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# Hippocampal spatial navigation: interneurons take responsibility

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The hippocampal formation has a central role in spatial navigation. The recording of individual neuronal activity in the awake freely moving rat during a spatial navigation began with the landmark studies of O'Keefe & Dostrovsky (1971) and Ranck (1973). Two types of hippocampal CA1 neurons, designated as complex spike cells and theta cells, have been identified on the basis of their firing rates, action potential width, and locations in the hippocampus (Ranck, 1973). These two classes of cells were later identified as excitatory pyramidal cells and fast-spiking inhibitory interneurons. These and subsequent studies have demonstrated that hippocampal pyramidal cells exhibit peaks in their activity in particular regions of the environment (place field) and revealed a changing phase relationship with the ongoing rhythmic activity of the network as the animal moves across the field (phase precession) indicating the central role of these cells in spatial processing. In contrast, interneurons have been regarded as time signal generators providing a temporal context for spatial processing in hippocampal networks, rather than directly contributing to space-specific activity.

In the CA1 area, 21 types of GABAergic interneurons have been described so far (Klausberger & Somogyi, 2008). These can be grouped into three main types: perisomatic and dendritic inhibitory interneurons, and GABAergic cells specifically innervating other inhibitory interneurons. Dendritic inhibition regulates the efficacy and plasticity of excitatory synaptic inputs, whereas perisomatic inhibition controls the output, and can thereby synchronize the discharge of large groups of principal cells (Freund & Buzsáki, 1996). The involvement of interneurons in rhythm generation, such as theta and gamma network oscillations, is well documented. However, a growing body of evidence indicates that the role of interneurons extends beyond that of rhythm generation. For example, during exploratory behaviour on a linear track, GABAergic interneurons also show spatially selective discharge and phase precession, suggesting that they participate in a finely tuned local interaction with pyramidal cells (Ego-Stengel & Wilson, 2007). Spatial firing of interneurons and principal cells often showed parallel changes, suggesting that the discharge of the interneurons could be simply driven by the principal cells. In other instances, however, spatially specific firing of hippocampal place cells may be determined by an associated location-specific decrease of interneuron activity ('Off' field) that can release place cells from inhibition (Wilent & Nitz, 2007).

In a recent issue of *The Journal of Physiology*, Hangya *et al.* (2010) provided novel insights into the role played by interneurons in hippocampal spatial navigation. Using simultaneous recording from CA1 place cells and interneurons in freely moving rats, they demonstrated that place cell–interneuron pairs with both similar (positively correlated) and complementary (negatively-correlated) firing patterns coexist in the hippocampus. Unexpectedly, the complementary spatial firing patterns can be observed in the presence of positive temporal correlation in firing of pyramidal cell–interneuron pairs. In addition, both types of correlation were detected in the presence and absence of putative monosynaptic connections from pyramidal cells to interneurons. These results suggest that location-specific firing of hippocampal interneurons is not a simple consequence of their activation by a pyramidal cell with a similarly positioned place field but reflects a more complex interaction between these cell types within hippocampal microcircuits during spatial navigation.

Investigating the phase preference of interneurons relative to the theta rhythms recorded in the pyramidal cell layer, Hangya and colleagues (2010) find that regardless of the sign of spatial correlation (positive or negative) most of the interneurons discharged on the positive phase of theta oscillations. On the basis of their phase preference, the authors suggest that these interneurons represent perisomatic inhibitory interneurons, putative basket and axo-axonic cells. The precise identity of neurons recorded in freely moving animals is a critical question for this and related studies. Current identification is based on differences in the action potential waveform, firing rates and some other properties (e.g. Csicsvari *et al.* 1998; Hangya *et al.* 2010) and this method does not allow for the separation of the distinct types of fast spiking perisomatic inhibitory interneurons. Moreover, some dendrite-inhibiting interneurons located in strata pyramidale and oriens may also exhibit the fast firing phenotype. As different subclasses of fast spiking inhibitory cells based on their distinct intrinsic and synaptic properties could differentially be involved in spatial navigation, additional, more precise morphological and physiological identification of the recorded cells is required.

For a more complete understanding of the role of interneurons in spatial navigation, we need to also address the impact of non-fast spiking interneurons. Recent data suggest that an activity-dependent release of endocannabinoids from active place cells during late theta cycles can modulate the temporal profile of perisomatic GABA release by CCK-immunopositive non-fast spiking interneurons and may shape the pattern of theta related discharge of principal cells (Losonczy *et al.* 2010). Furthermore, we need information on how GABAergic cell types selectively innervating other inhibitory interneurons are involved in formation of spatial firing patterns. This information will help us to understand how hippocampal microcircuits incorporating the place cells and various classes of interneurons are built and function during spatial navigation. In this respect, *in vivo* approaches, such as juxtracellular and whole-cell patch-clamp recordings (Klausberger *et al.* 2003; Lee *et al.* 2009; Epsztein *et al.* 2010) in awake animals in combination with subsequent anatomical identification of recorded neurons, will certainly facilitate progress in this area.

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