Sensory biology

Doubt cast on magnetic sensing in flies

Eric J. Warrant

It has long been thought that the fly *Drosophila melanogaster* can detect Earth's magnetic field and offers an ideal system in which to examine this enigmatic sense. However, a rigorous replication of key studies fails to support this idea. **See p.595**

Earth's magnetic field is a remarkably stable compass cue used by many terrestrial and aquatic animals for navigation and orientation[1], and the list of organisms known to sense it is growing steadily. Among the organisms on the list is the fruit fly *Drosophila melanogaster* (Fig. 1), whose magnetic sense was first implicated more than 50 years ago[2] and was highlighted again in a landmark study in 2008 (ref. 3). These discoveries were exciting, given that *Drosophila* has such a small and experimentally accessible nervous system, and that the veritable trove of tools available for genetic modification of this insect raised the possibility of finally discovering the physiological basis of the elusive magnetic sense. But now, on page 595, Bassetto *et al.*[4] cast doubt on the existence of a magnetic sense in this species. They present an incredibly rigorous set of experiments that examined around 110,000 flies and failed to replicate the results of either the landmark 2008 study[3] (which examined a few hundred flies) or a watershed 2014 study[5].

Any sensory biologist who has dared to work on the magnetic sense of animals knows it is notoriously difficult. For one thing, the stimulus itself – Earth's magnetic field – lies outside our own sensory realm. We can't see, hear or feel it, and we have immense difficulty picturing magnetic stimuli in our minds.

To make matters worse, we have little idea how animals sense magnetic fields, and absolutely no idea where the magnetosensory organ (or cells) are located on or in the body. There are several hypotheses[1], from the action of tiny particles of ferrous magnetite that are physically attached to the ion channels of mechanosensory neurons and open and close the channels as the animal turns in the field, to the triggering of a light-dependent quantum-mechanical mechanism activated in magnetically sensitive cryptochrome (Cry) proteins embedded in a type of receptor that detects light (a photoreceptor) in the eye[1].

To add to these dilemmas, work also suggests that the magnetic sense is extremely 'noisy'[6], easily overwhelmed by other senses[7], knocked out by human-generated radiofrequency noise[8] and badly disturbed if magnetic objects are placed unwittingly in the vicinity of experimental apparatus. It is little wonder that the field of magnetosensation is riddled with arguably wild claims[9], debates about experimental results[10] and controversy.

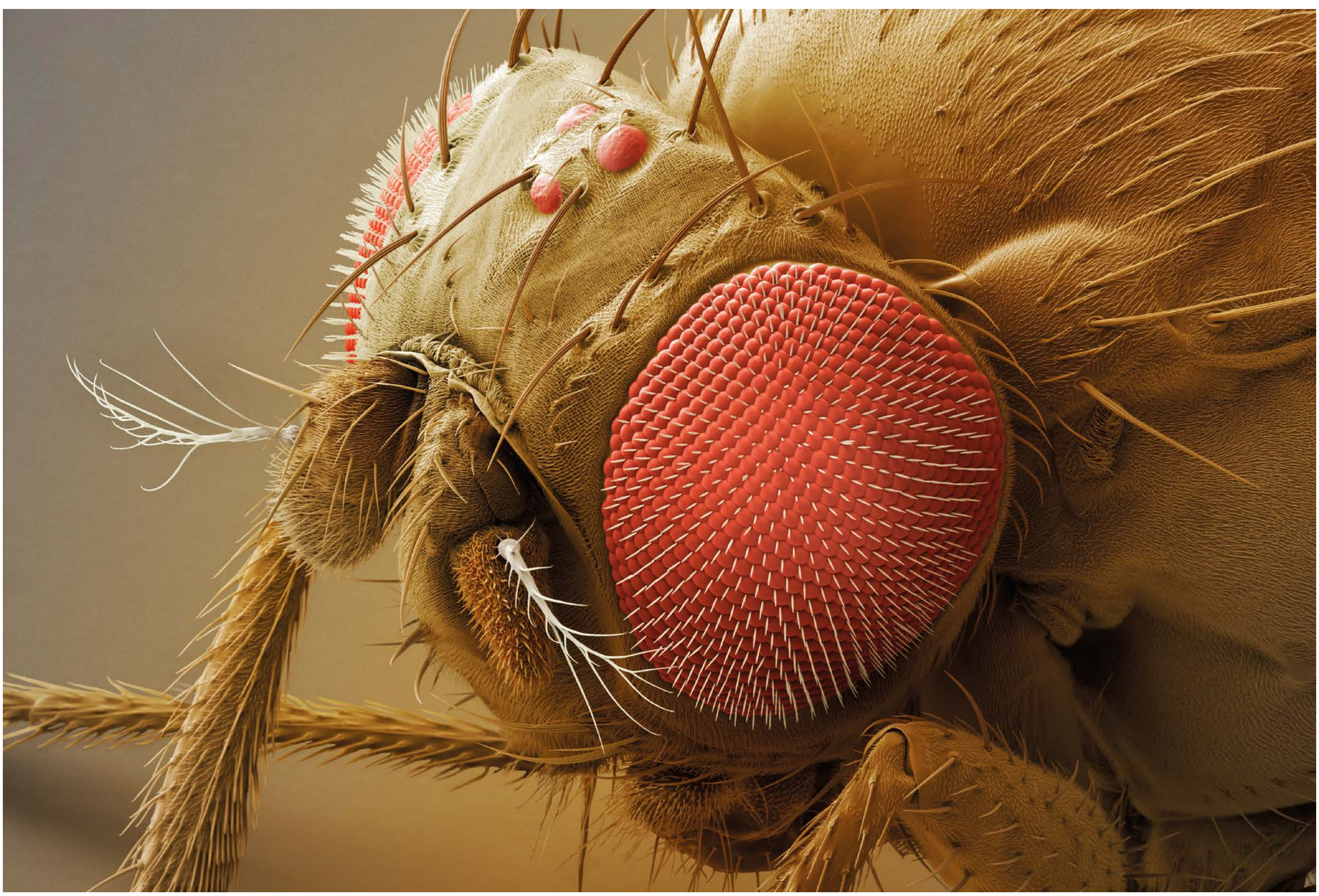

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Figure 1 | The fly *Drosophila melanogaster*.

For the 2008 study[3], around 100 flies were trained to associate food with a magnetic field that was roughly ten times the strength of Earth's, after which the flies were placed in a device (a two-choice tubular T-maze) used to examine behavioural preferences. Each of the two arms of the device was surrounded by a magnetic coil, but only one of these coils produced the learnt magnetic field. With broad-spectrum illumination (light with a wavelength of 300–700 nanometres), flies preferentially aggregated in the arm with the magnetic field. But when the blue–ultraviolet part of this spectrum (light with a wavelength of less than 420 nm) was removed, the flies distributed uniformly between the two arms, apparently oblivious to the magnetic field. Blue–ultraviolet light seems to be required for a magnetic sense that depends on Cry (ref. 1), and because Cry-deficient mutant flies failed to detect the magnetic field in broad-spectrum light, the authors concluded that *Drosophila*'s magnetic sense is Cry-based.

In the wake of this ground-breaking claim, a number of papers were published — some in high-profile journals — showing similar results (see references in ref. 4). The authors of the 2014 study[5] harnessed the ability of the fly to climb against gravity (negative geotaxis) to test the animal's magnetic sense, and found that in dim blue light, the climbing tendency was high in the absence of a static magnetic field, but poor when the field was present. With or without the field, climbing was poor in the absence of blue light or when Cry-deficient mutant flies were tested. These results support a Cry-based magnetic sense in *Drosophila*.

Bassetto and colleagues tried to replicate the two influential studies from 2008 and 2014 using the same strains of flies. They received blueprints of the apparatus used in 2008, which enabled them to manufacture an exact copy, and the authors of the 2014 paper supplied the actual apparatus used in their study.

In highly controlled conditions, with apparatus placed in an electromagnetically shielded chamber inside a non-magnetic building that blocked external background radiofrequency noise, Bassetto *et al*. rigorously repeated the 2008 study, testing 984 sets of 100 flies over 48 months (97,658 flies in total). The authors found no preference for magnetic fields in the T-maze experiment.

Likewise, when Bassetto and colleagues attempted to replicate the results of the 2014 study using almost 11,000 flies, they failed to detect a difference in fly climbing tendency in dim blue light either with or without an applied magnetic field. When they reassessed the statistical approaches and sample sizes used in the two earlier studies, Bassetto *et al.* concluded that most of the original results were probably false positives, indicating magnetic sensitivity where it didn't actually exist.

Bassetto and colleagues' study is incredibly rigorous, with extremely large sample sizes. It also used appropriate statistical methods and assumptions, and the experimenters were not told of the magnetic conditions used in each experiment. The work was performed in arguably the best-controlled environment for magnetic experimentation in the world, purpose-built to be free of magnetic artefacts and radiofrequency noise. Therefore, the results the authors obtained raise serious doubts about the presence of a magnetic sense in *Drosophila*.

But do the authors definitively debunk the existence of a magnetic sense in *Drosophila*? Possibly, although there are now at least 15 publications reporting that this sense does exist, with many indicating a Cry-based mechanism. Can all of them be wrong? Again, possibly — and for similar reasons — but this is a serious call to make. Exact replication is notoriously difficult because, for instance, the states of the flies (such as health, age or reproductive state) and environments (such as season, time of day, temperature or humidity) in the original and replicate experiments might have differed.

Nonetheless, Bassetto *et al*. have raised a major red flag over the likelihood of *Drosophila* having the capacity for magnetic sensing. Hopefully this will encourage further replication studies, as well as entirely new studies, to scrutinize the magnetic sense of *Drosophila* with the same level of rigour as the work undertaken by Bassetto and colleagues.

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1. Mouritsen, H. *Nature* **558**, 50–59 (2018).
2. Wehner, R. & Labhart, Th. *Experientia* **26**, 967–968 (1970).
3. Gegear, R. J., Casselman, A., Waddell, S. & Reppert, S. M. *Nature* **454**, 1014–1018 (2008).
4. Bassetto, M. *et al. Nature* **620**, 595–599 (2023).
5. Fedele, G., Green, E. W., Rosato, E. & Kyriacou, C. P. *Nature Commun*. **5**, 4391 (2014).
6. Johnsen, S., Lohmann, K. J. & Warrant, E. J. *J. Exp. Biol*. **223**, jeb164921 (2020).
7. Dreyer, D. *et al*. *Curr. Biol*. **28**, 2160–2166 (2018).
8. Engels, S. *et al*. *Nature* **509**, 353–356 (2014).
9. Meister, M. *eLife* **5**, e17210 (2016).
10. Malkemper, E. P. *et al*. *Commun. Biol*. **6**, 242 (2023).

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Allergies

The immunology that underlies picky eating

Marc E. Rothenberg

Humans can be picky eaters. One such behaviour is an aversion to food associated with food allergy. The immunological basis for this response has been uncovered in mice, revealing the role of neuroimmune connections. **See p.634 & p.643**

Allergic diseases are on the rise, affecting 30–40% of the global population[1]. Research often focuses on the illness and death associated with these and other immune-mediated diseases, but emerging evidence suggests that allergies also provide some protection and benefit. Food aversion, for instance, can limit exposure to harmful stimuli, acting as a defence strategy to prevent further damage. Yet how allergy and food aversion are connected mechanistically has been unclear. Writing in *Nature*, Plum *et al.*[2] (page 634) and Florsheim *et al.*[3] (page 643) report evidence in mice that the arm of the immune system involved in allergic responses communicates with the brain, and thereby leads to food avoidance.

The authors report that this avoidance response involves a neuroimmune pathway that requires antibody responses (relying on a type of antibody termed IgE). The pathway also depends on activation of a population of gut-resident immune cells called mast cells, which produce and release molecules called leukotrienes that are normally associated with promoting inflammation (Fig. 1).

The brain and immune system communicate readily through, for example, a system (called the efferent hypothalamic–pituitary–adrenal axis) that regulates production of a potent anti-inflammatory hormone called cortisol. This communication is bidirectional, and the immune system can activate structures outside the brain called afferent nerve fibres. These fibres are extensions of sensory neurons that connect to the brain and generate molecules called cytokines in the brain.

What is often unappreciated is that these biological responses can be altered through learning or conditioning — the brain can

Correction

The image of a fly that originally accompanied this article was not, as stated, *Drosophila melanogaster*. The image has now been replaced.