61 days afterwards) and at long wavelengths (up to 5 micrometres). The emission spectra contain a line feature near 2 µm, similar to one seen in the GW170817 event. Building on a previously reported theoretical study[11], the authors suggest (but do not prove) that this line arises from tellurium, an r-process element.

Levan *et al.* and Yang *et al.* carried out modelling of the kilonova signatures, which suggested that a mass equivalent to one-twentieth to one-tenth of the mass of the Sun was ejected from the source of the GRB, and that this ejecta contained heavy elements (lanthanides) produced by the r-process. This corroborates what was indicated by studies of GW170817 – that kilonovas were a substantial, and possibly dominant, contributor to the production of r-process elements in the Universe.

The idea that a long GRB such as GRB 230307A could be produced by a compact-object merger was suggested in 2021, when another long GRB (GRB 211211A) showed possible signatures of a kilonova[12,13]. So what is going on in these events? There are three possible explanations. First, it could be that GRB 230307A was derived from the collapse of a massive star, as expected for long GRBs, but that it happened to make a kilonova, rather than a brighter supernova. Some simulations suggest that a collapsar can produce and expel r-process elements[14], but the yields would probably be about tenfold more than what was observed for GRB 230307A.

A more compelling argument – which both Levan *et al.* and Yang *et al.* favour – is that GRB 230307A arose from a compact-object merger that somehow resulted in a long GRB. Although the small disks produced in such mergers should rapidly accrete onto the resulting black hole, simulations[15] published in 2023 suggest that the power of a GRB engine might initially depend not only on the amount of mass that accretes on the black hole, but also on the magnetic field of the accreted debris. The mass feeding the black hole might dwindle quickly, but the magnetic field of the mass inflow might increase, and provide a relatively constant power to the engine over timescales that match the durations of long GRBs. If this theory is correct, then compact-object mergers could produce either long or short GRBs, depending on the magnetic-field geometry and whether the merger produces a black hole or a hypermassive neutron star.

Finally, an overlooked scenario could be responsible. One possibility is a white dwarf merging with a black hole or a neutron star. White dwarfs have a much bigger radius than do neutron stars, and so their debris disks are large and the characteristic accretion timescales would be roughly consistent with the duration of long GRBs[16]. Material ejected from a disrupted white dwarf might produce a radioactive afterglow[17], but this ejecta would probably lack the peculiar heavy elements that give rise to a distinctive red hue. This scenario has not yet been investigated in detail, and further modelling of such white-dwarf mergers might resolve the contradiction.

The puzzles posed by GRB 230307A will inspire continuing theoretical and observational studies. Fortunately, it might be only a matter of time before gravitational waves from an unusually long GRB are detected,

"The JWST observations provided unprecedented emission spectra of a kilonova."

which would definitively tell us whether or not the burst arose from a compact-object merger – and, if it did, what the masses of the component objects were. In the meantime, the misbehaviour of GRB 230307A is a reminder that the Universe is more interesting than the pedantic classifications of humans suggest.

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Neuroscience

A neural circuit that keeps flies on target

Katherine Nagel

Studies reveal how neuronal populations in the fruit fly brain work together to compare the direction of a goal with the direction that the fly is facing, and convert this into a signal that steers the fly towards its target. **See p.808 & p.819**

Animals of all kinds show a remarkable ability to navigate, whether it is to the location of a remembered food source or back to the safety of a nest. To accomplish this kind of goal-directed movement, brains have evolved specialized navigation centres – the hippocampus in vertebrates and the central complex in insects – that allow each animal to build an internal map or compass of its environment. Although the way in which these maps are built by neural circuits has been studied for many years, neuroscientists are still trying to understand how the maps allow an animal to orient towards a goal. On pages 808 and 819, respectively, Mussells Pires *et al.*[1] and Westeinde *et al.*[2] reveal the detailed mechanisms by which the insect brain converts a map-like representation of direction into goal-oriented steering.

The essence of a map is that it stays the same as an animal moves through space – the map is tied to coordinates of the animal's spatial environment (for example, north, south, east and west) rather than to the animal's left or right. Turning such a map into a steering command requires some form of comparison. For example, if a map tells you that treasure is northeast and you are currently pointing north, you can compare these two directions and determine that your best course of action is to turn right by a few degrees.

How might a neural circuit make this comparison? A possible answer first emerged from reconstructions of the brains of sweat bees (*Megalopta genalis*)[3] and, later, fruit flies (*Drosophila melanogaster*)[4]. By painstakingly tracing and reconstructing neurons and their synaptic connections using electron microscopy images, researchers revealed surprisingly precise and selective connectivity

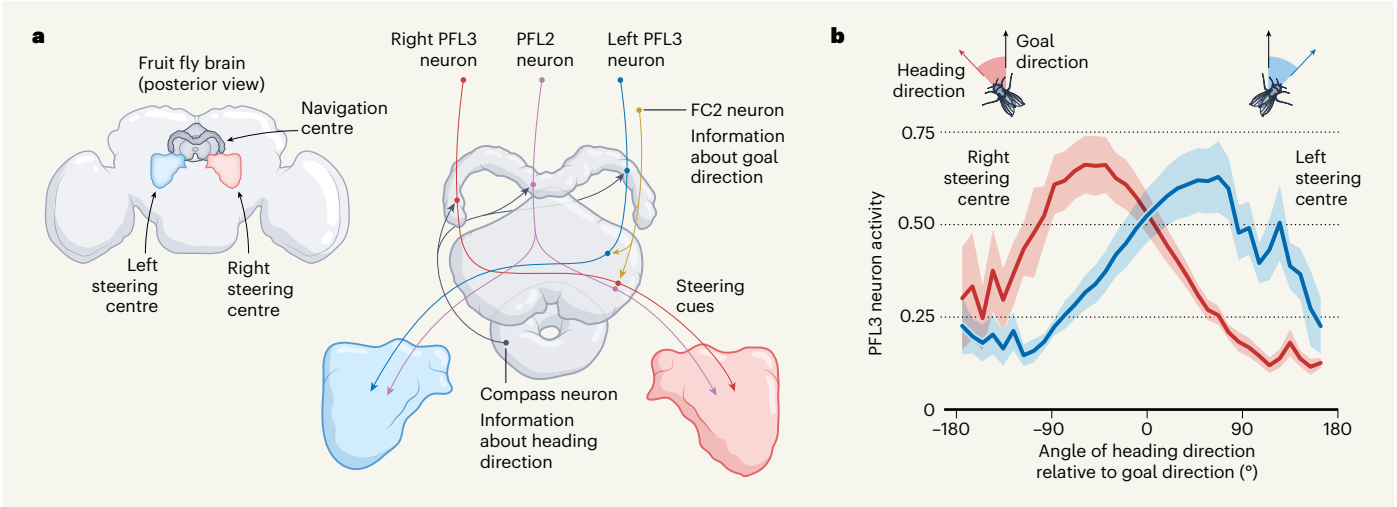

Figure 1 | A neural circuit in the fruit fly brain that enables goal-directed steering. **a**, In the navigation centre of the fruit fly (*Drosophila melanogaster*) brain, compass neurons encode information about the direction in which the fly is facing (heading direction). Mussells Pires *et al.*[1] find that FC2 neurons encode information about the position of a visual stimulus (goal direction). These two sets of neurons input into PFL3 and PFL2 neurons, which connect to regions of the brain that control steering. **b**, Both teams measure PFL3 neuronal activity, and find that the right steering centre is most active when the goal is to the right of the fly, and the left is most active when the goal is to the left. Westeinde *et al.*[2] also find that PFL2 neurons are most active when the fly is facing in the opposite direction to its goal (not shown). Together these neurons integrate information about the heading direction and goal direction, and enable the fly to stay on course as it steers towards a target. PFL3 neuron activity is expressed as baseline-normalized fluorescence measurements that report neuronal activity following navigation behaviour. (Graph adapted from Fig. 5 in ref. 1.)

between individual types of neuron. One circuit in the insect brain — the compass network — builds a map of the direction in which the animal is facing (its heading direction)[5]. These compass neurons communicate with another set of neurons, known as PFL3 neurons, that send projections to, and form connections with, an area of the brain involved in steering.

There are two sets of PFL3 neurons: one on the left and one on the right side of the brain. Neurons in each hemisphere form an array across the navigation centre and communicate with the steering centres on the opposite sides, suggesting that they might translate the compass map into a steering command (Fig. 1a). Curiously, PFL3 neurons receive input from the compass network, but there is a characteristic 'offset' between the direction encoded by compass neurons and that encoded by PFL3 neurons. This means that PFL3 neurons should be preferentially responsive (tuned) to heading directions that are to the left or right of the way in which the animal is currently pointing. Guided by this connectivity pattern, these earlier studies[3,4] proposed that PFL3 neurons might allow an insect to make a direction comparison, computing whether a left or right turn would bring its heading direction in line with a goal.

The latest studies[1,2] validate and extend the predictions of these models. Each group developed a different genetic tool to target PFL3 neurons in the brains of fruit flies. The researchers recorded the activity of these neurons as flies performed a navigational task called menotaxis, in which the fly adopts a straight course at an angle to a visual stimulus (the goal)[6]. Both groups found that PFL3 neurons are tuned to the heading direction, but that the neurons' activity is modulated by the direction of the goal. When the goal was to the fly's right, PFL3 neurons that connect to the right steering centre showed stronger responses, whereas when the goal was to the fly's left, neurons connecting to the left steering centre showed stronger responses (Fig. 1b). Together, these experiments provide strong support for the model that PFL3 neurons compare map-like representations of heading direction and goal to drive targeted steering.

In addition to finding support for the PFL3 steering model, Mussells Pires *et al.* identified a second group of neurons upstream of PFL3 neurons that can specify a goal direction.

"Internal maps of the environment are found in the brains of many animals, including humans."

Known as FC2 neurons, these neurons also form an array but they remain in the navigation centre rather than projecting out to the steering centres (Fig. 1a). Using a laser to artificially stimulate different parts of this array, Mussells Pires and colleagues found that flies adopted distinct orientations with respect to the visual stimulus. Unlike compass neurons, FC2 neurons do not change their firing when the fly turns, suggesting that they encode a map-like representation of the animal's goal.

These data are consistent with findings published last year for migratory monarch butterflies (*Danaus plexippus*): a population of neurons in the navigation centre was thought to track the butterfly's goal, not its heading direction, and the active population of neurons shifted only when the experimenter used electric shocks to force the butterfly to adopt a new goal[7]. They are also consistent with studies of another population of upstream local neurons in the fly navigation centre that produce orientations relative to wind direction when artificially stimulated[8]. Taken together, these studies suggest that insects might be able to learn and store multiple goal directions in different local neuron populations of the navigation centre. Understanding how distinct goals are learnt, remembered and prioritized during behaviour is a major focus for future research in the field.

The study by Westeinde *et al.* revealed another aspect of goal-orientation circuitry: a set of anti-goal neurons called PFL2 neurons (Fig. 1a). These were known to send signals to both sides of the steering centre, but with a distinct offset, effectively tuning them to directions 180° away from the fly's current heading direction[4]. By taking recordings from these neurons during menotaxis, Westeinde *et al.* found that the cells respond most strongly when the fly is pointing 180° in the opposite direction of its goal. Artificially activating these neurons caused the fly to slow down and increase its turning. The fly, therefore, is able to stay on target by combining three sets of steering neurons: right and left PFL3 neurons help the fly to stay on track when it makes small deviations from its goal, and PFL2 neurons turn the fly when it ventures too far off course.

Both studies provide strong experimental

evidence that PFL3 and PFL2 neurons can generate goal-directed steering, as predicted by theoretical models — but they stop short of showing that these neurons are required for all goal-directed steering. Mussells Pires *et al.* investigate the effects of silencing PFL3 neurons in a task designed to assess memory of wind direction, which the authors show is dependent on the compass network. However, the effects of silencing PFL3 neurons are only modest. This might be because the genetic line used by the authors labels, and therefore silences, only a subset of neurons. Future studies will be needed to determine how PFL neurons as a population contribute to goal orientation during complex behaviours.

Although the current studies focused on flies, internal maps of the environment are found in the brains of many animals, including humans. In vertebrates, navigational abilities are strongly linked to the hippocampus, which forms maps of both real and abstract environments. How these maps are translated into locomotor commands remains unclear. A study in Egyptian fruit bats (*Rousettus aegyptiacus*) found that a subset of neurons in the hippocampus is tuned to both the direction and distance (the vector) between the animal and the location of a hidden goal platform[9]. Another study found that place cells (neurons that fire when an animal is in a particular location in its environment) show directional tuning towards a goal when rats navigate a series of moving platforms[10].

Both of these coding schemes are reminiscent of the fly brain, in which the direction of a goal is represented by the pattern of activity across an array of neurons. Defining the precise neural architectures that allow insects to convert such maps of the environment into steering commands for the body might therefore help to reveal how human brains navigate both real and imaginary spaces.

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Forum: Structural biology

Energetic laser pulses alter outcomes of X-ray studies

Cutting-edge X-ray sources have enabled the structural dynamics of proteins to be tracked during biochemical processes, but the findings have been questioned. Two experts discuss the implications of a study that digs into this issue. **See p.905**

The paper in brief

- **Ultrashort, intense X-ray pulses generated at facilities known as X-ray free-electron lasers (XFELs) have been used to probe light-induced structural changes in proteins.**
- **Light-responsive proteins typically absorb one optical or ultraviolet photon in natural settings, but could absorb more from the intense 'pump' lasers used to induce structural changes in these studies.**
- **Such unnatural absorption of multiple pump photons might force proteins to behave in ways that are not biologically relevant.**
- **Questions have therefore been raised about how these studies should be interpreted.**
- **Barends *et al.*[1] now show that the structure of a model protein changes in different ways depending on whether single or multiple photons are absorbed.**

Richard Neutze

Imperfect experiments can be informative

Structural changes that occur in proteins during biochemical reactions can be measured using a technique called time-resolved X-ray diffraction (TR-XRD). In this method, reactions are initiated in protein crystals, and X-ray pulses are used to record X-ray diffraction data at selected times after initiation. TR-XRD has produced structural insights into the pathways of diverse biological processes[2], including photosynthesis, sensory signalling, ion transport and photodissociation — the light-induced breakage of bonds between proteins and their ligand molecules.

For light-sensitive proteins, a pump laser pulse is used to initiate the reaction of interest. All molecules probed in a crystal contribute to the measured X-ray diffraction pattern, yet typically only a subpopulation is activated by the pump laser. A quantity known as the crystallographic occupancy estimates the fraction of molecules in a crystal that are activated. Raising the pump-laser fluence — the energy delivered per unit area by the pump laser onto a crystal — can increase the crystallographic occupancy, but more than one photon can be absorbed by the protein at high laser fluences[3,4].

Barends *et al.* studied structural changes that occur in the carbon monoxide complex of the protein myoglobin (MbCO) after pump-laser-induced photodissociation of CO from the iron atom of a haem group (Fig. 1). This process was previously studied using TR-XRD at time resolutions of 7.5 nanoseconds (ref. 5) and 150 picoseconds (1 ps is 10^{-12} seconds; ref. 6) using relatively large protein crystals (dimensions in the range of about 0.1 to 0.3 millimetres) and X-ray pulses from a synchrotron facility, which is a less intense X-ray source than an XFEL.

A 2015 study by some of the same researchers as Barends *et al.* used extremely short, intense XFEL pulses to record TR-XRD data from tens of thousands of much smaller MbCO crystals (average size 15 micrometres × 5 μm × 3 μm). This thereby achieved a time resolution of 250 femtoseconds (1 fs is 10^{-15} s) and revealed ultrafast conformational changes of the protein as photodissociation occurs[7]. But because those experiments used a high pump-laser fluence, Barends *et al.* have now repeated their study using a lower fluence that ensures single-photon excitation of MbCO.

The authors used their TR-XRD data to determine difference Fourier maps, which show differences in electron density in MbCO before and after activation. Barends *et al.* found that lower pump-laser fluences yield lower crystallographic occupancies in maps produced 10 ps after protein activation. For this time delay, differences between structural