To determine the neural circuit within which RMG functions, the authors inspected the essentially complete anatomical wiring diagram of the *C. elegans* nervous system[6]. They find that this pair of neurons is connected by gap junctions — hollow proteins that allow electrical currents to flow between cells — to seven other neurons, six of which are sensory (Fig. 1a). This pattern of connectivity immediately suggested a hub-and-spoke arrangement with RMG at the centre. But how does this circuit function in social feeding?

In search of an answer, Macosko *et al.*[4] chose the chemosensory neuron ASK, which integrates food and pheromone signals emitted by hermaphrodites[7]. In *npr-1*-defective social feeders, inactivating ASK and its sister chemosensory neurons reversed the effect of *npr-1* mutation, causing the animals to be solitary. Moreover, restoring the function of ASK, and just one other sensory neuron, in these animals caused aggregation, bordering and locomotion speed to return to nearly the levels seen in social strains, suggesting that ASK can promote social feeding.

The next obvious question was how the ASK–RMG spoke of the circuit might act to regulate foraging style. ASK is required to attract males to hermaphrodites[8], and Macosko and colleagues show that it signals the presence of pheromones by a reduction in its activity. These clues prompted the authors to test whether social and solitary strains might differ in their behavioural responses to pheromones. Whereas pheromones repelled solitary animals (as previously shown[8,9]), they attracted the *npr-1*-defective social strains. This striking observation has two key implications. First, it points to pheromones as the missing, long-range sensory cue that attracts worms into feeding groups. Second, it brings *C. elegans* aggregation closer to the orbit of behaviours that are more than just metaphorically social.

Macosko *et al.* also find that a pulse of pheromones reduces ASK activity to a much greater extent in the *npr-1*-defective social strain than in the solitary strain. This observation provides a clue as to how the RMG–ASK spoke of the circuit might function. In one model, RMG resides in either a low (solitary feeding) or a high (social feeding) activity state, depending on the activity of NPR-1 and, possibly, on the concentration of neuropeptides (Fig. 1b). The state of RMG activity is communicated electrically to ASK through gap junctions, with the result that membrane potential in ASK is set respectively low or high. When ASK is in its low state, there is little activity to inhibit. But when it is in its high state, a pheromone pulse can more strongly inhibit it. Thus, RMG switches the dynamic range of ASK's pheromone response.

In support of this model, the researchers[4] show that pheromone-induced synaptic responses in the interneuron AIA — the main postsynaptic target of ASK — are small in the solitary strain and large in the social strain.

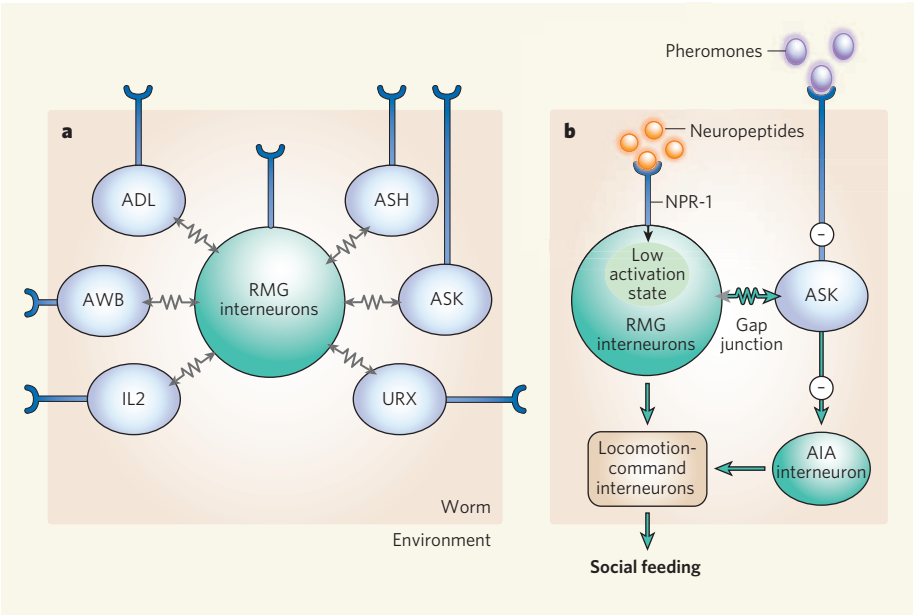

Figure 1 | The RMG hub-and-spoke circuit. a, RMG interneurons are connected to six types of sensory neuron (ASH, ASK, URX, IL2, AWB and ADL) covering a wide range of sensory modalities. The circuit might operate in two directions simultaneously. In the centripetal direction, RMG could integrate signals across several modalities to assess the quality of the local environment. In the centrifugal direction, RMG could set the dynamic range of the sensory neurons' response. **b**, For instance, Macosko and colleagues' data[4] indicate that RMG interneurons might send electrical signals through gap junctions to ASK, tuning the extent of this sensory neuron's response to pheromones. When NPR-1 is absent or its activity is low, RMG activation is high, leading to ASK's strong response to pheromones and so its relatively strong signals to locomotion-command interneurons through AIA interneurons, which might promote social feeding. Negative signs indicate inhibition; all other connections are positive.

Thus, from the point of view of the neurons in the social strain that get their news about the proximity of other nematodes from ASK, it would seem as though the animal has encountered a bigger change in pheromone concentration, presumably leading to a stronger orientation response. It would be interesting to determine whether AIA is required for aggregation responses.

An attractive feature of the hub-and-spoke motif is that, if its gap junctions pass ionic currents bidirectionally (as many do), then the circuit ought to operate simultaneously in opposing directions. In the centrifugal direction, RMG should broadcast to sensory neurons of various modalities its assessment of the animal's internal state, encoded by neuropeptides, thereby redirecting the attentions of the animal according to its needs. In the centripetal direction, by simple laws of current flow in circuits, RMG's membrane voltage should be a weighted average of the state of the sensory neurons, providing a balanced assessment of the local environment. We do not yet know whether the hub-and-spoke circuit as a whole functions as proposed. The evidence that one of the seven spokes (RMG–ASK) functions centrifugally now provides the impetus to test other spokes as well.

As neuroscientists contemplate large-scale anatomical reconstructions of other nervous systems[10], it can be argued that costly wiring diagrams are not worth the expense because of unavoidable ambiguities in the final result. Macosko and colleagues' work[4] provides a bracing example to the contrary, for without the guidance of the *C. elegans* wiring diagram[6], one might have lost sight of this rich vein of inquiry. ■

Shawn R. Lockery is at the Institute of Neuroscience, 1254 University of Oregon, Eugene, Oregon 97403, USA.
e-mail: shawn@chinook.uoregon.edu

1. de Bono, M. & Bargmann, C. I. *Cell* **94,** 679–689 (1998).
2. Gray, J. M. *et al. Nature* **430,** 317–322 (2004).
3. Persson, A. *et al. Nature* doi:10.1038/nature07820 (2009).
4. Macosko, E. Z. *et al. Nature* **458,** 1171–1175 (2009).
5. Coates, J. C. & de Bono, M. *Nature* **419,** 925–929 (2002).
6. White, J. G., Southgate, E., Thomson, J. N. & Brenner, S. *Phil. Trans. R. Soc. Lond. B* **314,** 1–340 (1986).
7. Schackwitz, W. S., Inoue, T. & Thomas, J. H. *Neuron* **17,** 719–728 (1996).
8. Srinivasan, J. *et al. Nature* **454,** 1115–1118 (2008).
9. White, J. Q. *et al. Curr. Biol.* **17,** 1847–1857 (2007).
10. Helmstaedter, M., de Kock, C. P. J., Feldmeyer, D., Bruno, R. M. & Sakmann, B. *Brain Res. Rev.* **55,** 193–203 (2007).

Corrections

● In the News & Views article "Quantum chemistry: The little molecule that could" by Chris H. Greene (*Nature* **458,** 975–976; 2009), the equivalent for 1 millikelvin should have been given as 100 billionths of an electronvolt, not 4 billionths.

● In one of the obituary articles about John Maddox, "Maddox by his successor" by Philip Campbell (*Nature* **458,** 985–986; 2009), Nietzsche was misspelled.