, physiology, and function. In part, this is due to the sheer complexity of the brain. In that sense, despite a significantly reduced size in comparison to the mouse brain, for example, the fly brain is exquisitely complicated in its connectivity pattern and compartmentalization. Related to that is the fact that studying the brain requires sophisticated tools, both genetic and technical, to carefully dissect its development, physiology, function, and eventually degeneration and to eventually link these different aspects to the genetic logic(s) underlying them.

The past decade has witnessed a massive expansion in the extent and sophistication of the genetic tool kit of *Drosophila*. Because of the generic nature of genetic approaches, brain research has benefited significantly from essentially all of these approaches. In addition, increasingly clever and technologically sophisticated behavioral assays have led to an increase in the number of laboratories studying behavioral encoding using *Drosophila* as a model system. Much more recent developments and expansions of these tools mean that we are on the verge of a veritable revolution in our understanding of the genetic, cellular, and network properties of the formation and function of the fly brain.

This book is intended as a general introduction to the ideas and concepts behind the methods, tools, and tricks that *Drosophila* neuroscientists utilize to decode the secrets of their favorite enigma. It is by no means intended to be an exhaustive survey of the approaches used in studying the fly brain. Rather, it provides cutting-edge examples of the tools and techniques used today in the research aimed at understanding the fly brain as a model for understanding how brains are organized and how they encode innate behaviors and learn new ones. The major purpose is to equip current and future *Drosophila* neurobiologists with a set of cutting-edge tools and the ideas underlying them so that fly neurobiologists are able not only to exploit these techniques but also to develop them further to suit their particular needs.

In this sense, there are perhaps two aims of this volume that are essential to emphasize in introducing it. The first idea is that the major unifying focus of the different chapters is the concept of a neuronal circuit, defined as a series of synaptically connected neurons subservient to a particular behavioral modality. This is why, after an introduction to the general anatomy of the fly brain and its compartmental organization, all chapters dealing with anatomical analysis focus on cellular and subcellular morphologies. These chapters range from presenting the reader with currently available genetically encoded neuronal markers to methods for generating labeled single neurons, imaging them at very high resolution and reconstructing those images, eventually into circuit diagrams. Although each of these chapters uses examples in different neuronal lineages and at different developmental stages, the basic tools and methodologies apply equally well to any neuron or circuit the reader wishes to study. Once assembled, a circuit functions via synaptic communication between its members in order to allow the animal to encode, produce, and learn behaviors. The classical approach to circuit function is electrophysiological recording of neuronal activity. An emerging, and increasingly powerful, alternative is visualization of synaptic activity through genetically encoded indicators. Part II of the book provides two powerful examples of these two approaches. Importantly, one chapter deals with studying neuronal physiology at larval stages and the other in the adult brain. This is in order to cover the two major forms of the *Drosophila* life cycle that are heavily used by researchers. In a very similar vein, Part III of the book provides assays for larval as well as adult behavioral paradigms.

The second major aim of the book is to have a current and futuristic "feel" to it. To this end, two elements were incorporated into the book's concept. First, the choice of contributors is intended to reflect a relatively "young" group of fly neurobiologists who are nonetheless at the forefront of developing tools for the study of brain development, anatomy, and function. In fact, the lead authors of almost all chapters describe approaches that they themselves have developed and that are setting new standards for neuronal circuit analysis. Here, it is important to emphasize that there are many, many more such talented scientists in the field developing at least equally exciting approaches. However, it is simply impossible to include the entire spectrum of tools currently available. Thus, this book by no means claims comprehensiveness, but rather provides a relatively limited selection of many equally good approaches, but which nonetheless covers a broad spectrum of modern concepts and techniques. The choice of the contributors is also intended to provide methods that are constantly being updated by the authors themselves. We hope that this allows the user direct access to the source of further information about an insight into most of the methods. Second, we included a final Part IV which includes chapters on relatively recent developments that are still finding their way into broader use and are still being further optimized by many workers in the field. Specifically, we hazard to predict that more hardcore molecular, ex vivo and even in vitro approaches that have proven very powerful in gaining insights into the working of mammalian neurons will become increasingly used in *Drosophila* neurobiology research to complement the classical in vivo genetic approaches. On the subject of prediction, we also assume the risk of predicting that developmental, anatomical, physiological, and behavioral vision research in *Drosophila* will likely rise to significant prominence in the medium-term future of fly neuroscience. This is why one of the two chapters in Part II and both chapters of the behavioral section apply their tools strongly or exclusively to the visual system. The fly visual system has lagged behind other models mainly due to the complexity and density of its connections. However, the rapid progress being made at mapping the entire fly brain connectome means that the complexity of the visual system will change from being a foreboding into being an enticing problem to solve.

In closing, and on behalf of all the authors, we hope that readers will find in this book the information and tools necessary to carry out their current experiments and—more importantly—further advance the progress of the *Drosophila* neurobiology field and neurobiology in general.

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http://www.springer.com/978-1-61779-829-0

The Making and Un-Making of Neuronal Circuits in Drosophila
(Ed.)B.A. Hassan
2012, XIV, 278 p. 48 illus., 39 in color., Hardcover
ISBN: 978-1-61779-829-0
A product of Humana Press