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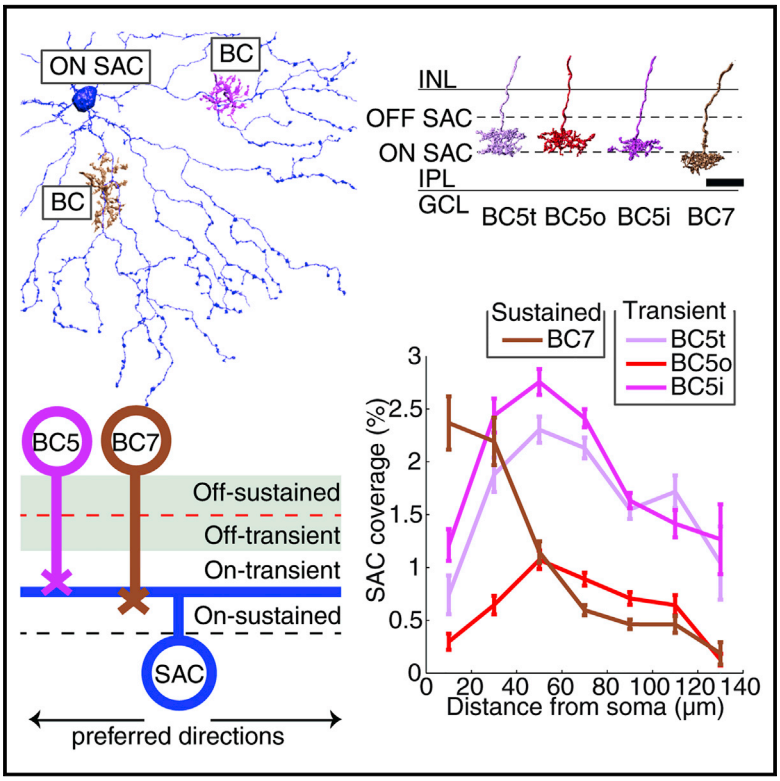
Analogous Convergence of Sustained and Transient Inputs in Parallel On and Off Pathways for Retinal Motion Computation

Graphical Abstract



Highlights

- We analyzed serial electron microscopic images of a mouse retina
- On starburst amacrine cells (SACs) and bipolar cells (BCs) were reconstructed
- We defined an additional On BC type in the course of classifying On BCs
- Sustained and transient BC types are wired to SAC dendrites at different distances

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In Brief

Greene et al. find that in the mouse retina, sustained and transient On bipolar cell (BC) types are wired to dendrites of On starburst amacrine cells (SACs) at different distances from the SAC soma. This wiring specificity may support retinal computation of the direction of a moving stimulus.

Greene et al., 2016, Cell Reports *14*, 1892–1900
March 1, 2016
http://dx.doi.org/10.1016/j.celrep.2016.02.001

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Analogous Convergence of Sustained and Transient Inputs in Parallel On and Off Pathways for Retinal Motion Computation

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http://dx.doi.org/10.1016/j.celrep.2016.02.001

SUMMARY

Visual motion information is computed by parallel On and Off pathways in the retina, which lead to On and Off types of starburst amacrine cells (SACs). The approximate mirror symmetry between this pair of cell types suggests that On and Off pathways might compute motion using analogous mechanisms. To test this idea, we reconstructed On SACs and On bipolar cells (BCs) from serial electron microscopic images of a mouse retina. We defined a new On BC type in the course of classifying On BCs. Through quantitative contact analysis, we found evidence that sustained and transient On BC types are wired to On SAC dendrites at different distances from the SAC soma, mirroring our previous wiring diagram for the Off BC-SAC circuit. Our finding is consistent with the hypothesis that On and Off pathways contain parallel correlation-type motion detectors.

INTRODUCTION

The starburst amacrine cell (SAC) is a key player in retinal computation of the direction of a moving stimulus. Ablation of SACs impairs the optokinetic reflex, a behavior that depends on computation of visual motion (Yoshida et al., 2001; Amthor et al., 2002). Both ablation (Yoshida et al., 2001; Amthor et al., 2002) and reversible inactivation (Vlasits et al., 2014) of SACs reduce direction selective (DS) responses in ganglion cells, which receive synaptic input from SACs. SAC dendrites are preferentially activated by visual stimuli that move outward from the soma to the dendritic tips (Euler et al., 2002; Lee and Zhou, 2006; Hausselt et al., 2007).

The proposed mechanisms for DS of SAC dendrites fall into several categories. According to inhibitory cellular hypotheses, dendritic biophysics causes inhibitory input to SACs to have effects that depend on dendritic location (Borg-Graham and Grzywacz, 1992; Gavrikov et al., 2003). In inhibitory circuit hypotheses, GABAergic synaptic connectivity between SAC dendrites depends on the difference between their preferred directions (Lee and Zhou, 2006; Münch and Werblin, 2006). In excitatory cellular hypotheses, SAC biophysics causes excitatory input to SACs to have effects that depend on dendritic location (Tukker et al., 2004; Hausselt et al., 2007; Oesch and Taylor, 2010).

Recently, we proposed an excitatory circuit hypothesis based on specificity of wiring between bipolar cells (BCs) and SACs. The proposal was based on anatomical evidence that sustained and transient BC types are connected to SACs at locations that are near and far from the SAC soma, respectively (Kim et al., 2014). Such "space-time wiring specificity" could make the BC-SAC circuit function as a correlation-type motion detector (Borst and Euler, 2011) and is consistent with the observed outward preferred direction of SAC dendrites.

Like many other retinal neurons, the SAC comes in both On and Off types. The On SAC resembles a reflection of the Off SAC across a plane through the middle of the inner plexiform layer (IPL) (Figures 1B and 1D). Probably due to this striking symmetry, DS and its mechanisms are often assumed to be similar between On and Off SACs. However, published studies of SACs were typically restricted to a single type. Physiological studies of DS were carried out for On SACs (Euler et al., 2002; Lee and Zhou, 2006; Hausselt et al., 2007), while our anatomical study of BC-SAC wiring specificity was carried out for Off SACs (Kim et al., 2014).

Here, we find evidence that the On BC-SAC circuit possesses a space-time wiring specificity analogous to that shown previously for the Off BC-SAC circuit. We reconstructed a large set of On BCs and On SACs from e2198, a dataset of mouse retinal images from serial block-face scanning electron microscopy (Briggman et al., 2011). Based on the resulting high-resolution information about the anatomy of single cells, we have succeeded in subdividing BC5 into three types that we call BC5t, BC5i, and BC5o. This finding confirms Helmstaedter et al. (2013), who were previously able to distinguish just two BC5 types, but predicted the existence of more. Our definition of a third BC5 type increases the total count of cone BC types to 13.