

The Role of the Radical Pair Mechanism in Avian Magnetoreception

Kevin B. Henbest (1), Jingjing Xu (2), Lauren E. Jarocha1 (1), Tilo Zollitsch (1), Marcin Konowalczyk (1), Sabine Richert (1), Matthew J. Golesworthy (1), Tommy L. Pitcher (1), Gabriel Moise(1), Joseph S. Takahashi (3), Stefan Weber (4), Henrik Mouritsen (2), P. J. Hore (1), Stuart R. Mackenzie (1), Christiane R. Timmel (1)

Department of Chemistry, University of Oxford, Oxford OX1 3QR, UK, (2) AG Neurosensory Sciences/Animal Navigation, Institut für Biologie und Umweltwissenschaften, Carl-von Ossietzky Universität Oldenburg, 26111 Oldenburg, Germany, (3) Department of Neuroscience, University of Texas Southwestern Medical Center, Dallas, TX 75390-9111, USA, (4) Institut für Physikalische Chemie, Albert-Ludwigs-Universität Freiburg, 79104 Freiburg, Germany.

christiane.timmel@chem.ox.ac.uk

Although it has been known for half a century that night-migratory songbirds can detect the strength and direction of the Earth's magnetic field for the purposes of orientation and navigation, the primary sensory mechanisms responsible for this fascinating feat are still obscure. Schulten's suggestion in 1978 [1] that this capability might be driven by a quantum mechanical process involving a pair of photoinduced radicals was long considered to be an exotic and highly unlikely hypothesis. However, with the discovery of cryptochromes [2], a family of blue light photoreceptor proteins, this radical pair hypothesis has taken centre stage in the discussion of animal magnetosensitivity and is now, arguably, the most likely mechanism to drive this fascinating process.

Here we report that the photochemistry of cryptochrome 4 from the night-migratory European robin (*Erithacus rubecula*, *Er*Cry4) is indeed magnetically sensitive *in vitro*, and compare the results to those found for Cry4 from two non-migratory bird species, chicken and pigeon. Site-specific mutations of *Er*Cry4 in combination with Electron Paramagnetic Resonance studies are used to demonstrate the roles of four successive flavin-tryptophan radical pairs in generating magnetic field effects and in stabilising potential signalling states [3].

- [1] Schulten, K.; Swenberg, C. & Weller, A. Z. Phys. Chem., 111, 1–5 (1978)
- [2] Ahmad, M. & Cashmore, A.R., *Nature*, **366**, 162–166 (1993)
- [3] Xu J. et al., Nature, **594**, 535-540 (2021)

