

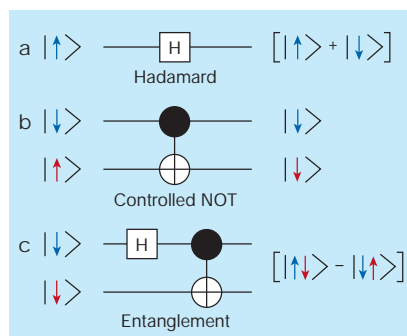
**Figure 1 Bell states for a two-particle system.** The arrows represent the spin state of each particle (coded red and blue), which may be either 'up' or 'down'.

four 'maximally entangled Bell states', shown in Fig. 1. Such Bell states have the paradoxical property that the particles always 'know' about each other, even if they are separated by huge distances<sup>5</sup>; this property is commonly associated with the 'non-locality' of quantum mechanics. Entanglement such as this is a basic ingredient of quantum computation (Fig. 2) and hence is no longer just a toy for laboratory science<sup>6,7</sup> but also a tool for the technological world. But how can specific entangled states be constructed on demand?

For a deterministic entanglement of two quantum degrees of freedom, the two constituents must interact in a controlled manner. This has already been achieved in atomic optics, by manipulating a pair of trapped beryllium atoms using a sequence of laser pulses<sup>8</sup>. But now the solid-state camp is catching up: Pashkin *et al.*<sup>4</sup> have brought two superconducting qubits into a controlled state of interaction.

These qubits encode information using charge rather than spin. In a superconductor, charge is carried by pairs of electrons, known as Cooper pairs. In Pashkin and colleagues' experiment, the qubits are micrometre-size specks of superconductor, each connected to a superconducting 'reservoir'. By quantum mechanical tunnelling, a Cooper pair might jump from the reservoir onto a qubit. Then, analogous to the spin 'up' and 'down' states, the qubit can be in a state with no excess Cooper pairs, or one excess Cooper pair — or a superposed state of both. The superconducting energy gap, which is a natural barrier against the dissociation of Cooper pairs, protects these solid-state qubits from decoherence.

Using lithography and evaporation techniques, Pashkin *et al.* fabricated two qubits on an insulating wafer, connected through a capacitor (see Fig. 1 on page 824). Each qubit coupling to the superconducting reservoir (called a Josephson junction) results in a mixing between the charge states of that qubit, and the capacitive connection between the qubits leads to the mixing of two-particle states, and hence entanglement of the qubit pair. Following the principle demonstrated by Nakamura *et al.*<sup>9</sup> for a single qubit, Pashkin *et al.*<sup>4</sup> trace the evolution of the mixing of these two-particle states over



**Figure 2 Quantum logic.** The quantum state of an individual qubit is described as a complex superposition of two basis states, here denoted by  $|\uparrow\rangle$  and  $|\downarrow\rangle$ . a. Acting on a single qubit, the operation known as 'Hadamard' transforms  $|\uparrow\rangle$  or  $|\downarrow\rangle$  into the symmetric or antisymmetric superpositions  $[|\uparrow\rangle \pm |\downarrow\rangle]$ . b. Adding one non-trivial two-qubit operation to the set of single-qubit rotations defines a complete and universal set of gate operations. The operation 'Controlled NOT' flips the target spin (red) if the control spin (blue) points downwards (or else leaves the target unchanged). c. Two-qubit states are complex superpositions of the four basis states  $|\uparrow\uparrow\rangle$ ,  $|\downarrow\downarrow\rangle$ ,  $|\uparrow\downarrow\rangle$  and  $|\downarrow\uparrow\rangle$ . Applying the two operations 'Hadamard' and 'Controlled NOT' to one of the two-qubit basis states produces a maximally entangled Bell state.

time, monitoring the charge oscillations produced with a current probe.

Although they have not yet been able to create and measure a specific entangled state, a numerical analysis shows that the qubit pair does evolve through a maximally entangled state, bringing us closer to the construction of a solid-state quantum logic gate to produce deterministic entanglement. The next step could be to introduce time-controlled switching of the interaction and subsequent readout, measuring the degree of

entanglement through the amplitudes of the final state expressed in the Bell-state basis<sup>10</sup>.

Astounding progress has been made over the past few years in the experimental development of quantum computing. In quantum atom optics, entanglement of four particles has been achieved<sup>11</sup> and entangled ions are being used to test quantum mechanical relations known as Bell's inequalities<sup>12</sup>. Shor's factorization algorithm has been implemented<sup>13</sup> with a seven-qubit molecule using NMR techniques, successfully identifying the factors of 15 as 3 and 5. From their first appearance a few years ago<sup>9,14,15</sup>, superconducting qubits have already matured into effective and efficient devices<sup>16,17</sup>, and now Pashkin *et al.*<sup>4</sup> have demonstrated the first step towards their deterministic entanglement. These are firm foundations for the development of a solid-state quantum processor, but considerable effort will be needed to direct the complex choreography of a real quantum algorithm. ■

Gianni Blatter is at the Institute of Theoretical Physics, ETH-Hönggerberg, CH-8093 Zürich, Switzerland.

e-mail: blatterj@phys.ethz.ch

- Raimond, J. M., Brune, M. & Haroche, S. *Rev. Mod. Phys.* **73**, 565–582 (2001).
- Monroe, C., Meekhof, D. M., King, B. E., Itano, W. M. & Wineland, D. J. *Phys. Rev. Lett.* **75**, 4714–4717 (1995).
- Gulde, S. *et al. Nature* **421**, 48–50 (2003).
- Pashkin, Yu. A. *et al. Nature* **421**, 823–826 (2003).
- Einstein, A., Podolsky, B. & Rosen, N. *Phys. Rev.* **47**, 777–780 (1935).
- Glauber, J. F. & Shimony, A. *Rep. Prog. Phys.* **41**, 1883–1927 (1978).
- Aspect, A., Grangier, P. & Roger, G. *Phys. Rev. Lett.* **49**, 91–94 (1982).
- Turchette, Q. A. *et al. Phys. Rev. Lett.* **81**, 3631–3634 (1998).
- Nakamura, Y., Pashkin, Yu. A. & Tsai, J. S. *Nature* **398**, 786–788 (1999).
- Hill, S. & Wootters, W. K. *Phys. Rev. Lett.* **78**, 5022–5025 (1997).
- Sackett, C. A. *et al. Nature* **404**, 256–259 (2000).
- Rowe, M. A. *et al. Nature* **409**, 791–794 (2001).
- Vandersypen, L. M. K. *et al. Nature* **414**, 883–887 (2001).
- Friedman, J. R. *et al. Nature* **406**, 43–46 (2000).
- van der Wal, C. H. *et al. Science* **290**, 773–777 (2000).
- Vion, D. *et al. Science* **296**, 886–889 (2002).
- Yu, Y., Han, S., Chu, X., Chu, S.-I. & Wang, Z. *Science* **296**, 889–892 (2002).

## Neurobiology

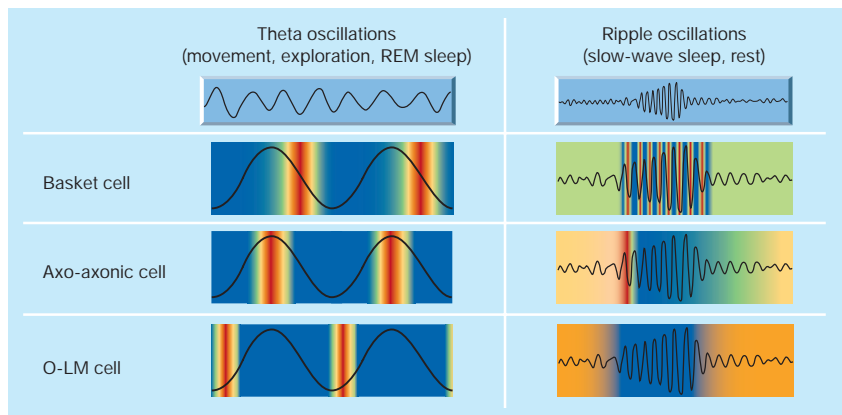
# Interneurons take charge

Edvard I. Moser

The brain's hippocampal region contains many classes of interneurons, which, it transpires, show different patterns of activity. They might contribute to memory by shaping the dynamics of neuronal networks.

Learning something new — and recalling what you've learned — involves large numbers of nerve cells, distributed throughout different parts of the brain. Neuronal assemblies in the hippocampus, for instance, are thought to be essential in encoding, consolidating and retrieving memories. These neuronal networks alternate between several functional states, each characterized by a temporally structured

pattern of electrical activity that may facilitate a particular aspect of memory processing. On page 844 of this issue, Klausberger *et al.*<sup>1</sup> present results that bring us closer to understanding the precise but varied ways in which distinct classes of hippocampal neurons impose such network states. Their study focuses on interneurons — small neurons that are involved in the local processing of nerve signals. They find that these



**Figure 1 Interneurons and electrical oscillations.** The figure shows the activity profiles of three types of hippocampal interneuron during two brain states, based on the findings of Klausberger *et al.*<sup>1</sup>. Colours indicate the probability that a given interneuron will fire (maximum red, minimum blue). During theta oscillations, basket cells fire on the descending phase of local theta waves, axo-axonic cells fire just after the peak, and O-LM cells fire at the trough. During ripple oscillations, basket cells discharge one or several phase-locked spikes, axo-axonic cells fire only at the beginning of the ripple sequence, and O-LM cells become silent. The variation within each group is small, suggesting that classes of interneurons exert precise control over distinct aspects of hippocampal network dynamics.

cells, which generally have inhibitory activities, seem to work together in a strictly coordinated manner to control assemblies of excitatory pyramidal nerve cells.

In particular, the new results<sup>1</sup> show that the dynamics of hippocampal networks are related to the diversity in the hippocampal interneuron population. Pyramidal cells are relatively uniform in their structure and behaviour. But interneurons form distinct classes, in terms of their shape, the inputs to which they respond, the other neuron populations they connect to, and the specific parts of neurons with which they make contact<sup>2–4</sup>. Klausberger *et al.* now show that morphologically distinct classes of hippocampal interneurons also contribute differently to network states.

The authors recorded the electrical impulses (spikes) generated by three types of hippocampal interneurons — basket cells, axo-axonic cells, and oriens–lacunosum-moleculare (O-LM) cells — during two network states in anaesthetized rats. One of these states is characterized by theta oscillations (which have a frequency of 4–10 Hz), the other by short ripple oscillations (120–200 Hz) on a background of more irregular activity. In conscious animals, theta oscillations are associated with movement and exploration, whereas ripples are associated with inactivity and slow-wave sleep<sup>5</sup>.

The three classes of interneurons exhibited distinct, state-dependent patterns of activity (Fig. 1). For instance, during theta oscillations, basket cells fired on the descending phase of each wave, axo-axonic cells just after the peak, and O-LM interneurons at the trough. During ripple oscillations, basket cells discharged one or more phase-locked spikes; axo-axonic

cells fired at the beginning of each ripple sequence; and O-LM cells became totally silent. The implication is that the three classes of interneurons, through their characteristic patterns of activity, make specific contributions to the production of hippocampal network states.

It remains to be seen, however, exactly what these contributions are. For example, what is the function of the sudden drop in activity of O-LM cells during ripple oscillations? As interneurons generally inhibit other nerve cells, this drop in activity means a drop in inhibition. Axons from O-LM cells target the outermost portion of pyramidal-cell dendrites — the area in which pyramidal cells receive excitatory inputs from another brain region, the entorhinal cortex, which mediates highly processed sensory information to the hippocampus. So does the drop in inhibition amplify the cortical input? Does it enable the excitatory synapses (connections) between entorhinal cells and hippocampal cells to become modified, and do such changes occur specifically during ripple oscillations? During ripples, pyramidal cells tend to fire in patterns that are reminiscent of their firing during recent awake behaviour<sup>6</sup>. Such 'reactivation' may contribute to memory consolidation in the hippocampus and the neocortex<sup>8</sup>, where the permanent storage of memories is thought to take place<sup>7</sup>. Are O-LM cells involved in this process?

Moreover, what is the function of the precisely timed firing of basket cells and axo-axonic cells during ripple and theta oscillations? Does it synchronize the output from hippocampal pyramidal cells to the neocortex<sup>8</sup>? And, if so, how do the neocortical target neurons respond to such output?

To determine how the interneurons' precise control of network dynamics contributes to hippocampal functions such as memory processing<sup>9</sup>, the analysis must be extended to behavioural studies in conscious animals. Functional diversity in the hippocampal networks of conscious rats was first studied 30 years ago<sup>10</sup>, when nerve impulses recorded in the hippocampus were observed to originate from either 'complex-spike cells' or 'theta cells'. The complex-spike cells discharged at low rates but in bursts; theta cells were more active but their spikes were also more dispersed. These two types of neurons had the properties expected of pyramidal cells and interneurons, respectively. Their identity was eventually verified by staining the recorded neurons in anaesthetized rats<sup>11</sup>; this confirmed that spike parameters and spike patterns can indeed predict the morphology of hippocampal neurons.

The results of Klausberger *et al.*<sup>1</sup> show that a similar approach can be used to distinguish between classes of interneurons. The spike activity generated by interneurons in a given class varies little, suggesting that state-dependent activity patterns provide valid signatures of basket cells, axo-axonic cells and O-LM cells in anaesthetized rats. Can these differences be extrapolated to awake animals? Similar profiles of activity have been observed during corresponding network states in anatomically unidentified hippocampal interneurons in conscious rats<sup>12</sup>. Obviously, there are differences between the awake and anaesthetized conditions<sup>13</sup>, but the new results represent a first step towards a physiological classification scheme that could be used to relate variations in activity profiles to particular interneurons and to specific memory operations<sup>14</sup>.

For these results to be applied to behavioural studies, other types of hippocampal interneurons must be analysed in a similar way. The criteria that distinguish between basket cells, axo-axonic cells and O-LM cells in the study by Klausberger *et al.* might be less useful in samples that also contain other interneuron classes. It may be necessary to explore additional parameters, such as waveform shape — which is known to distinguish pyramidal cells from some interneurons<sup>10,11</sup> — as well as other network states and the cells' responses to specific drugs.

A physiologically based classification system for analysing behaviour represents one of two developments that should advance our understanding of hippocampal interneurons. The other is the genetic manipulation of mice, which may soon allow scientists to examine neuronal networks and memory processes when the function of particular interneurons has been genetically altered. Together, these new tools have the power to uncover the most fundamental

principles of memory formation in the neuronal assemblies of the hippocampus. ■  
**Edvard I. Moser is at the Centre for the Biology of Memory, Norwegian University of Science and Technology, MTF5, 7489 Trondheim, Norway.**  
 e-mail: edvard.moser@cbm.ntnu.no

1. Klausberger, T. *et al.* *Nature* **421**, 844–848 (2003).
2. Buhl, E. H., Halasy, K. & Somogyi, P. *Nature* **368**, 823–828 (1994).
3. Freund, T. F. & Buzsáki, G. *Hippocampus* **6**, 347–470 (1996).
4. McBain, C. J. & Fisahn, A. *Nature Rev. Neurosci.* **2**, 11–23 (2001).
5. Buzsáki, G. *Neuroscience* **31**, 551–570 (1989).

6. Wilson, M. A. & McNaughton, B. L. *Science* **265**, 676–679 (1994).
7. Squire, L. R. & Alvarez, P. *Curr. Opin. Neurobiol.* **5**, 169–177 (1995).
8. Cobb, S. R., Buhl, E. H., Halasy, K., Paulsen, O. & Somogyi, P. *Nature* **378**, 75–78 (1995).
9. Paulsen, O. & Moser, E. I. *Trends Neurosci.* **21**, 273–278 (1998).
10. Ranck, J. B. Jr *Exp. Neurol.* **41**, 461–531 (1973).
11. Henze, D. A. *et al.* *J. Neurophysiol.* **84**, 390–400 (2000).
12. Csicsvari, J., Hirase, H., Czurko, A., Mamiya, A. & Buzsáki, G. *J. Neurosci.* **19**, 274–287 (1999).
13. Fox, S. E. & Ranck, J. B. Jr *Exp. Brain Res.* **62**, 495–508 (1986).
14. Fyhn, M., Molden, S., Hollup, S., Moser, M. B. & Moser, E. I. *Neuron* **35**, 555–566 (2002).

## Animal behaviour

# How self-organization evolves

P. Kirk Visscher

Self-organized systems can evolve by small parameter shifts that produce large changes in outcome. Concepts from mathematical ecology show how the way swarming bees dance helps to achieve unanimous decisions.

Work published in *Proceedings of the Royal Society*, Mary Myerscough<sup>1</sup> has taken a novel approach to the modelling of group decision-making by honeybee swarms when they are in search of a new home. Bees ‘waggle dance’ to communicate locations of food in foraging, and of potential nest sites when a colony moves during swarming. Myerscough treats the scout bees dancing for alternative sites as populations, and models their growth and extinction with the tools of mathematical ecology. From this approach it is evident how a slight difference in the way the dance-language ‘recruitment’ of other bees is structured in foraging and house-hunting influences the outcome of each process.

The choice of a new home site by a swarm of honeybees is a striking example of group decision-making. When a swarm clusters after leaving its natal colony (Fig. 1), scouts search the countryside for cavities with the appropriate volume and other characteristics<sup>2</sup>. They then return to the swarm, and communicate the distance to and direction of the sites that they have found with waggle dances<sup>3</sup>, just like those used for communicating locations of food sources in foraging<sup>4</sup>. Usually, the scouts find and report several sites, but in time dances cease for all but one of them, and finally the swarm flies to the selected cavity. Self-organizing processes such as this, in which a complex higher-order pattern (here, the development of a consensus on the best site) arises from relatively simple responses of individuals with no global view of the situation, are receiving increasing attention as biological mechanisms for elaborating complexity<sup>5</sup>.

The population-biology metaphor is appropriate for analysing honeybee dance information. Bees recruited by dances for



Figure 1 Honeybee swarm in search of a new nest site.

a particular site may visit it and in turn dance for new recruits, so dances reproduce. But nest-site scouts may cease dancing before they recruit at least one other dancer: the population of dancers for that site then declines, and may become extinct. Myerscough’s approach incorporates key aspects of the dynamics of nest-site recruitment, and can accommodate differences that are specific to the nest site or the individual bee. The populations of dancers have ‘age structure’ in the sense that some dances are a scout’s first dance for a nest site, others follow a second trip, and so on. This is similar to population growth with discrete generations, which can be represented in a standard tool of mathematical ecology: a Leslie matrix. The ‘age structure’ patterns also can incorporate an important difference in dance language use between nectar foraging and house-hunting. In foraging, the number of waggle runs that a bee performs when returning with food increases and then levels off with successive dances by that bee (Fig. 2a). In contrast, in house-hunting, the number of waggle runs (which initially depends on the quality of the site) generally declines with each successive dance (Fig. 2b),

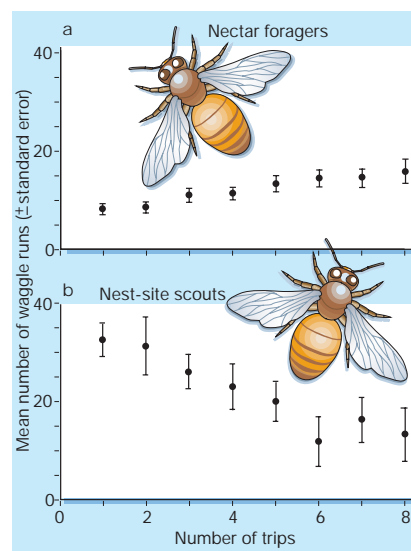


Figure 2 Different patterns of dance-language performance in nectar foragers and nest-site scouts. These graphs plot the number of waggle runs in the recruitment dances performed after each return trip to the colony for successive instances where each individual bee danced<sup>10</sup>. a, Nectar foragers continue to dance for many trips. (Here, 93% of 40 foraging bees in 3 colonies danced on more than 8 trips; most danced on more than 50 trips.) b, Nest-site scouts, searching for a new home following swarming, perform dances with more waggle runs at first, but soon cease to dance entirely. (Here, fewer than 5% of 86 bees in 3 swarms performed more than 8 dances.) Myerscough’s analysis<sup>1</sup> suggests that this difference in dance performance underlies the difference in outcome: in foraging, it is desirable to recruit new foragers for several sites; in swarming, unanimity for a single site must be reached.

and each scout soon ceases dancing entirely. This gives different patterns of ‘age-specific fecundity’ to the dancing bee populations.

Because the mathematical theory of models of this type is well developed, Myerscough’s approach has an analytical payoff. It is straightforward to predict whether a population of dancers for a site will increase or decline. But this is a dynamic process, because only a limited number of scouts can be recruited. As a result, whether dancers for a particular site increase or decrease in number depends both on the quality of the site and on the populations of other dancers. The dancing for a site may increase while competing dances are rare, but then decline in favour of other sites with greater ‘fecundity’ (that is, those that elicit a greater number of waggle runs of dancing per trip by scouts). Such dynamics are typical of swarms<sup>3,6,7</sup>, with the outcome that the highest-quality site among those discovered is usually selected<sup>8</sup>.

The most striking result of this approach is that it shows how certain special features of the dance in the context of house-hunting