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Review

Waves of differentiation in the fly visual system

Makoto Sato [a,b,*], Takumi Suzuki [a], Yasuhiro Nakai [a]

[a] Brain/Liver Interface Medicine Research Center, Graduate School of Medical Sciences, Lab of Developmental Neurobiology, Kanazawa University, Japan
[b] PRESTO, JST, Japan

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ABSTRACT

Sequential progression of differentiation in a tissue or in multiple tissues in a synchronized manner plays important roles in development. Such waves of differentiation are especially important in the development of the *Drosophila* visual system, which is composed of the retina and the optic lobe of the brain. All of the components of the fly visual system are topographically connected, and each ommatidial unit in the retina corresponds to a columnar unit in the optic lobe, which is composed of lamina, medulla, lobula and lobula plate. In the developing retina, the wave of differentiation follows the morphogenetic furrow, which progresses in a posterior-to-anterior direction. At the same time, differentiation of the lamina progresses in the same direction, behind the lamina furrow. This is not just a coincidence: differentiated photoreceptor neurons in the retina sequentially send axons to the developing lamina and trigger differentiation of lamina neurons to ensure the progression of the lamina furrow just like the furrow in the retina. Similarly, development of the medulla accompanies a wave of differentiation called the proneural wave. Thus, the waves of differentiation play important roles in establishing topographic connections throughout the fly visual system. In this article, we review how neuronal differentiation and connectivity are orchestrated in the fly visual system by multiple waves of differentiation.

Contents

Introduction

During the development of complex neuronal circuits in the brain, sequential progression of neuronal differentiation may provide clues to the establishment of precise and repetitive neuronal connections. The *Drosophila* visual system is the best example among such systems studied to date. All of the components of the fly visual system (retina, lamina, medulla, lobula and

* Correspondence to: Graduate School of Medical Sciences, Kanazawa University, b43-1, bldg B, 13-1 Takaramachi, Kanazawa, Ishikawa 920-8641, Japan. Fax: +81 76 234 4239.
E-mail addresses: makotos@staff.kanazawa-u.ac.jp, Ćsatouma@mac.com (M. Sato).
URL: http://fsosato.w3.kanazawa-u.ac.jp/indexE.html (M. Sato).

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lobula plate) appear to contain similar numbers of columnar structures and are topographically connected (Fig. 1A, Fischbach and Dittrich, 1989). Of these components, the development of at least the retina, lamina and medulla is accompanied by waves of differentiation (Tomlinson and Ready, 1987; Selleck et al., 1992; Yasugi et al., 2008). Additionally, waves of neuronal differentiation concomitantly produce waves of neuronal projections, arborizations and connections. Thus, synchronization and orchestration among different parts of the visual system are necessary to establish precise neuronal circuits throughout the fly visual system. A similar developmental strategy is also found in vertebrate visual system (Kollros, 1982; Mumm et al., 2006; Neumann and Nuesslein-Volhard, 2000; Raymond et al., 1983; Yang et al., 2009) and olfactory system (Gong and Shipley, 1995). Thus, extensive study of the fly visual system may provide great insights into developmental neurobiology in other systems that display waves of differentiation.

Cajal established the basis of modern neuroscience and neuroanatomy by extensive Golgi studies of the vertebrate central nervous systems. However, he was interested in insect nervous systems in his later years and was surprised at the complex and precise connections of the neuronal circuits found in the insect nervous systems, especially in the optic lobe, the visual center of the insect brain (Cajal and Sanchez, 1915; Sanes and Zipursky, 2010). The visual information along the two-dimensional sheet received in the retina (compound eye) is transmitted to the optic lobe in the brain with its two-dimensional topographic relationship preserved (Fig. 1A). Due to the retinotopic connections throughout the optic lobe, each columnar structure found in the optic lobe corresponds to an ommatidial unit in the retina. Additionally, the optic lobe contains multiple layered structures composed of neuronal processes that are orthogonal to the columnar structures (Fig. 1A, Fischbach and Dittrich, 1989). Thus, insect brains are as complex as vertebrate brains and share structural characteristics, such as columnar and layered structures.

Among many insect species, *Drosophila melanogaster* is one of the most advanced model organisms for developmental neurobiology, providing us with powerful molecular genetic tools and resources. In the history of the developmental neurobiology of the fly visual system, molecular mechanisms of photoreceptor neuron differentiation were extensively studied in the late 1980s to the early 1990s (Freeman, 1997). Subsequently, mechanisms of photoreceptor axon targeting have been extensively studied since the late 1990s (Hadjieconomou et al., 2011; Melnattur and Lee, 2011). Compared to the significant progress in our understanding of photoreceptor neuron differentiation and axonal targeting, we know relatively little about the mechanisms of development of the optic lobe, to which photoreceptor neurons project. However, recent progress in our understanding of optic lobe development has revealed the presence of differentiation waves in the development of the lamina and medulla that are similar to that of the morphogenetic furrow in the retina (Huang and Kunes, 1996; Selleck et al., 1992; Yasugi et al., 2008). The waves of differentiation not only yield sequential production of neurons but also enable sequential neuronal projections and connections with other neurons. Thus, the orchestration of multiple waves of differentiation found in different parts of the optic lobe may be a key to understanding the formation of neuronal circuits in the fly visual system. In this article, we review recent advances in the developmental neurobiology of the fly visual system by focusing on the roles of such waves in the formation of neuronal circuits in the brain.

Basic structures of the *Drosophila* visual system

The *Drosophila* retina is composed of 750–800 ommatidial units, each containing eight different types of photoreceptor

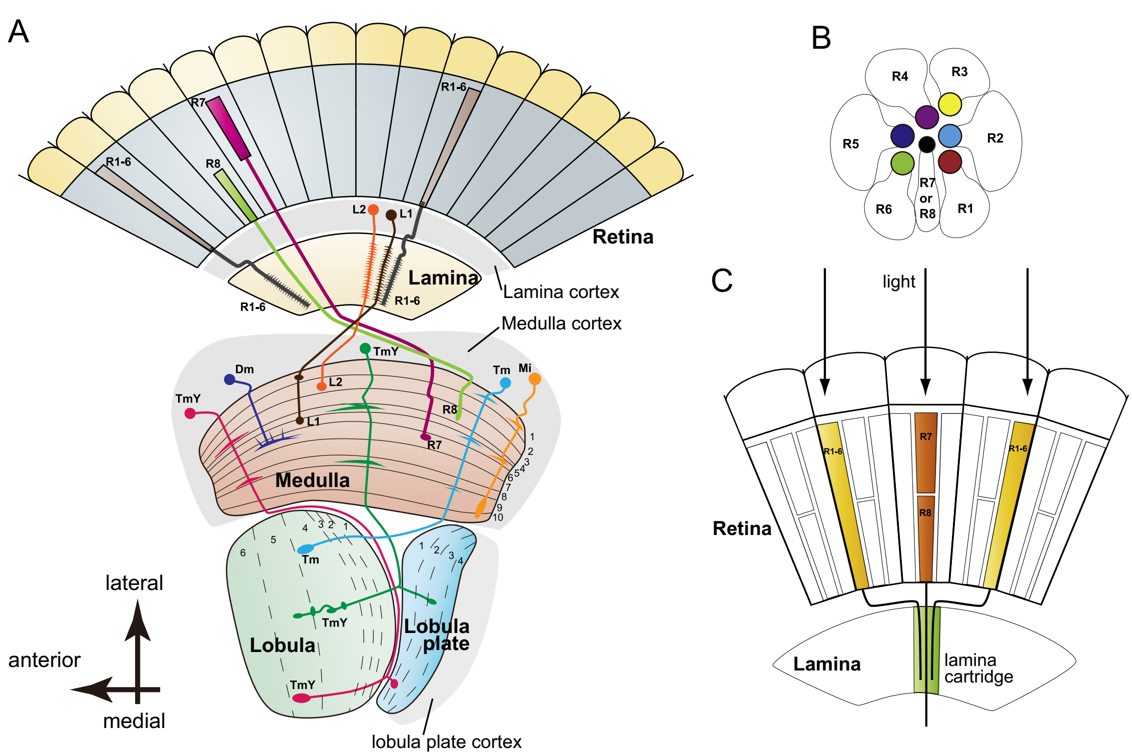

Fig. 1. Schematic drawings of the adult *Drosophila* visual system: (A) a horizontal section of the visual system including the retina, lamina, lobula and lobula plate, (B) a lateral view of the ommatidial unit. The colored circles are the rhabdomeres of photoreceptor cells, R1–8 and (C) a lamina cartridge processes visual stimuli originating from a same point in the visual space that are received by R7/8 placed at the center of an ommatidia and R1–6 in the neighboring ommatidia. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)