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## Spatial Representation: Maps in a Temporal Void

It has been suggested that the matrix-like firing structure of entorhinal grid cells is caused by interference between membrane oscillations at slightly different theta frequencies. A recent report suggests that grid signals can be generated in the absence of theta oscillations.

Lisa M. Giocomo and Edvard I. Moser

Spatial representation in mammals is thought to depend on place-specific neurons in the hippocampus and entorhinal cortex. 'Place cells' in the hippocampus fire in a single location within the environment, reflecting the encoding of complex relationships between self-motion and external landmarks [1]. Place cells receive input from grid cells in the entorhinal cortex – place-modulated neurons whose firing locations define a periodic triangular array covering the entirety of the animal's environment [2,3]. Grid cells are thought to provide the metrics for spatial representation and navigation [3,4].

The mechanism generating the periodic grid map remains one of the biggest unresolved questions. One class of computational models suggests that the spatial periodicity of grid cells is derived from the theta rhythm, a prominent hippocampal-entorhinal network oscillation in the 6–10 Hz frequency

range [5,6]. In these models, a periodic spatial signal is formed by interference between a velocity modulated oscillation and a baseline oscillation at slightly different theta frequencies [7–9]. Implicit to the 'oscillatory interference' models is a breakdown of grid patterns in the absence of theta oscillations. Recent work suggests that some species may navigate at least partially without theta activity. While nearly continuous theta oscillations are a prominent characteristic of electro-encephalogram (EEG) signals during foraging in rodents, theta waves appear more intermittently in other species, including bats [10] and humans [11]. The sporadic nature of the theta activity is maintained during movement in bats [10]. In a recent paper, Yartsev and colleagues [12] take advantage of this species variability to determine whether grid cells can exist in the absence of theta oscillations.

Yartsev *et al.* [12] recorded single-unit activity from the

hippocampus and medial entorhinal cortex of Egyptian fruit bats as the animals crawled around a large enclosure in search of food. Under these conditions, place cells and grid cells could both be identified. Grid cells showed all the cardinal features of rodent grid cells, including a hexagonal firing lattice, co-localization of cells with similar grid orientation and grid spacing, offsets in firing phase of co-localized neurons, an increase in scale along the dorsal to ventral axis, and velocity modulation of the firing rate. The medial entorhinal cortex of bats also contained the same functional cell types as in rodents; pure grid cells, conjunctive grid-head direction cells, pure head direction cells and border cells. These results are significant for two reasons. First, the data show that grid cells are present in a species that is phylogenetically distant from rodents [13] (Figure 1). In spite of this distance, the cytoarchitecture of the hippocampal and entorhinal cortices of bats and rodents is very similar. The formation of grid structure may depend on the common architectural features. A second and more important point is the observation of grid structure in the apparent absence of theta activity. Theta oscillations were present only in one-second long bursts with an average interval between the bursts of 37 seconds in the entorhinal cortex. Between the bursts, theta oscillations

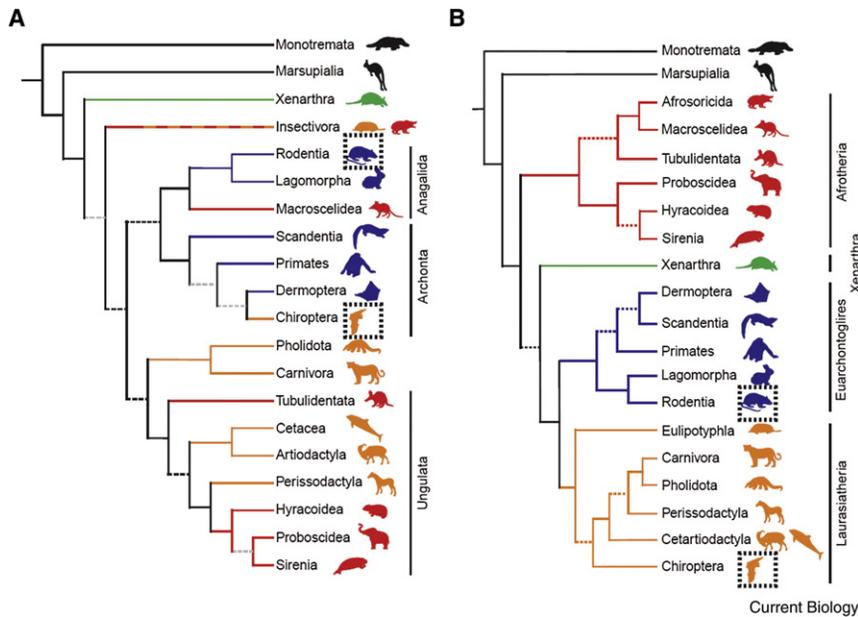


Figure 1. Bats are not flying rodents. Phylogenetically, bats and rodents branch off early. (A) The prevailing morphological tree of the placental orders. (B) The emerging molecular tree of the placental orders. (Figure adapted from [13].)

were not detectable, neither in local field potentials nor in autocorrelations of discharge in individual cells (Figure 2). Notably, the grid pattern was equally prominent during these theta-free intervals as in analyses of the entire recording session.

The persistence of spatial periodicity between the theta bouts is potentially cataclysmic for the oscillatory interference models of grid cells. The intermittent nature of the theta oscillation in bats is fundamentally different from the continuous activity used to generate grid patterns in the oscillatory interference models. However, it may be somewhat premature to discount these models entirely. We will consider three factors. First, and most importantly, the low firing rates of the grid cells in the bat study may mask an underlying pattern of theta modulation. Speaking against this possibility is the fact that theta modulation was not present in the multiunit data, although it cannot be excluded that a common phase relationship among theta-modulated cells was lost between the theta bouts to an extent that prevents peaks in the autocorrelogram. The authors should determine if theta modulation is present when higher-rate data from rats (e.g. publicly available data from [3]) are downsampled to the average

rates of the bat study for similar trial durations. Second, it cannot be ruled out that oscillatory interference takes place, in some form, at higher frequencies than theta. Example traces showed clear evidence of gamma activity in the bat, although these oscillations were short-lasting and varied in frequency. Such supra-theta oscillations may give rise to periodic spatial signals, although the existing models would require substantial revision if this were the case. Finally, the entorhinal network may *in principle* have more than one mechanism for producing grid activity and different mechanisms may be applied to various extents in different species or behavioral conditions. Work on simpler preparations suggests that an apparently uniform pattern of network activity can be generated by a number of mechanisms [14] and it is possible that rodents have evolved mechanisms to exploit the continuity of theta to generate grid fields. On the other hand, it would be extremely surprising if a dual set of mechanisms resulted in grid cells with exactly the same properties and an identical functional organization. Evidence in favour of a role for theta oscillations in grid formation in rats was recently reported in two studies [15,16].

These studies showed a clear loss of grid structure after blocking the theta rhythm by inactivation of the medial septum. The two studies are correlative, however, and grid activity may have disappeared for reasons besides the blockade of theta rhythm, such as the loss of cholinergic input or the drop in firing rates. This should be tested directly.

If grid cells are produced by a theta-independent mechanism in bats, what then is that mechanism? A series of theta-independent models has suggested that grid patterns are generated from local network activity. In one class of network models, activity moves across attractor networks of recurrently connected neurons in proportion to the speed and direction of the animal's movement [4,17,18]. Other network models point to Hebbian competitive learning as the principal mechanism for spatial periodicity [e.g., 19]. The presence of grid cells in the absence of theta waves does

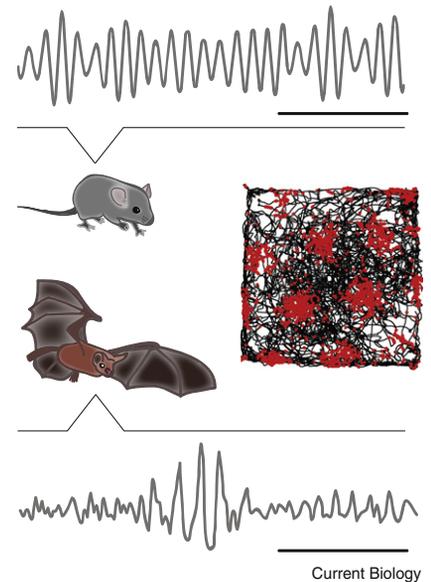


Figure 2. Theta oscillations are fundamentally different in bats and rodents. Despite the different nature of theta rhythms in rodents (top left) and bats (bottom left), medial entorhinal grid cells are present in both (right). The trajectory of a rat in a 1.5 x 1.5 meter box is shown in black and spikes are plotted in red. Top: theta rhythms are present continuously during movement in rodents. An example from a rat is shown. Trace in grey filtered at 6–11 Hz. (Adapted with permission from [20].) Bottom: theta rhythms occur sporadically during movement in bats. Trace in grey filtered at 4–25 Hz. (Adapted with permission from [12].) Black line represents one second.

not contradict any of these models but also does not directly test any of their predictions.

The bat study [12] has implications beyond the dissociation of grid patterns from theta oscillations. The presence of spatial encoding in the absence of theta activity raises questions about the role of theta rhythms more generally. In rats, theta rhythms are thought to organize sequences of spatial firing and link distributed cell ensembles during key functions of the hippocampus such as memory encoding and retrieval [6]. Is such synchronization not required for spatial performance in bats? Can bats store and retrieve place sequences without theta oscillations and are such sequences represented in the same way in bats and rodents? What is the function of the theta bouts; do they shape the activity of the network during the subsequent seconds, and are such effects necessary for spatial firing and spatial performance? The demonstration of grid cells in the absence of detectable theta oscillations in Egyptian fruit bats is a fresh input which undoubtedly will guide theoretical and experimental studies during the next years.

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## Invertebrate Evolution: Bringing Order to the Molluscan Chaos

While the seven classes within the phylum Mollusca are clearly defined morphologically and molecularly, relationships between them have long been contentious. Two recent phylogenomic studies take an important step forward with intriguing implications for their evolution.

Maximilian J. Telford<sup>1</sup>  
and Graham E. Budd<sup>2</sup>

The phylum Mollusca is second only to the arthropods in terms of numbers of species (>100,000). Not only are the molluscs speciose, they are also highly disparate (compare a giant squid, a snail and an oyster), so much so that it has proved difficult to identify features they all share; this disparity has led to more than a century of dispute over the relationships between molluscan classes. This phylogenetic confusion has fostered the production of competing versions of the infamous

'hypothetical ancestral mollusc' — a clunky assembling of key features of living molluscs into a limpet-like archetype that has long acted as a restraining dead hand on the understanding of molluscan evolution. Two recent studies [1,2] using phylogenomic-scale molecular data sets bring a significant new degree of order to this chaos and promise a solid basis for future reconstructions of molluscan evolution.

The phylum Mollusca contains seven easily distinguished classes (Figure 1), of which the edible ones (Gastropoda — snails, whelks

and winkles; Cephalopoda — *calamari*; and Bivalvia — *moules marinière*) are immediately familiar, whilst the Scaphopoda (tusk shells) and Polyplacophora (chitons), although absent from most seafood platters, are easy to find on rocky shores or in shallow water. Much less familiar are the Monoplacophora, a single-shelled group known only, until the discovery of living examples in 1952, from 400 million year old fossils, and the shell-less Aplacophora (Caudofoveata and Solenogastres, or, if you prefer, the Chaetodermomorpha and Neomeniomorpha). The Aplacophora are more worm-like than molluscan, yet they possess typical molluscan features such as a radula (rasping tongue) and ctenidia (gills).

Along with their intrinsic interest, Molluscs are important for understanding broader animal relationships because of the intriguing organisation they possess. Hints of