

Per expression was rescued in the  $LN_v$  neurons, the morning activity peak was restored, but when it was rescued in both the  $LN_v$  and  $LN_d$  neurons, both the morning and evening activity peaks were normal.

Both groups also found that the 'morning' oscillator, maintained by the  $LN_v$  neurons, can be maintained in sustained darkness, whereas the 'evening' oscillator cannot, although this is difficult to reconcile with findings that the morning peak, but not the evening peak, is progressively lost when wild-type flies are placed in darkness. It is likely that these two oscillators, although they can act independently, are functionally coupled under normal circumstances to allow them to be coordinated and to respond flexibly to challenges such as seasonal changes.

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### References and links

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**FURTHER READING** Hastings, M. H. *et al.* A clockwork web: circadian timing in brain and periphery, in health and disease. *Nature Rev. Neurosci.* **4**, 649–661 (2003)

through the  $G\alpha_q$  pathway or decreased signalling through the  $G\alpha_o$  pathway resulted in dopamine resistance. These results and others fit a model in which DOP-3 signals through  $G\alpha_o$  to inhibit locomotion, and DOP-1 antagonizes this effect by signalling through  $G\alpha_q$ .

Dopamine signalling in worms shows striking parallels with the dopamine system in mammals. In both types of animal, D1- and D2-like receptors are expressed at different levels in the same neurons, and can have opposing effects on behaviour. As in worms, D1 receptors in mammals can activate  $G\alpha_q$  signalling, and D2 receptors can activate  $G\alpha_o$  signalling, although it has not been previously shown that these pathways mediate their antagonistic effects. Moreover, dopamine in both worms and mammals can act extrasynaptically as a neurohormone. If these parallels hold true for other details of dopamine signalling, results from studies of *C. elegans* could give important insights into how mammalian dopamine receptors function.

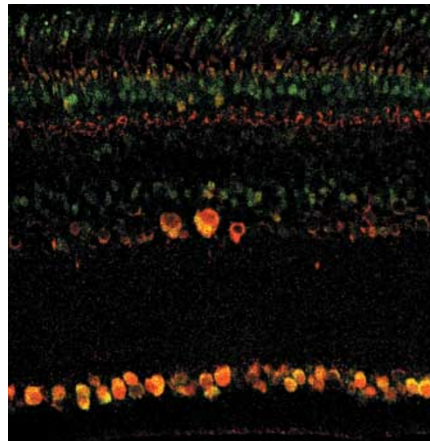
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#### WEB SITE

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Left: retina section of garden warbler, stained with CRY1 (green) and c-Fos (red). Figure reproduced, with permission, from The National Academy of Sciences USA. Right: a garden warbler. Image courtesy of H. Mouritsen, University of Oldenburg, Germany.



### SENSORY SYSTEMS

## Homing in on magnetic orientation

Migratory birds use the Earth's magnetic field for homing and navigation. How they do this is not clear, but theoretical biophysicists have predicted that photoreceptor molecules in the retina might be involved in sensing magnetic fields. Reporting in the *Proceedings of the National Academy of Sciences*, Mouritsen and colleagues investigated the expression of cryptochromes (CRYs) — blue-green photoreceptors that are important in the regulation of circadian rhythms — in the retina and their association with neuronal activity during magnetic orientation.

Biophysicists have proposed that magnetic sensing might be based on the sensitivity of a class of chemical reactions called radical-pair reactions to magnetic fields. In a radical-pair reaction, absorption of light through a photoreceptor molecule, such as a CRY, induces the transfer of an electron from one molecule to another and results in a pair of molecules each with an unpaired electron. These unpaired electrons have particular spin states that can be affected by an external magnetic field, which might alter downstream chemical and biological events.

This theoretical analysis is supported by the fact that magnetic sensing in migratory birds is light-dependent: they can sense magnetic fields under blue and green light but become disorientated under dim red light. This observation also indicates that CRYs might be involved in radical-pair reactions in magnetoreception. In this study, Mouritsen and colleagues identified two CRY isoforms in the retina of migratory garden warblers — the cytosolic gwCRY1 and the nuclear gwCRY2. As molecules that serve as magnetoreceptors must be orientated in the cell and, therefore, are more likely to be localized in

the cytosol in association with cytoskeletal proteins, the authors focused on gwCRY1.

In the retina of non-migratory zebra finches, expression of CRY1 is high during the day and drops markedly at night. In migratory garden warblers, CRY1 is expressed during both day and night in the retinal ganglion cells and a specific group of cells in the retina called displaced ganglion cells that have been implicated in magnetoreception. Interestingly, expression of CRY1 is absent in displaced ganglion cells in zebra finches.

The authors then analysed the functional relevance of CRY expression for magnetoreception by studying the expression of c-Fos and ZENK — markers of light-dependent neuronal activation — in migratory and non-migratory birds. They found that both c-Fos and ZENK were strongly expressed in the retina of garden warblers at night during magnetic orientation, and the expression co-localized with CRY1 in all ganglion cells and displaced ganglion cells. By contrast, c-Fos is only weakly expressed during the night in the retina of zebra finches, and expression of c-Fos in displaced ganglion cells does not correlate with that of CRY1.

Although direct functional evidence is still lacking to support a definitive role for CRYs in magnetoreception, the study is an encouraging step towards unravelling the molecular mechanisms of magnetic orientation.

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