

# Introduction

The fly sat upon the axle tree of the chariot-wheel and said, what a dust do I raise!

—Aesop

An important question in developmental biology is how a single-celled embryo gets transformed into a multicellular three-dimensional organism with complex structure and functions. The quest to understand this important facet of development resembles the search for the holy grail of modern day biology. Patterning and development of an organism require production of specific number of cells whose fate is determined by a genetic circuitry. Any perturbation in this finely tuned process results in defects. Therefore, the basic cell biological process of cell proliferation, cell differentiation, and cell death play important roles in sculpting an organ during organogenesis. In developmental biology, it is important to unravel the mechanism of fate assignment and differentiation.

The time tested *Drosophila melanogaster* (fruit fly) model has played a central role in developmental biology during the twentieth century. The *Drosophila* model has a long genetic legacy, beginning with Thomas Hunt Morgan in early 1900 (Morgan 1911). A judicious blend of molecular and developmental genetics has proved beyond doubt that *Drosophila* is a valuable model for addressing important questions of modern day biology. There are several thousand people whose work/lives center around the little fruit fly *Drosophila melanogaster*. In recent years, the emphasis of their studies has shifted from inheritance to development and disease. In the hands of a small number of particularly imaginative scientists, traditional genetics, experimental embryology, and new molecular genetic techniques have been combined to build a picture of developmental mechanisms. To date, *Drosophila* has maintained its status as a trusted and highly versatile model to study patterning, growth, and disease. Among all the adult body structures, the *Drosophila* eye, because of its simple structure, and easy amenability to mutations and genome-wide screens has become an important tool in the hands of Drosophilists.

The study of developing eye from a two-dimensional eye primordium to a three-dimensional adult eye and visual system, and use of eye model to study patterning, growth, development, evolution, and disease is the topic of the current book. The *Drosophila* eye has been intensively studied to explore cell biological processes like cell fate specification, patterning, growth, and cell signaling, etc. Understanding

the generation and functioning of eye as an organ, our primary sensory modality, is important. We are curious to know how the visual system assembles.

It is now almost 37 years since the seminal paper from Ready et al. (1976) described the development and structure of *Drosophila* compound eye. The discovery of morphogenetic furrow (MF), a wave of differentiation, which is initiated from the posterior margin of the eye imaginal disc and sweeps in the anterior direction (Ready et al. 1976), is considered to be a major milestone in *Drosophila* eye field. It results in differentiation of retinal precursor cells to photoreceptor neurons. It was known that adult appendage develops from a group of cells set aside during embryonic development, which grows during larval stages and then metamorphose into adult appendages. Tomlinson provided the electron microscopic view of cellular events that follow the formation of morphogenetic furrow (Tomlinson 1985). Generation of monoclonal antibodies to detect early cell differentiation was another major landmark (Fujita et al. 1982). Enhancer trap technique using P element-mediated transgenesis proved to be an important tool that still remains an asset in the arsenal of modern day fly geneticist's tool kit (Bellen et al. 1989; Grossniklaus et al. 1989; Wilson et al. 1989). Another important milestone was demonstration of structural and functional similarity in the genetic circuitry involved in eye development in flies and humans (Halder et al. 1995; Quiring et al. 1994). These studies completely changed the outlook of the eye field. Halder et al. (1995) reported the master selector gene concept in the eye where they demonstrated that *eyeless (ey)* *Drosophila* homolog of *PAX-6* gene could reprogram other tissues and generate ectopic eyes in the wing, leg, and antenna. These studies provided a great impetus to the *Drosophila* eye model, which, by then, was also used to address questions for human disease. The evolution of *Drosophila* eye research cannot be complete without mentioning the contributions of Seymour Benzer, Walter Gehring, and Gerald M Rubin. The hard work of Gerald Rubin and his collaborators came to fruition when fly genome was published in the year 2000 (Adams et al. 2000; Myers et al. 2000; Rubin et al. 2000). It was instrumental in validating the observation of Gehring's group that there is a strong conservation in the genetic circuitry of flies with that of humans and other vertebrates. It completely changed the field and put the fly model on the forefront among all other animal models. These discoveries led to generation of new genetic and molecular technology, and put *Drosophila* eye model system on the forefront of biological research to address important questions related to human diseases like retinal diseases, neurodegenerative disorders, cancers, etc. Furthermore, the *Drosophila* eye model provided more versatility to study basic cell biological processes of patterning, growth, cell proliferation, and cell death and to carry out genome-wide screens.

This picture is new and exciting, although far from complete. It represents the beginnings of a real understanding of how one animal is designed and built. This book, which is written for the students as well as the specialists, aims to give an up-to-date glimpse of that picture. However, the field is developing so fast that some of the things may change; therefore, we have tried to use well-established material. We have made an attempt to provide an overview of approaches used in the fly eye model. We have dealt with the basic question of patterning of how eye develops starting from

early events of specification to molecular mechanisms involved in transition of eye from a monolayer epithelium to a three-dimensional structure. During this transition, one of the hallmark events is formation of the morphogenetic furrow (MF). This book also highlights events of morphogenesis, cell polarity, cell adhesion, and negative regulation of neural patterning in developing *Drosophila* eye. Other areas discussed in this book are use of *Drosophila* eye model to understand protein homeostasis network, organ size control mechanism, and genetic basis of neurodegeneration. The book also encompasses an important aspect of development and evolution during early eye development as well as larval eye or Bolwig's organ.

The collection of chapters in this book helps us celebrate hundred plus years of research using *Drosophila* eye model, and provides a blueprint of future research directions and frontiers in this field. We hope you enjoy reading this book as much as we did. We would like to end with a quotation (Dryden J (1696) from: The epilogue to The Husband his own Cuckold, lines 35–37):

Fools change in England, and new fools arise'  
For, tho' th' immortal species never dies,  
Yet ev'ry year new maggots make new flies. . . .'

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