novel sequences whose function remains to be discovered, opening new avenues of research. Other genes could help to refine the results from quantitative trait loci analysis, in which large chromosomal regions are linked to specific phenotypes. Finally, the existence of region-specific genes should lead to the identification of the sequences that regulate their restricted expression, which could then be used to drive the region-specific expression of any transgene.

The differences in gene expression might be subtle but they provide some valuable signposts for future work.

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**WEB SITE** C. Barlow's laboratory


**that a lower level of oscillatory activity is preserved in spite of the drugs. Could these remaining oscillations be related to the state-dependent retrieval that is observed (so they tell me) after drug intake?**

*Juan Carlos López*


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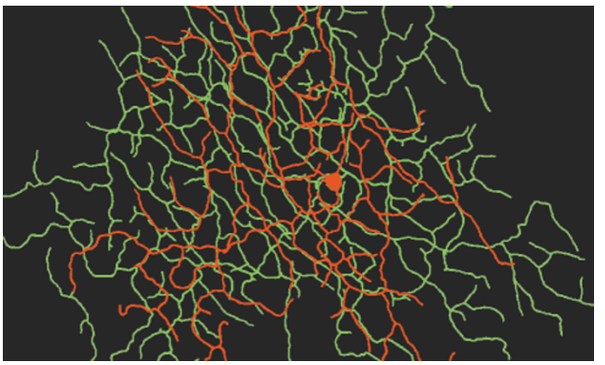
**WEB SITE** Tamas Freund's department

A reconstructed On–Off DSGC, with the soma and proximal (On) dendrites in red and distal (Off) dendrites in green. Image supplied by David Vaney, University of Queensland, Australia.

VISION

# A sense of direction

**Horace Barlow and William Levick first described the properties of the direction-selective ganglion cells (DSGCs) in the retina way back in the mid-1960's. They reported that the most common type of DSGC, which is activated by the onset and termination of light (On–Off DSGC), responds preferentially to image motion, the direction of which is aligned with one of four axes (up, down, forward or backward). Despite the intervening years and the relative simplicity of the retinal system (the DSGCs are located only two or three synapses from the photoreceptors), the precise locus and mechanism of direction selectivity in the retina has remained elusive.**

**Although image motion in both the preferred direction and the opposite 'null' direction activates interneurons that excite the DSGCs, electrophysiological evidence indicates that the excitation in the null direction is cancelled by spatially offset input from inhibitory interneurons. Conversely, in the preferred direction, the excitation and inhibition are not spatially and temporally coincident, and the excitation therefore escapes the inhibition. This circuitry therefore provides a mechanism for direction selectivity. But where and how does the interaction between excitation and inhibition occur?**

**Logically, the null-direction inhibition could act either presynaptically on the excitatory inputs to the DSGCs or postsynaptically on the dendrites of the DSGCs. A report in the September 29 issue of *Science* suggests that spatially asymmetric inhibition acts postsynaptically. Recordings made in rabbit retina whole-mounts by Taylor, He, Levick and Vaney showed that the DSGCs responded strongly to a stimulus moving in the preferred direction and only weakly to a stimulus moving in the null direction or orthogonal directions. However, when the patch clamp was used to load the DSGC with chloride, thereby preventing the excitatory and inhibitory channels in the DSGC membrane from interacting, the difference between the synaptic currents elicited by image motion in the preferred and null directions disappeared, consistent with a postsynaptic site. These results show that direction selectivity is conferred by null-direction inhibition, acting postsynaptically on ganglion cell dendrites. The simplicity of this system should now allow the precise characterization of the computational properties of dendrites, and this may have far-reaching implications for our view of computation in the brain.**

*Peter Collins*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**ENCYCLOPEDIA OF LIFE SCIENCES** Dendritic Spines
**WEB SITES** Rowland Taylor | David Vaney


DEVELOPMENT

# Sim and Sonic

The patterning of embryonic neural tissue provides the template for development of the mature nervous system and consequently must proceed with remarkable precision. Sonic Hedgehog (Shh), a protein secreted by the axial mesoderm and the ventral midline of the developing central nervous system, is a key regulator of these patterns of cellular growth and differentiation. Along the dorso-ventral axis, a gradient of Shh activity guides the establishment of a variety of cell fates. The role of Shh seems to be more complex along the antero-posterior axis and is thought to depend on interactions between Shh and other signalling pathways, although the genes coordinating *Shh* expression are poorly understood.

A report from Epstein *et. al.* in *Development* demonstrates that within the ventral areas of diencephalon, members of the basic helix–loop–helix–PAS (bHLH–PAS) protein family could activate *Shh* transcription. By assessing the temporal and spatial overlap between known transcription factors and an *Shh* reporter construct expressing *lacZ* in rostal regions, this group revealed that Sim2, a member of the bHLH–PAS family, may function as a *Shh* activator in developing ventral diencephalon. Moreover, mis-expression of *Sim2* in transgenic mice led to ectopic expression of *Shh*. Although *Shh* expression was maintained in $Sim2^{-/-}$ mutants, it was absent from rostral midbrain and caudal diencephalon of embryos carrying a dominant-negative transgene that disrupts the function of bHLH–PAS proteins. These results indicate that Sim2 and possibly other members of the bHLH–PAS family may be important new regulators of *Shh* expression.

*Peter Collins*


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