

in the hexamer is probabilistic, and not held to a particular firing order as prescribed by concerted or sequential models (Figure 2). As the authors point out, this mechanism is also well suited to the biological properties of the system. When an unfolded polypeptide chain is translocated through the hexameric ClpX ring, each segment of the substrate is conformationally and chemically unique and may be located anywhere in the ring. At any given time, one ClpX subunit may be better positioned than another to interact with the substrate. As the enzyme need not follow a specified firing order, the subunit best positioned to interact with the substrate can hydrolyze ATP, driving that particular round of unfolding and translocation.

Is the probabilistic model for AAA+ ATPase motor function used by other proteins? Many AAA+ machines act on heterogeneous substrates, suggesting that this mechanism would be advantageous for other members of the family. In addition, mechanisms that invoke a specified firing order for motor function require specific, ordered interactions between subunits. The probabilistic mechanism is not bound by such constraints and can function similarly with the

wide array of quaternary structures adopted by diverse AAA+ enzymes. When appropriate linkers can be designed, comparable experiments with other AAA+ ATPase machines will determine whether the probabilistic model is indeed a general mechanism and will provide new insights into how these remarkable machines function.

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Insect Navigation: No Map at the End of the Trail?

Although the hunt for cognitive maps in insects may not have reached the end, the search itself has been fruitful in sharpening our understanding of the ways that insects navigate through familiar surroundings.

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Almost every year new discoveries increase one's appreciation of the behavioural sophistication of ants and bees, making one wonder how the cognitive capacities of these small-brained animals measure up to those of much larger-brained mammals. Studying cognitive

capacities is particularly informative within a behavioural domain, such as navigation, where different species do roughly similar things. A paper by Wehner and colleagues [1], published recently in *Current Biology*, introduces an interesting new method for asking how flexibly ants use landmark memories when navigating within familiar terrain.

Habits often mask behavioural flexibility. On our habitual route to work, we tend to perform, as if in a trance, a sequence of stereotyped actions that are often cued by landmarks along the route. Should we be stopped for directions mid-route, then we may wake up and, as we formulate a reply, become aware of the many types of spatial memories that we have at our disposal, but which are normally masked while we follow our route. By pointing in the direction of the requested location, we can communicate its position relative to where we are. Or we can give a sequence of instructions that describe a route to the location, possibly choosing between several routes. Such route instructions, moreover, are

likely to include a description of prominent landscape features which serve as sign-posts or beacons along the way. The flexibility that allows us to imagine a variety of possible routes to an arbitrarily chosen goal or to figure-out its direction, we take as evidence for having what is loosely called a cognitive map [2] which endows landmarks with positional information.

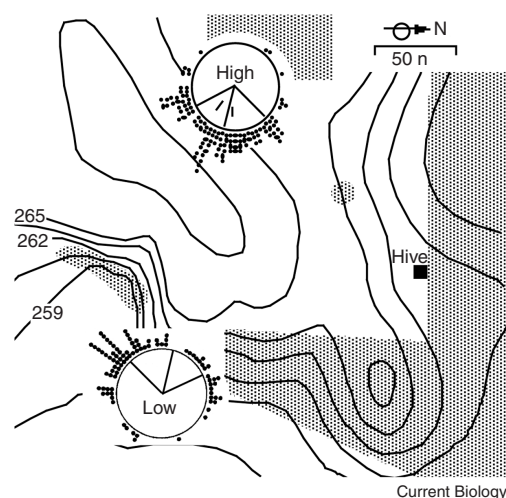
Insects such as ants and honeybees also exhibit a remarkable variety of navigational memories. But are these memories organised to allow a similar degree of flexibility as that available to humans? Ants travelling from their nest to a foraging site establish idiosyncratic and stereotyped routes [3]. Many species form routes by laying pheromone trails, but the routes of desert ants depend upon the acquisition of visual memories [4]. Landscape features remembered as landmarks can act as beacons, guidelines or sign-posts that trigger memories of subsequent route-segments.

Ever since Gould [5] raised the question in the mid 1980s, it has been asked repeatedly whether an insect's habitual route-following might mask a richer representation of familiar terrain in which landmarks provide positional information that could support more flexible feats of navigation [6–8]. This question is often posed in terms of a forager's ability to take a novel shortcut to a familiar goal. For an experiment to give a useful answer, one must have evidence that at least three conditions are met. First, the release site must be familiar. Second, foragers must be motivated to travel towards the goal — either a food-site or nest. Third, guidance should not be available from landmarks near the goal or along a habitual route to the goal.

An exemplary study by Dyer [9] to test whether food-motivated foragers are able to take novel shortcuts to a familiar food-site illustrates the difficulties of doing such experiments. Two groups of honeybees were trained to one of two feeder locations — one higher

Figure 1. Novel shortcuts require a view of the goal.

Honeybees trained to a low-lying feeder (Low) were captured on leaving the hive and released at a higher location (High). The bees could look down on landmarks surrounding their trained feeder, and the majority of the vanishing bearings (from High) were towards their trained feeder (Low). The vanishing bearings in the converse experiment (from Low), in which the released bees could not see their trained feeder, were split between the direction they would have taken had they not been displaced (Hive to High) and the return direction to the hive (Low to Hive). (Adapted from [9].)



than the other — in a slightly hilly landscape (Figure 1). Bees trained to one location were captured on leaving the hive and released at their non-trained location to see whether they flew along the shortcut to their trained feeder. The choice of release sites ensured an asymmetry in the visual cues available to the released bees. From the high release site the bees could look down on landmarks surrounding their low-lying trained feeder. While a minority followed the compass cues from the hive or took a path back to the hive, the majority did indeed take the shortcut.

In contrast, from the low-lying release site, bees could not see the landmarks surrounding the high-location feeder to which they had been trained. These foragers did not take the shortcut: the majority flew in the compass direction they would have taken from the nest (showing that they retained a food-ward motivation), while a sizeable minority took the route back to the hive (showing that they recognised the landscape, but used landmark features in a home-motivated fashion). With pre-training to the low-lying feeder location all bees followed route-cues back to the hive. Foragers were thus able to use familiar landmarks flexibly (in the sense of recognizing them from unexpected locations or motivational states) but only as indicators of a particular goal or

route. But might the bees' propensity to go home have masked something more map-like?

In their new displacement experiment on the Australian ant, *Melophorus*, Wehner *et al.* [1] made sure that the ants were familiar with landmarks at a release site, while reducing as far as possible the chances that the ants' habit of following routes could mask the use of any positional memories that the ants might have. *Melophorus* inhabits an environment with abundant grass tussocks and occasional trees that can serve as landmarks. Two long, low barriers placed in this terrain led the ants to follow a one-way foraging circuit between their nest and a feeder with a 2–5 m separation between the food-ward and homeward paths (Figure 2A).

The ants apparently established idiosyncratic routes through this terrain to reach the feeder. This point is important, as consistent routes, which differ between individuals, provide the evidence that foragers have indeed learnt landmark features for use in navigation. Ants returning from the feeder were captured close to the nest and released at a point in the middle of the food-ward route. Normally, the ants encountered this release site only when they were motivated to go to the feeder. What would the ants do when they viewed familiar landmarks at the release site in a

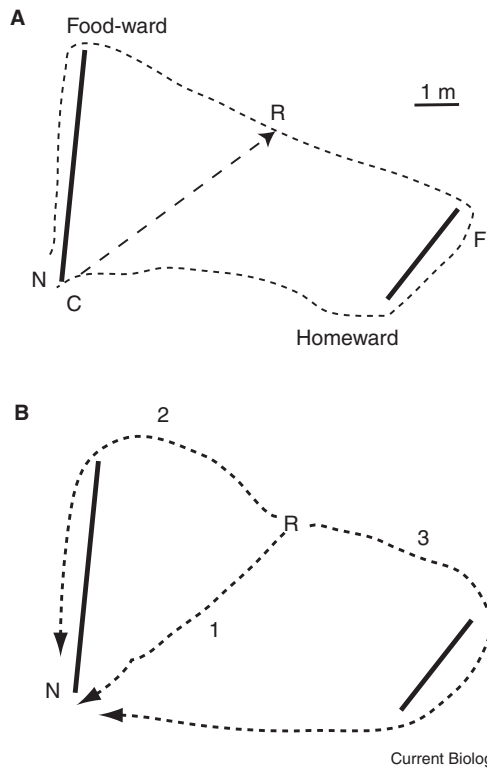


Figure 2. The ants' one-way circuit.

Low barriers (thick lines) encouraged ants to follow different paths to the feeder and on the way home. (A) Ants caught on their way home (C) when close to the nest (N) were released (R) on their path to the food (F). (B) Three possible routes to the nest that the ants failed to take.

homeward motivational state? Might this unusual situation uncover hidden positional memories?

Displaced ants on release performed a search that was partly biased by landmarks, and which led some of the ants to encounter their homeward route. The majority of these ants then joined the route and, as would be predicted [10], followed the route cues home. Most significant is what the ants failed to do while searching, as these failures indicate memories that the ants either have not acquired or do not use.

The first notable thing that the ants did not do was to take a direct path back to the nest (Figure 2B). One kind of memory that would have allowed them to take this shortcut is a landmark-associated path integration memory. Path integration is the process by which ants and bees keep track of their position with respect to their start point at the nest — not by means of landmarks, but by integrating their path as indicated by their sky compass and some kind of odometer [11]. Using the results of its path integration, an ant or bee

can return from any position it has reached in a direct line to its nest without knowledge of the terrain it covers. Insects could make their navigation more versatile by storing path integration states at prominent locations and associating these path integration memories with landmark memories [12]. The recall of a path integration state when an animal is displaced to a familiar site could then allow the animal to produce a direct path to any location with stored path integration coordinates.

That *Melophorus* did not take the shortcut when displaced to a location on their familiar one way circuit [1] is consistent with experiments on another desert ant, *Cataglyphis fortis*. These experiments tested whether familiar landscape features along a route can reset the state of an ant's path integrator. There was no sign of resetting either on the way to the feeder [13], at the feeder [14], at prominent landmarks on the way home [14,15], or at the nest [16]. Rather than being used in association with landmark memories, path integration appears to be reserved as an independent source of

information about a forager's position based only on movement information from the current trip.

The second notable thing that the ants did not do was to retrace their food-ward route back to the nest (Figure 2B), suggesting that ants have not incidentally learnt the route in reverse. That the ants took neither the reverse route nor the shortcut home suggests in addition that the ants have not incorporated the landmark memories into some kind of cognitive map [1] or general landscape memory [8]. In general the question of whether insects such as ants or honeybees have cognitive maps is hard to settle definitively. First, there is no general agreement about what constitutes a cognitive map [17]. Second, it is not always straightforward to decide whether experimental results can be safely accepted as evidence for or against map-like representations. It is hard to refute the possibility that apparently 'map-like' behaviour [18] can be explained by direct visual guidance through cues belonging to a learnt route [9]. Equally, it is difficult to discount the possibilities that insects showing no map-like behaviour either have too little experience to acquire positional memories (individuals may take longer to acquire maps than routes), or too much route experience to use them. While one could argue that in Wehner *et al.*'s experiment [1] the ants had not explored the interior of the foraging circuit and so had no opportunity to incorporate the landmarks there into a general landscape memory, the same argument could not be applied to the ants' failure to reverse their familiar food-ward route. Instead, the ants seem to limit the use of landmark memories to recognising goals or triggering procedural instructions for following routes [3,4,10,14].

The third notable thing that the homebound ants mostly failed to do was to follow the food-ward route (Figure 2B). In contrast, when these ants hit the homeward route, the majority joined it immediately and followed it all the way to the nest. In this case, the

ants' motivational state determines so strongly which landmarks the ants use that most home-motivated ants ignore the food-ward route entirely. In a study with the two routes closer together, displaced home-motivated ants had the opportunity to choose between the routes; they then joined their homeward route in preference to the food-ward one [10]. That such a preference can be triggered by motivational state is borne out by experiments on wood ants showing that visual memories for the ant's homeward or food-ward route can be primed selectively simply according to whether or not the ant has fed [19].

The segregation of memory-use according to motivational state makes good sense. Often food-ward and homeward routes are intertwined so that an insect that did not prime memories according to motivational state might well retrieve the memory for the wrong route and so be guided in the wrong direction. Ants seem not to be misled in this way. Similarly, on our way to work we may pass the pub that we will visit on our way home. In our hurry we may or may not notice the pub, but we will certainly not stop and go in. In humans, such motivational priming will probably influence

whether we notice a landmark, the recognition of the landmark, as well as the triggering of any actions associated with the landmark. In this respect, insects and humans may not greatly differ. Nonetheless, big brains undoubtedly have their uses, even for navigation.

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Tubulogenesis: An Inside Job

New work shows that a dynamic and highly patterned apical extracellular matrix regulates epithelial cell shape and tube size from within the lumen of the *Drosophila* tracheal system.

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Size does matter. While endlessly debated in social circles, this is unquestionably true for the normal function of the epithelial and endothelial tubes that comprise such organs as the vascular system, lung and kidney. The enlarged tubules in a polycystic kidney, for instance, literally crush the surrounding normal tubules, while narrowed blood vessels can cause ischemic tissue injuries.

Surprisingly, the molecular and cellular mechanisms of tube-size regulation are poorly understood, and therapeutics to intervene in conditions such as polycystic kidney disease are non-existent. However, a flurry of papers, including those by Luschnig *et al.* [1] and Wang *et al.* [2] in this issue of *Current Biology*, have now defined a new mechanistic framework for understanding epithelial tube-size regulation in one of the best studied models for tubulogenesis, the *Drosophila*

tracheal system [3]. Importantly, the combined results have implications for understanding not only tube-size control, but also the mechanisms of specialized apical secretion, the role of extracellular matrix (ECM) in controlling cell shape, and possibly conserved signaling or morphogenic roles for what has been considered an invertebrate specific oligosaccharide.

The stage was set for the Wang and Luschnig papers [1,2] by recent papers from the Samakovlis, Uv, Krasnow, Casanova and Nüsslein-Volhard groups that showed that the genetically programmed tripling of the diameter of the tracheal tubes requires the formation of a transient luminal chitin-based