Cognitive architecture of a mini-brain: the honeybee

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Honeybees have small brains, but their behavioural repertoire is impressive. In this article we focus on the extent to which adaptive behaviour in honeybees exceeds elementary forms of learning. We use the concept of modularity of cognitive functions to characterize levels of complexity in the honeybee brain. We show that behavioural complexity in the honeybee cannot be explained by independent functions of vertically arranged, domain-specific processing modules, but requires horizontal integration in a central state, and we identify neural mechanisms that may underlie domain-specific processing and central integration. The honeybee may serve as a useful model for the study of intermediate levels of complexity in cognitive functions and the search for their neural substrates.

Insects have traditionally been considered simple and small reflex automata. However, this particular view overlooks the fact that insects, like most living organisms, flexibly process information in order to adapt to their environment. Behavioural processes that range from gathering sensory information through perception and decision-making to the resulting appropriate actions allowing the animal to cope with a changing environment can be identified in insects. As cognition can be defined in a broad sense as the sum of such processes[1], we must consider insect behaviour from a cognitive perspective.

The traditional way of conceptualizing insect behaviour is to assume sets of independent sensory–motor routines, each of which is responsible for a particular task that the insect must perform. For example, insect pheromones trigger sexual behaviour, appropriate care of larvae, and defensive behaviour, among others. Also, the pattern of polarized light in the sky reliably orients navigation, and the speed and time of the flow field experienced during flight gives a direct measure of the distance flown. Such routines have specific inputs and thus resemble features of domain-specific processing modules as characterized by Coltheart[2] with reference to Fodor's original notion of modularity of mind[3] (Box 1). Although such processing modules refer to rather simple cognitive functions, the concept of vertical modularity and the characteristics of modules provide a useful frame to ask whether behaviour can be explained solely on the basis of separately acting modules, each having its own particular input and providing a specialized output. The insect processing modules are fast and informationally encapsulated because they are innately specified or tuned to selective and simple forms of learning. The operations of such modules correspond to a vertical processing that is mandatory (automatic). Their neurobiological basis is given by simple circuits of few neurons or, in some cases, by single identified neurons[4–6]. The basis of insect behaviour might thus consist of stacks of such modules, lacking horizontal processing across them. Accordingly, we should expect rather limited cognitive functions: insects should exhibit only elementary forms of learning and specific adaptations to rigid environmental conditions.

However, insects are evolutionarily extremely successful, having penetrated all habitats and outnumbering by far all other multicellular organisms, both in absolute and in species numbers[7]. The insect brain must therefore provide intelligent solutions to a wide range of ecologically relevant problems in order to assure such evolutionary success. Such solutions arise not only from the single domain-specific modules, but essentially, from the possibility of horizontally combining several modules at a central level of integration (see Box 1). In doing so, new and richer behaviour can be produced. Thus studies on insect cognition should determine the specific contributions of vertical and horizontal processing to the behavioural richness observed in insects. It is possible to address this question in the honeybee by focussing on adaptive aspects of its behaviour. In a natural context, honeybees exhibit a great variety of domain-specific sensory–motor routines. Many modules are addressed under such conditions and may potentially produce behaviour. How do they interact? Do single, isolated modules rule behaviour, or do they feed into a central state where information from other modules is 'consulted'? Underlying these questions is the motivation to unravel the neural basis of processing modules and their interactions. There is a fair chance of attaining this goal in the honeybee, because of its relatively simple nervous system and because electro- and optophysiological measurements can be performed in the bee brain, often from identified neurons and neuropils, while the animal is learning and responding[8].

A small brain for rich behaviour
The honeybee brain has a volume of approximately 1 mm³ and contains around 960,000 neurons. Despite this small size, the honeybee displays an extremely rich behavioural repertoire. A social lifestyle is obligatory, and a single bee cannot survive

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Box 1. Cognitive architecture of an insect brain

Vertical modularity

Domain-specific processing modules

- characterized by their specific input (key stimuli, see Fig. I) and their specific motor programs
- innately-specified or tuned to selective and highly-prepared forms of simple learning
- informationally encapsulated: restricted to a particular sensory–motor task; no horizontal connections between processing modules; vertical processing is mandatory
- automatic; that is, fast both with respect to their specific sensory–motor connections and their restricted forms of learning

Value systems

- processing modules specified for providing value information to subsets of domain-specific processing modules
- provide horizontal connections to domain-specific modules. These are restricted and not reciprocal
- neural implementation: dominated by sets of dedicated neurons

Central integration

- horizontal processing of inputs from domain-specific and value-specific processing modules
- integrated representation of information from several to many modules
- creation of new behaviour (e.g. configural and context-dependent forms of learning; categorization and abstraction, relational learning, navigation according to a mental map)
- neural implementation: multiple parallel neuron architecture

Examples of vertical modularity

- pheromone-released behaviours: feeding behaviour of larvae; aggression and defence
- phototactic open-sky reaction
- path integration during search flights
- distance estimation from the visual flow field experienced during flight
- dance communication, relationship between dance movements to distance and direction of indicated site
- sun compass, relationship of sun azimuth and time of the day as guide in navigation and dance behaviour
- detection of polarized light pattern in the sky
- quality estimation of potential nest sites

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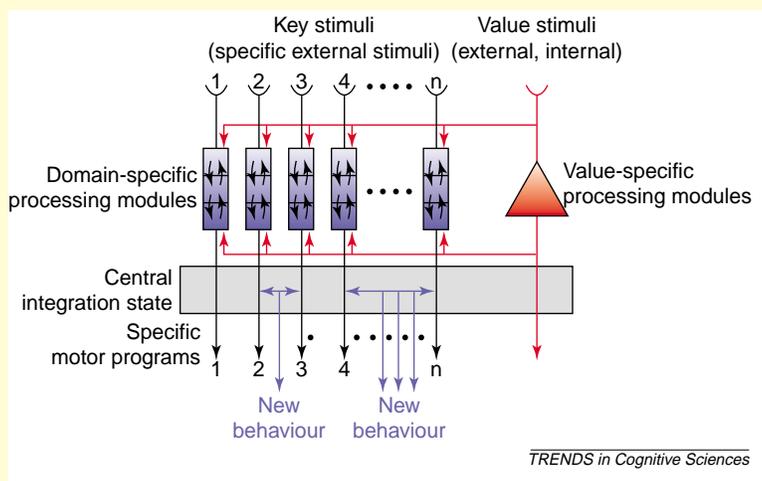
Fig. I. See text for details.

very long independent of the colony. Outside the hive bees navigate over distances of several kilometres using landmark constellations and celestial cues (azimuthal position of the sun, polarized light pattern of the blue sky). They visit hundreds of flowers in quick and efficient succession for gathering food, inspect potential new nest sites, and learn and memorize the local cues characterizing places of interest. Bees exchange information through ritualized body movements, called the 'waggle dance'. This dance transmits information about the vector flown towards an attractive food source or nest site[9]. Hive bees attending such a 'dancing' bee learn the distance to the food source from the speed of movement and the flight direction relative to the sun from the angle of the waggling phase relative to gravity. Sensory capacities and motor performances are highly developed. Bees see the world in colour, perceive shapes and patterns, and resolve movements achromatically with a high temporal resolution. Their olfactory sense allows them to distinguish a large range of odours; their mechanosensory perception is also extremely rich.

The neural organization of the brain combines two design principles: dedicated neurons and multiple parallel neuron architecture. The dedicated neuron principle is based on the existence of single neurons that serve as identifiable functional elements in sensory-motor routines and which can be repeatedly and reliably identified due to their unique morphology. Such neurons are characteristic of the invertebrate nervous systems and provide the mechanistic basis for domain-specific modules.

A particularly striking neuron in the bee brain is VUM_{mx1} (ventral unpaired median neuron of the maxillary neuromere 1), which serves the function of a value system. Activity in this neuron constitutes the neuronal representation of the food reward in appetitive associative olfactory learning[10] (Box 2). Because VUM_{mx1} converges only with the olfactory, not with other sensory pathways in the bee brain, it may be the specialized reward system for olfactory cues. Other value systems may exist for other sensory modalities. In any case, VUM_{mx1} provides an example of a value-specific processing module based on a single identified neuron that is specialized in informing a subset of domain-specific modules about the outcome of their actions.

Multiple parallel neuron architecture indicative of higher-order integration is represented by the mushroom bodies (MBs), which are central, prominent structures in the insect brain (Fig. 1). In the bee brain, each MB consists of approximately 170,000 tightly packed, parallel and rather similar neurons. The MBs receive compartmentalized multisensory input (olfactory, visual, mechanosensory)[11], and their output neurons are multimodal[12,13]. Such a multimodal convergence suits the MBs for higher-order multimodal computations, in particular, for relational,

Box 2. A single neuron represents the value system in olfactory learning in the honeybee brain

(a) The VUM$_{mx1}$ neuron belongs to a group of 15 ventral unpaired median neurons of the sub-oesophageal ganglion, and its soma is located in the maxillary neuromere 1. All 15 neurons differ in the structure of their dendritic arborization. The dendrites of VUM$_{mx1}$ arborize symmetrically in the brain and converge with the olfactory pathway at three sites (delimited by a red dashed line in Fig. I), the primary olfactory centre, the antennal lobe (AL), the secondary olfactory integration area, the lip region of the mushroom bodies (MB), and the output region of the brain, the lateral horn (LH). VUM$_{mx1}$ responds to sucrose solution both at the antenna and the proboscis with long lasting spike activity, and to various visual, olfactory and mechanosensory stimuli with low frequency spike activity.

(b) Behavioural learning of an olfactory stimulus can be induced by substituting the sucrose reward in PER conditioning (see Box 3) by an artificial depolarization of VUM$_{mx1}$ immediately after olfactory stimulation (forward pairing). If depolarization precedes olfactory stimulation (backward pairing), no learning is observed. The same forward-backward effect is seen when sucrose is used as the reward under similar experimental conditions[a]. In all cases the bees' response is quantified in terms of the number of spikes of M17, a muscle controlling the movement of the proboscis. The results thus show that VUM$_{mx1}$ constitutes the neural correlate of the US in associative olfactory learning.

(c) Intracellular recordings of VUM$_{mx1}$ during training and tests with a reinforced (CS$^+$) and a non-reinforced odour (CS$^-$).

(i) Intracellular recording of VUM$_{mx1}$ during differential conditioning to two odours, a forward-paired one (CS$^+$), and a backward-paired one (CS$^-$). Such a conditioning leads to an enhanced response of VUM$_{mx1}$ to CS$^+$ but not to CS$^-$.

(ii) After differential conditioning, presentation of the CS$^+$ alone activates VUM$_{mx1}$ but presentation of the CS$^-$ alone does not, a fact that supports second-order conditioning, a phenomenon documented in PER conditioning[b]. In this case, if a new CS is followed by the learned CS$^+$, it will be associated transitively with VUM$_{mx1}$ activation.

(iii) If the US follows the presentation of the CS$^+$, the response of VUM$_{mx1}$ to the US is greatly reduced, and even inhibited. In contrast, the response of VUM$_{mx1}$ to the US after the presentation of the CS$^-$ remains normal. This indicates that differential conditioning leads to different reward-related responses, depending on whether the reward is expected (after CS$^+$) or not (after CS$^-$). Asymptotic acquisition of CS$^+$ may,

therefore, result from a loss of reinforcing strength of the reward as predicted by the Rescola and Wagner model[c]. Furthermore, this property of VUM$_{mx1}$ is sufficient to explain the behavioural phenomenon of blocking and may thus reflect its neural substrate. When animals are conditioned to a mixture of two stimuli (AB$^+$) containing a previously conditioned stimulus (A$^+$), then their response to the second stimulus (B), when presented alone, is reduced compared to that of animals which had been conditioned to the mixture (AB$^+$) alone and were subsequently also presented with B. Learning about the first stimulus (A$^+$) 'blocks' learning about the second stimulus (B$^+$) during compound conditioning. The issue of whether honeybees exhibit blocking is still being debated[d–f]. However, the fact that learning about a first CS$^+$ reduces the response of VUM$_{mx1}$ to a US implies that in subsequent compound conditioning, learning about a second CS$^+$ is impaired (i.e. blocked).

These results demonstrate that the single identified neuron VUM$_{mx1}$ is a sufficient neural substrate for the reinforcing function of the unconditioned stimulus sucrose in olfactory conditioning, and has properties that allow explaining second-order conditioning and blocking. It is still unknown whether VUM$_{mx1}$ itself or the other 14 identified VUM neurons of the sub-oesophageal ganglion belong to a general modulatory pathway also subserving non-associative forms of plasticity and arousal[g].

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context-dependent associations. The MBs therefore provide a potential substrate for central integration of diverse vertically-processing, domain-specific modules.

Computational strategies in associative learning

Associative learning is a fundamental property of nervous systems governed by rules applicable both across species and across modalities. Elementary
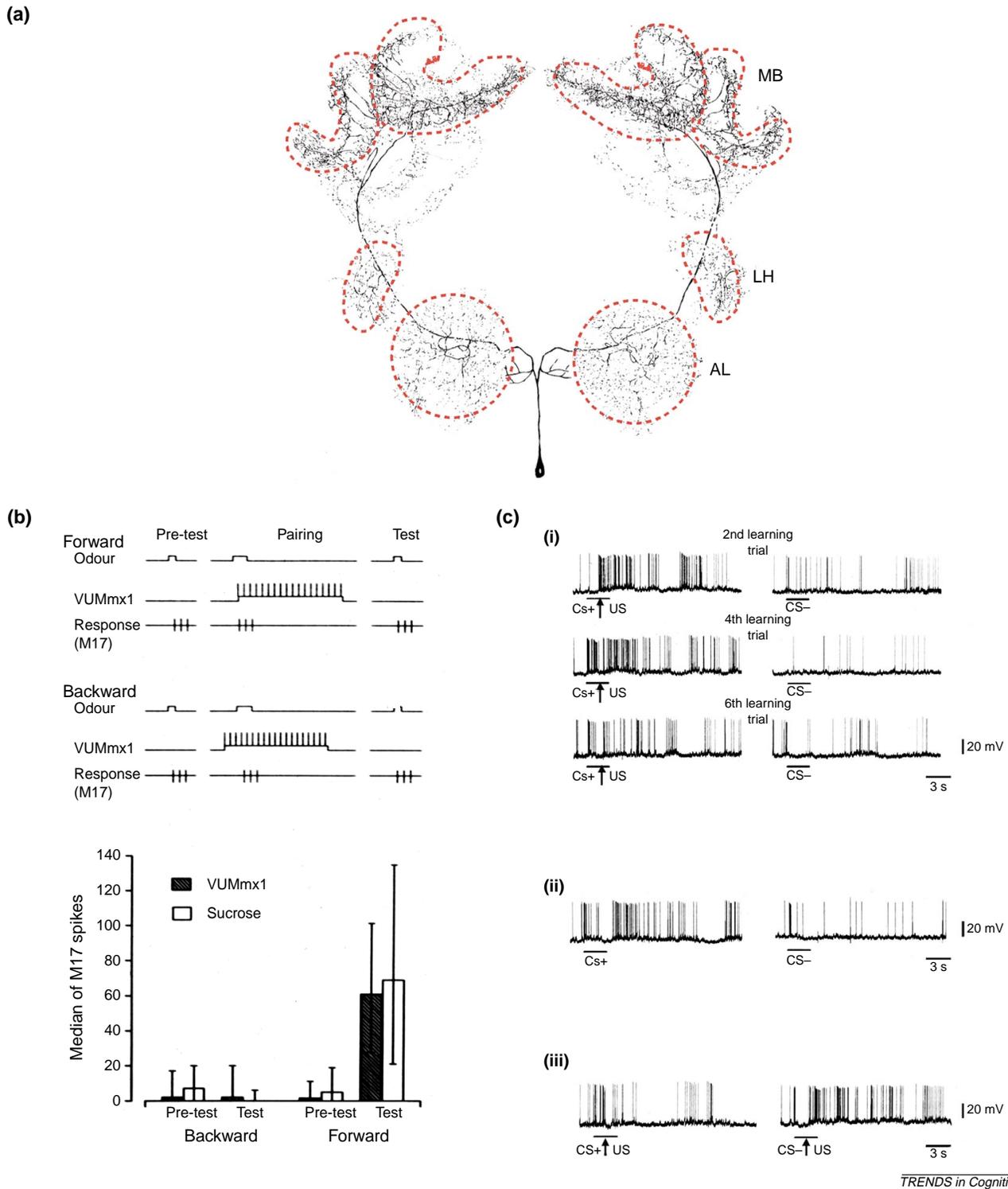
Fig. I. The VUM$_{mx1}$ neuron: a value system in olfactory learning in the honeybee (see text on facing page for details).

forms of associative learning can be viewed as domain-specific modules, because behaviour comes to be governed by linear associations in which specific stimuli trigger a conditioned response.

However, honeybees exhibit complex forms of associative learning that cannot be explained on the sole basis of elementary associations[14]. Such non-elementary forms of learning are indicative of
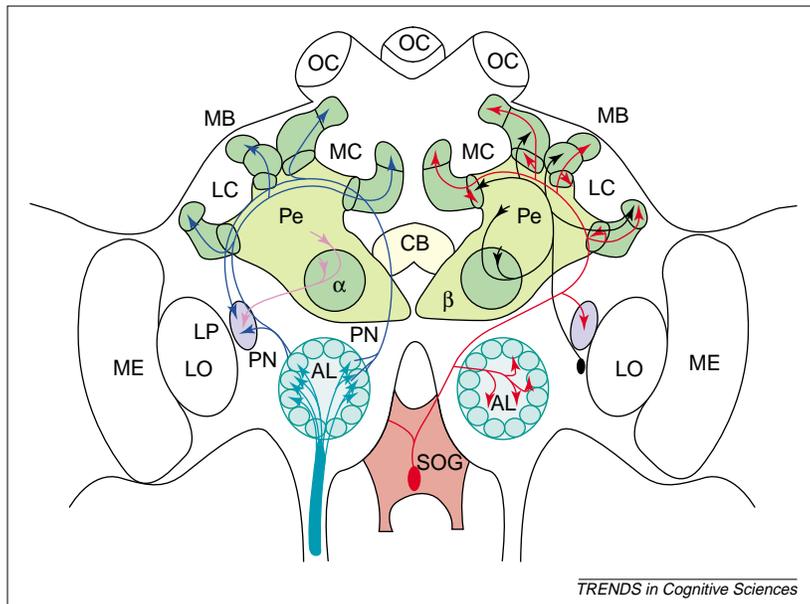
Fig. 1. The honeybee brain. A schematic view of the major neuropils of the central brain area excluding the eyes, showing the olfactory pathway. AL, antennal lobe (light blue), first-order neuropil, which receives the input of 60 000 chemosensory axons and where synapses between these input neurons, local interneurons and projection neurons are located in 156 spherical glomeruli; MB, mushroom body, second-order olfactory and higher-order visual and mechanosensory integration centre made of 170 000 densely packed and parallel neurons (green). These intrinsic neurons have widely overlapping dendritic branches in the calyx (MC, medial calyx; LC, lateral calyx), the input region of the MB, and similar axon shapes. The axons form the pedunculus (Pe). The calyx is segregated into modality-specific regions; the upper part is olfactory, the median part visual and the lower predominantly mechanosensory. The output regions of the MB are the α and β lobes. These are formed by two collaterals of the intrinsic MB neurons. An inhibitory feedback loop of MB is shown at right (black). PN, two neural tracts (blue arrows), which transmit olfactory information from the AL to the MB. LP, a third olfactory neuropil in the lateral protocerebrum (also called the lateral horn), which receives the input from the AL and the indirect input from the MB via extrinsic neurons (left side, violet arrows). Descending neurons run from there to the motor centre in the sub-oesophageal ganglion (SOG). The output neuron of the SOG is the ventral unpaired median neuron of the maxillary neuromere 1 (VUM$_{mx1}$, red). CB, central body; LO, lobula, and ME, medulla, two visual neuropils. OC, ocelli (three simple eyes). The organization of the honeybee MB constitutes an example of multiple parallel-neuron architecture. This neuropil is composed of multiple aligned neurons that can be flexibly organized into various functional ensembles.

different computational strategies in associative learning and could arise through horizontal combination of modules.

A robust and fast form of associative learning in honeybees is olfactory conditioning in harnessed bees[15] (Box 3). This preparation has been successfully used in studying elementary and configural forms of learning. Rules of elementary associative learning assume that in learning a compound, animals learn the associations between the reinforcer and the compound elements separately[16]. Contrary to this presumption, configural learning theories assume that, in learning a compound, animals build a new entity made from the conjunction of compound elements, and that a connection is made between this new configuration and the reinforcer[17,18]. The different processing strategies underlying elementary and configural olfactory learning can be illustrated by negative patterning discrimination.

In negative patterning two single stimuli are reinforced (A+, B+), while the compound is not (AB-). Solving this problem, that is responding less to the compound than to the single elements, can only be explained if configural associations are taken into account[17–19]. Otherwise, summation of the elementary associative strengths in the compound should result in stronger response to the compound than to the elements. Honeybees can solve negative patterning discrimination in olfactory conditioning of the PER (Deisig *et al.*, in preparation). The fact that bees can solve a negative patterning discrimination in olfactory conditioning of the PER and in colour/odour tasks[20] shows that lineal associations between single stimuli and the reinforcer are not the only ones underlying associative learning in honeybees.

Horizontal interaction between domain-specific modules

Experiments with free-flying bees have made it possible to uncover higher levels of behavioural complexity. Bees learn all the colours within their spectral range (from 300 nm to 650 nm), although with differing efficacy[21]. Similarly, bees learn different kinds of patterns and shapes, although more learning trials are usually required for this purpose[22,23]. Bees also learn to distinguish stimuli on the basis of motion cues[24–26].

Studies on pattern perception by honeybees have yielded results that cover a broad spectrum, ranging from matching with a template to categorization. Discrimination based on retinotopic matching between perceived patterns and a memorized template was suggested in many experiments (e.g. Wehner[27]). Visual categorization has been shown for orientation of black and white gratings and for bilateral symmetry. Bees easily learn orientation as an independent parameter[28,29]: if they are trained with a series of different patterns to discriminate vertical from horizontal stripes, they can transfer this information to different new patterns sharing the features vertical versus horizontal[28]. Similarly, bees learn to extract bilateral symmetry or asymmetry from a series of different, changing patterns and transfer this information to novel symmetrical and asymmetrical stimuli[30].

Thus bees show a primary level of categorization as they assign individual stimuli to categories based on the pictorial features of which they are composed[31]. Typically, a categorization experiment must involve a discrimination in which reward is not signalled by a single stimulus, but, rather, by a variety of stimuli that share some common characteristics, and a transfer to novel instances. Both conditions are fulfilled in these experiments. Orientation perception, however, may not imply a true abstract categorization, as it relies on the existence of well-defined orientation detectors found in the visual neuropils of the bee brain[32]. It suffices that, independently of pattern quality, the orientation of a novel pattern falls within the preferred orientation of the previously-activated detector for the novel pattern being recognized as the same as that previously reinforced. The same argument could hold

Box 3. Classical conditioning of the proboscis extension reflex (PER) in the honeybee

Harnessed honeybees can be conditioned to olfactory stimuli. Each bee is restrained in a tube such that it can freely move only its antennae and mouthparts (mandibles and proboscis). The antennae are the main chemosensory organs. When the antennae of a hungry bee are touched with sucrose solution, the animal will reflexively extend its proboscis to reach out towards the sucrose and suck it. Odours or other stimuli to the antennae do not release such a reflex in naive animals (Fig. Ia).

If, however, an odour is presented immediately before sucrose solution (forward pairing), an association is formed which enables the odour to release the proboscis extension response (PER) in a successive test (Fig. Ib). This effect is clearly associative and involves classical, and not operant, conditioning[a]. Thus the odour can be viewed as the conditioned stimulus (CS) and sucrose solution as the reinforcing, unconditioned stimulus (US). (Fig. Ic) The acquisition curves show a typical differential conditioning experiment: one odour is paired with sucrose (CS+)

and the other odour is presented unpaired (CS−) between CS+ trials. The bees learn to respond to the CS+ and not to the CS−. The physiological correlates of olfactory conditioning can be studied at different levels, ranging from the molecular and biochemical levels to that of single identified neurons and neuronal ensembles[b–d]. These studies are possible because bees prepared in a similar way to that shown here, but with their brains exposed for physiological recording, will also perform olfactory learning and display the conditioned PER.

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(a) Before conditioning **(b)** Conditioning After conditioning **(c)** Learning curves

Sucrose

Odor

CS+
Odor A
Sucrose
0 1 2 3 4 5 6 [s]

CS−
Odor B
No sucrose
0 1 2 3 4 5 6 [s]

CS+

CS−
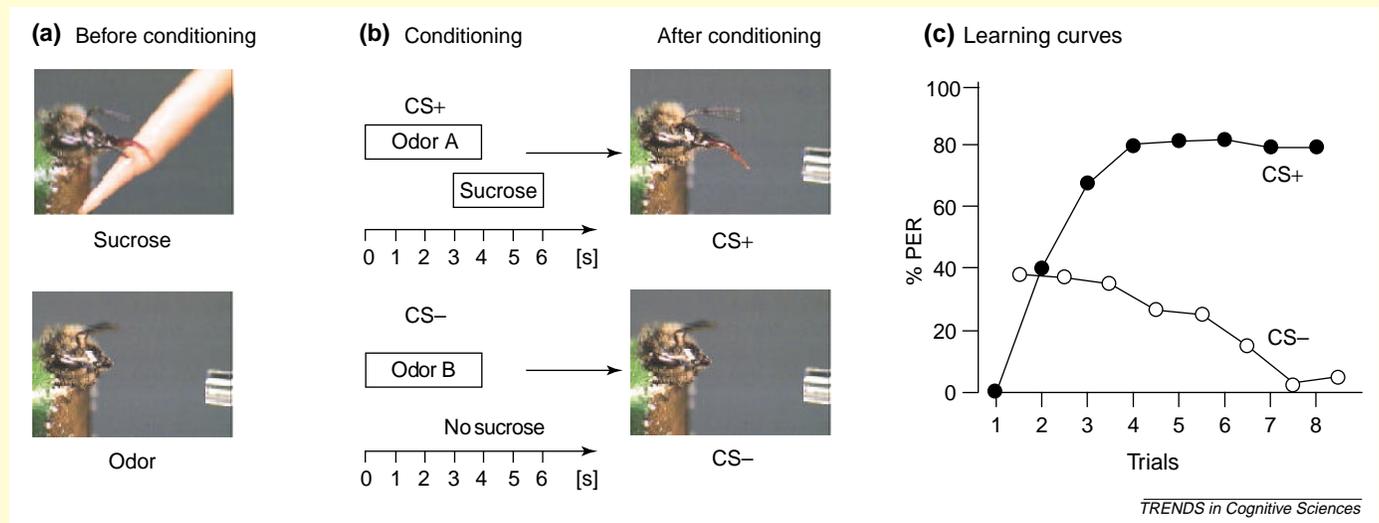
Fig. I. The proboscis extension reflex (PER) (see text for details).

for visual categorization based on symmetry if symmetry detectors were known. The mechanistic basis of symmetry perception in insects (as well as in animals in general) is, however, unknown.

Beyond categorization phenomena, bees can also learn to choose different colours[33] or different homing directions[34] at two places simultaneously, thus showing performances consistent with contextual learning[35]. Moreover, bees can also learn two different orientations of black-and-white gratings at two different places, the food source and the hive entrance, such that there is no transfer between these two places, even if the rewarded orientation in one location is the unrewarded one in the other location[36].

New behaviour indicative of horizontal interaction between domain-specific processing modules is also observed in maze training experiments. Bees learn to associate flight vectors with particular visual stimuli such as colours[37] or stripe orientations[38]. When presented with stripes

oriented in between the training values, they interpolate to new flight trajectories[38]. Furthermore, when bees are trained to fly into a dual-arm maze, they learn to associate a non-rewarded odour given at the entrance (mango or lemon) with a subsequent, rewarded colour (yellow or blue) presented in one of the arms of the maze and vice versa[39]. In that way crossmodal associations are established that allow for interaction between distinct modules. Bees can also be trained in a delayed matching-to-sample task in which they are presented with a changing non-rewarded sample (one of two different coloured disks, one of two different black-and-white gratings, vertical or horizontal, or one of two odours) at the entrance of the maze[40]. The bees are rewarded only if they choose the stimulus identical to the sample once within the maze. Bees trained with the colours and presented in transfer tests with gratings that they have not experienced before are able to solve the problem and choose the grating identical to the

(a)

(b) Route training

(c) Rotator feeding training

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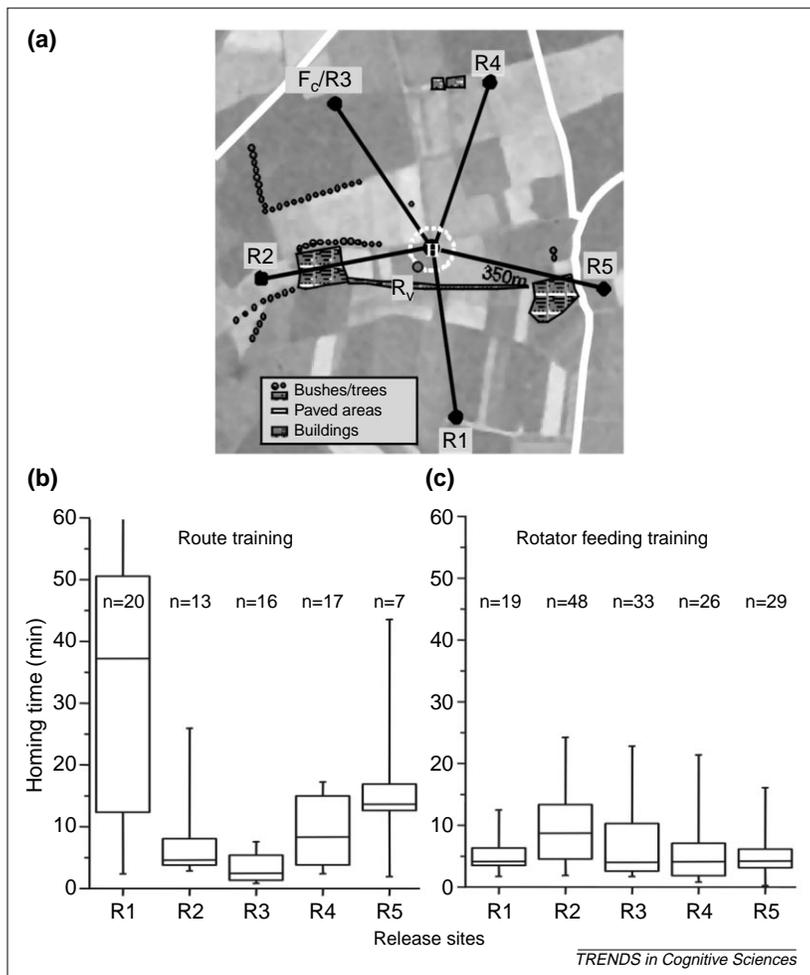
Fig. 2. Honeybee navigation. (a) Aerial map showing the hive (H) and five release sites (R1-5) for food. (b,c) The flight times from the five release sites to the hive after route training and (b) after rotating feeder training (c). (b) Because R3 was the site to which bees were trained, they return from this site the quickest, following their route memory. They take the longest time to return from R1 when trained to R3, because at R1 they head south-southeast, first applying the compass-vector of their route memory. However, if bees do not have a route memory because they had been trained to the rotating feeder (c), they are nearly as fast from any of the five release sites as the route-trained bees released at R3. This indicates that bees without route 'knowledge' apply their general landscape memory at any of the five release sites, which allows them to return quickly to the hive.

sample at the entrance of the maze. Similarly, bees trained with the gratings or odours and tested with colours in transfer tests also solve the problem and choose the novel colour corresponding to that of the sample at the maze entrance. Thus bees make a judgement regarding 'sameness' among objects in their environment. As bees can also solve a delayed non-matching-to-sample task, they can also form a concept of 'difference'[40].

Modularity in spatial navigation
Several modules contribute to honeybee navigation. The most important are path integration, distance estimation from visual flow field, the use of the sun and/or the polarized light pattern as a compass, and picture memories of important locations (hive, feeding site) as learned during stereotyped flight patterns. There is ample evidence for the use of each of these modules (see Ref. 41 for review) but the question again is: do these modules interact and if so,

how? A first answer is provided with the results of the following experiment: when bees are trained to forage at two feeding sites, one available only in the morning at 630 m from the hive heading 115° from north, and the other available only in the afternoon at 790 m from the hive heading 40° from north, they can be released at the 'wrong' site, that is, at the afternoon site in the morning, or vice versa, and they nevertheless fly straight back to the hive[34].

To achieve this, the bees needed to retrieve the memory for the correct route from long-term memory stores that were established during training and that connected local landmarks with the flight path to the hive. When these bees are released at a location halfway between the two feeding sites (at a place they had never been before) half of the bees fly straight back to the hive along a novel route, indicating that they integrated vector information related to the two feeding sites. The other half chose the correct compass direction that they would have flown if they were not captured[34].

Flying a new route in this context can be related to the interpolation capabilities shown by bees while negotiating a maze[38]. Additional experiments indicate that bees use two different kinds of spatial memory for navigation (Fig. 2). Consistent flights along fixed routes between the hive and a food source, and orientation flights when first departing from the hive establish two different kinds of spatial memory: (1) a memory for a fixed route (route memory), which stores a rich repertoire of sequential features between the hive and the food source and vice versa, and (2) a general landscape memory, in which all directions around the hive could be represented. This latter is a topographically organized memory that allows them to return to the hive if they were not trained along a route or if they had used their route memory.

The two kinds of memory can be studied separately using different procedures: (1) training along a route (Fig. 2; between the hive H and a feeder F_c at the site R3, and vice versa); and (2) training to a feeder that rotates close to the hive (RF_V, 5–10 m distance) several times a day such that no route is learned[42]. In the latter case, bees can only refer to their general landscape memory when released unexpectedly at any of the five new release sites (R1–R5) after having been collected at the feeder once they filled their crops and are ready to return to the hive. General landscape memory is inhibited by route memory because bees trained along a route and then released at a new site always fly in the wrong direction, following the vector corresponding to their route memory. If route memories are not available or are inactive in working memory (e.g. after having followed the route memory), the general landscape memory can be recruited by landmarks and guides the animal back to the hive.

The spatial representation allowing navigating without a route can be viewed as a set of vectors centred on the hive[43]. This type of vector map might be different from a cognitive map[44] insofar as it may
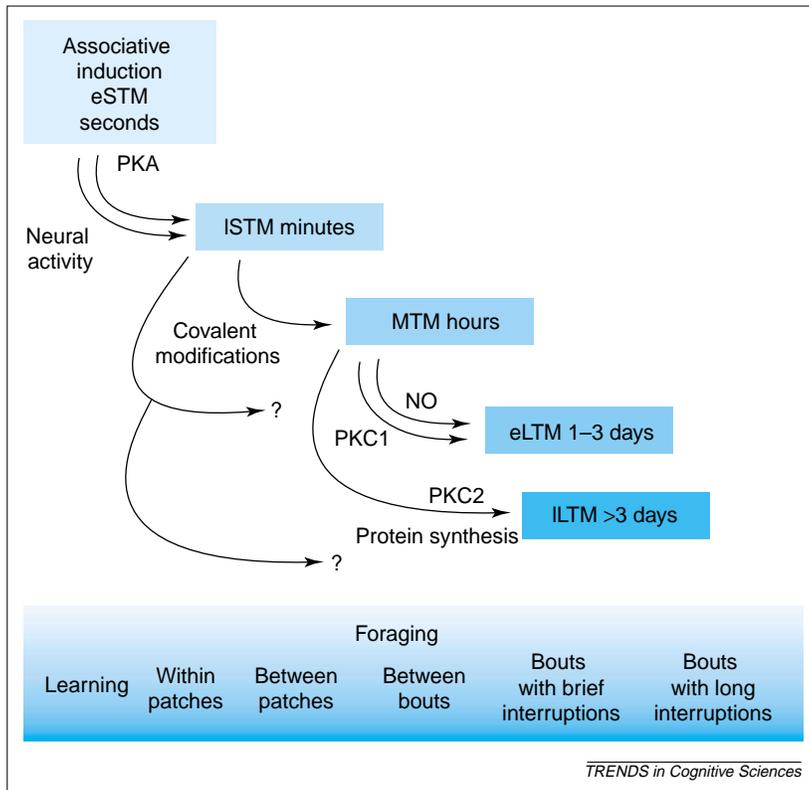
Fig. 3. Memory dynamics in the honeybee. Five memory phases are distinguished on the basis of retention scores, dependence on single or multiple learning trials, susceptibility to retrograde amnesic treatment (such as cooling or electric shock), participation of particular cellular reaction cascades (prolonged and enhanced activity of the protein kinases PKA and PKC, activity of NO synthase), and sensitivity to protein synthesis inhibition during the acquisition process and the time period immediately following. Early and late short-term (e- and l-STM) and middle-term memory (MTM) are initiated by a single learning trial; early and late long-term memory (e- and l-LTM) require multiple learning trials. l-LTM lasts for a lifetime even after only three learning trials. Consolidation during l-STM leads to enhanced retention scores and resistance to amnesic treatment. e- and l-LTM differ in the fact that e-LTM is not sensitive to protein synthesis inhibition, but l-LTM is. These memory phases are related to the sequence of events during natural foraging. Bees usually forage in patches of flowers where intra-patch choices occur at short intervals and inter-patch choices at longer intervals due to spatial separation of blooming flowers. Intra-patch choices do not usually require distinguishing between identical and different flowers. Inter-patch choices require distinguishing between identical and different flowers. Multiple learning trials in quick succession (massed trials) correspond to intra-patch choices. Such trials lead to faster consolidation than a single trial, but the resulting memory does not last as long as that resulting from spaced trials. Spaced trials correspond to inter-patch choices. They lead to improved retention and make memory more resistant to interference by new memory. In this case memory consolidation matches the time course of inter-patch choices. Inter-bout choices occur when bees have returned to the hive and started a new foraging trip. Under these conditions bees do not refer to a lasting working memory, but need to retrieve information about flower cues from a remote memory store. (Modified from Ref. 46.)

not allow novel short-cuts between any two points in space, but only between any point characterized by a landmark and the centre of navigation, the hive. Additional studies are necessary to determine whether bees also fly between a new release site and a known feeder. Tracing the bees' flights over long distances using the harmonic radar technique[45] indicates that bees might also choose to fly back to the feeding place, indicating a higher flexibility in the use of general landmark memory than has been considered so far (Menzel, Riley and Greggers, unpublished data).

Thus honeybee navigation constitutes a good example of the necessity to assume horizontal interactions between vertically arranged processing modules. The combinations of different kinds of

information giving origin to new behaviour can only result from horizontal interactions at a central level.

Memory dynamics and memory localization

Memory can be defined as an animal's capacity to retain acquired information and to use it for future behaviour. In the context of association theory, memory is the potential of a conditioned stimulus to activate an established associative link. However, learning might be viewed as a process of acquiring information rather than responses, and memory will then be a dynamic and self-organizing process of information storage. Support for such a cognitive interpretation of memory in the honeybee comes from the fact that olfactory memory formation is not identical with the process of acquisition. Memory needs time to develop, and proceeds through phases differing with respect to their susceptibility to interfering events, their content and their neural and cellular substrates[46] (Fig. 3).

The memory trace for olfactory cues is distributed and involves at least two of the three convergence sites between the olfactory pathway and the reward pathway constituted by the VUM_{mx1} neuron (Fig. 1). These sites are the antennal lobes and the MBs, the primary and secondary processing regions in the olfactory pathway, respectively[47]. Each of these two neuropils can establish its own memory trace independently of the other, and each trace controls the conditioned response. The two traces are, however, different at least with respect to their dynamics and are likely to store different information. The antennal lobe may possibly contain the substrates of elementary forms of association, and the MBs the substrates of configural and contextual associations.

Progress in unravelling the neural correlates of memory has been made for the antennal lobe by visualizing the changes in odour coding as a consequence of olfactory conditioning[48]. The antennal lobe is organized in glomeruli and odours are coded as specific spatial activation patterns of the glomeruli. These patterns can be imaged using calcium-sensitive fluorescent dyes[49]. As a result of conditioning, the neural representation of a trained odour becomes more pronounced and distinct from non-rewarded odours, but its general features do not change, indicating that learning at this level intensifies the neural code of the learned signal. Additional signatures of the neural code for the learned odour have not yet been detected but must exist, because bees are not confused by changing the intensity of the odour.

The temporal dynamics of five memory stages and their respective properties appear to reflect the sequences of events during foraging trips (Fig. 3). The cellular and neural machineries underlying the memory stages are basically similar to those known for other model systems (*Aplysia*[50,51], *Drosophila*[52], and the chick[53]), although each model system has its own temporal dynamics. This indicates that the

cellular and molecular machinery is flexible enough to adapt to the particular timing required under natural conditions.

Conclusion: modules of an insect mind

Studies on honeybee behaviour show that complexity can arise from a relatively simple nervous system that can be studied at a reductionistic level. The concept of modular organization used to interpret the behaviour of the honeybee postulates that complex behaviours may result from the horizontal integration of vertically arranged, domain-specific processing modules. Each of these modules is triggered by a specific input and produces a specific behavioural output. They are fast, automatic and encapsulated with respect to the information processed. Horizontal interaction provides novel and adaptive solutions. The cognitive architecture of the honeybee mini-brain thus consists of a network of interconnected modules that allows for stereotyped as well as flexible responses.

In concrete terms, the vertical modules may be sensory–motor routines, elementary processes in associative learning, or automatic processes of neuronal self-organization (such as those underlying the sequential organization of memory). The question that we originally raised was whether the explanation of insect behaviour could be reduced to a stack of such vertical processing modules or, whether it is necessary to assume that horizontal combinations between modules occur at a central state. Numerous examples show that the latter alternative is required for understanding the complexity of behaviour in the honeybee. Such an integration allows for consultation and comparison of different outputs corresponding to different contexts and stored in long-term memory, and thus for context-dependent decisions.

If we agree that behavioural complexity arises from a network of horizontally interconnected modules, the relevant problem that must be studied is that of the limits of horizontal connectivity. Characterizing not only what the bees do and learn, but also what they cannot do or learn, is of fundamental importance for understanding how a small brain with a reduced capacity (as compared with that of vertebrates) can extract the logical structure of the world in such an impressive way.

Studies of honeybee behaviour allow researchers to be optimistic when addressing the neural mechanisms within and between modular action. In this sense honeybees may serve as a useful model for the study of intermediate levels of complexity in cognitive functions and for the search for their neural substrates.

> **Outstanding questions**
>
> - In which sense is insect behaviour organized in modules?
> - Which examples of dedicated neurons and of multiple parallel neuronal architecture are known in the honeybee brain?
> - Do bees fulfil the requisites of a categorization experiment? Can honeybees categorize visual stimuli?
> - Which kinds of memories have been postulated to explain navigation performances in different sets of experiments in the honeybee? Why do bees trained to a distant food site fly in the wrong direction when released at an unexpected site which they know from their orientation flights?
> - How many memory phases have been distinguished in olfactory learning in the honeybee and how do they relate to foraging dynamics?

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fMRI and cognitive dysfunction in schizophrenia

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Despite being one of the most prevalent psychiatric conditions, schizophrenia is still poorly understood, with no clear objective biological marker. The advent of neuroimaging has enabled *in vivo* investigations to complement older techniques, and has revealed important insights. fMRI provides a means to assess the neurobiological theory that schizophrenia is caused by abnormal fronto–temporal lobe connections. In studies of language abnormalities, fMRI can explicitly assess the hypothesis that the normal lateralization of language is reversed in schizophrenia. Longitudinal fMRI studies, and studies examining the effects of medication, suggest that the technique has further potential to advance our understanding of this complex disorder.

A century ago Kraepelin described a group of psychiatric disturbances, which he saw as a single disease entity, the common feature of which was a loss of the internal connections of the psychic personality[1]. He termed this disease 'dementia praecox' because of the apparent degradation in function over time, and the young age of onset. His observations were later refined by Bleuler[2], who renamed the disease 'schizophrenia'.

SCHIZOPHRENIA (see Glossary) is a PSYCHOTIC DISORDER in which hallucinations and delusions are hallmark features, and impaired judgement and loss of contact with reality typically occur. The disease is characterised by a range of symptoms, frequently classified into POSITIVE and NEGATIVE SYMPTOMS (see Box 1). Positive symptoms refer to behaviours and cognitions that are not normally present in the general population, whilst negative symptoms refer to behaviours and cognitions that are absent in schizophrenia, but are normally present in the general population. Schizophrenia is a heterogeneous disorder, and individual symptom profiles may vary considerably. Although the core symptoms are occasionally seen in other disorders, the disturbances of word usage and linguistic expression seen in formal thought disorder, are unique and specific to schizophrenia.

Schizophrenia is relatively common, with a lifetime prevalence of approximately 1 in 100. Indeed,