

**INTRODUCTION****Beyond replay: Introduction to the special issue on hippocampal replay**

The hippocampus has at least two modes of operation: theta, which appears as a 6–10 Hz rhythm (in the rat) of repeating components with a 100–180 ms period, during which the hippocampal place fields sweep forward from a rat's current position ahead of the animal, and large amplitude irregular activity (LIA), which reveals a broader spectrum in the local field potential, and is punctuated by transient sharp wave–ripple complexes (SWRs, 150–200 ms bursts of coherent 150–200 Hz rhythms) and hippocampal replay events (Buzsáki, Leung, & Vanderwolf, 1983; Foster, 2017; O'Keefe & Nadel, 1978; Redish, 1999, 2016; Vanderwolf, 1969). These different modes have been seen in other animals as well from mice to bats<sup>1</sup> to monkeys to humans (Buzsáki, 2015).

When it was first observed that hippocampal cells “replayed” experiences by reactivating during rest and sleep following behavior (Nádasdy, Hirase, Czurkó, Csicsvari, & Buzsáki, 1999; Pavlides & Winson, 1989; Skaggs & McNaughton, 1996; Wilson & McNaughton, 1994), it was thought that replay was part of a consolidation process that wrote information from a transient memory storage in hippocampus to a long-term storage in cortex (see Sutherland & McNaughton, 2000; Redish, 1999 for reviews of the classic literature). While evidence still supports this original theory (Klitzing, Niethard, & Born, 2019), over the years, it has been found that these replays occur during waking states as well (Kudrimoti, Barnes, & McNaughton, 1999), differ between waking and sleeping states (Wikenheiser & Redish, 2013; Buzsáki, 2015), and change as animals become familiar with their environments (Cheng & Frank, 2008; Poe, Nitz, McNaughton, & Barnes, 2000; Shin, Tang, & Jadhav, 2019; Wu & Foster, 2014). Hippocampal representation during these “replay” events can show both forward and backward sequences (Davidson, Kloosterman, & Wilson, 2009; Foster & Wilson, 2006; Gupta, van der Meer, Touretzky, & Redish, 2010; Ólafsdóttir, Bush, & Barry, 2018; Shin et al., 2019), can reveal shortcuts the animal has never experienced (Dragoi & Tonegawa, 2013; Gupta et al., 2010; Ólafsdóttir, Barry, Saleem, Hassabis, & Spiers, 2015), and [sometimes] predict where the animal is going to go (Pfeiffer & Foster, 2013; Schmidt, Wikenheiser, & Redish, 2018; Shin et al., 2019; Singer, Carr, Karlsson, & Frank, 2013) but [sometimes] prefer where the animal has not been or is not going to go (Carey, Tanaka, & van der Meer, 2019; Gupta et al., 2010). Hippocampal replay has been found to interact with deep medial entorhinal cortex (Buzsáki, 2015; Chrobak & Buzsáki, 1996; Ólafsdóttir, Carpenter, & Barry, 2016), prelimbic cortex (Euston, Gruber, & McNaughton, 2012; Peyrache, Khamassi, Benchenane, Wiener, & Battaglia, 2009; Shin

et al., 2019), as well as other cortical areas (Buzsáki, 2015). Hippocampal replay events are aligned with value representations in the ventral striatum (nucleus accumbens core, Lansink, Goltstein, Lankelma, McNaughton, & Pennartz, 2009).

Functionally, disruption of hippocampal SWRs during sleep has been found to disrupt goal-related learning across days (Ego-Stengel & Wilson, 2010; Maingret, Girardeau, Todorova, Goutierre, & Zugaro, 2016), while enhancement of rewarding signals (medial forebrain bundle stimulation) during place cell activation during sleep creates goal-related learning (de Lavilléon, Lacroix, Rondi-Reig, & Benchenane, 2015). However, disruption of hippocampal SWRs during waking states produces changes in the ability to use working memory to plan and take correct paths (Fernández-Ruiz et al., 2019; Jadhav, Kemere, German, & Frank, 2012).

In this special issue, seven leaders in the field along with their teams present new data, reviews, and theoretical insights into the complexity that is hippocampal “replay.” We start with Pfeiffer (2020), who reviews the relationship of the content of replay to recent actions and future plans. Laventure and Benchenane (2020) review the evidence that sleep replay during SWRs really is causally involved in consolidation properties and in linking spatial signals with emotional valence. Cowen, Gray, Wiegand, Schimanski, and Barnes (2020) report interesting observations of the differences in waking SWR rates between young and aged animals, finding that younger animals showed higher rates, but that older animals emitted more ripples over the total time due to differences in their underlying behaviors. Todorova and Zugaro (2020) review the relation between hippocampal SWRs and extra-hippocampal neural structures, examining the relationship to other oscillations that occur during sleep and wake states. Hussin, Leonard, and Hoffman (2020) review the spatiotemporal features of SWRs in primates and compare their properties to behavioral effects in macaque monkeys. Zielinski, Tang, and Jadhav (2020) review the hippocampal-prefrontal interactions during theta and SWRs and suggest a theoretical complexity in their interactive roles as animals learn new tasks. Finally, Rusu and Pennartz (2020) provide a review placing SWRs in the context of large-scale theories of decision-making and behavior, suggesting that they play different roles in goal-directed versus habitual behaviors and comparing these roles to putative roles in contrasting theories of model-based and model-free learning, with a particular emphasis on the role of prefrontal-striatal loops and the relation to hippocampal SWRs.

Hippocampal replay is much more than “replay.” These seven papers provide new insights into hippocampal SWRs, replay, and their relationship with the rest of the brain and with behavior. We hope you enjoy this special issue.

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#### ENDNOTE

<sup>1</sup> The bat does not seem to have theta (Eliav et al., 2018) but does seem to show multiple modes of operation, including SWRs (Ulanovsky & Moss, 2007).

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