

# **Drift-diffusion dynamics of the hippocampal replay**

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## Abstract

**The hippocampus and associated brain areas exhibit striking replay activities. Replays are thought to be important in learning, memory and planning, and have important implications in developing learning algorithms in machine learning. Surprisingly, how to characterize the structure of replays remains controversial. Most existing methods rely on restrictive assumptions, by detecting replay activities based on the sequentiality of spike trains or the posterior probability decoded from a Bayesian framework. We develop a general and high-interpretable drift-diffusion framework to understand the structure of replays. The two key parameters (drift & diffusion parameters) in the model can be directly mapped onto the speed and quality of a replay event. Applications of this framework provide new opportunities to address important open questions in the study of replays, including: (i) whether replays follow random walk; (ii) whether many of the replay events are stationary; (iii) whether preplay exists. We expect that our approach will be broadly applicable in studying the structure and dynamics of replays.**

**Keywords:** neural coding; learning; replay; generative models

## Introduction

The mammalian hippocampus exhibits various forms of replay activities. Neural activities during sharp waves and ripples (SWRs) appeared to replay previous experience in forward or reverse orders, both during sleep (Skaggs & McNaughton, 1996) and awake immobility (Foster & Wilson, 2006). Replays were initially discovered in rodents, and more recently in humans (Schapiro, McDevitt, Rogers, Mednick, & Norman, 2018). Replays in the Hippocampus were found to be coordinated with neural activities in other brain regions, e.g., prefrontal cortex (Shin, Tang, & Jadhav, 2019) and visual cortex (Ji & Wilson, 2007). Replays are generally thought to play important roles in learning, memory consolidation, and planning (Foster, 2017; Stachenfeld, Botvinick, & Gershman, 2017). In machine learning, algorithms based on experience-based replay have been developed (Van de Ven, Siegelmann, & Tolias, 2020). These algorithms have been shown to increase the performance of learning in a variety of tasks and play an important role in reinforcement learning (Schaul, Quan, Antonoglou, & Silver, 2015; Mattar & Daw, 2018).

Despite of decades of research, detecting replays and characterizing their properties remain challenging. Classic approach relies on template matching, i.e., to assess how well a given population activity pattern during SWRs matches that during running (Wilson & McNaughton, 1994; Skaggs & McNaughton, 1996). However, many SWRs events can not be unambiguously classified according to this approach, making it difficult to analyze replays. Recent studies suggest replays may exhibit richer dynamics than initially considered, and such dynamics may have important implications in learning (McNamee, Stachenfeld, Botvinick, & Gershman, 2021).

Here we propose a general drift-diffusion framework to study the dynamical structure of replay events, building upon recent work that seeks to better describe the rich dynamics of replays (Denovellis et al., 2021; Krause & Drugowitsch, 2022).

Our framework generalizes the classic methods of analyzing replays, yet remains simple and highly interpretable. Preliminary applications of our method to hippocampal recordings during spatial tasks lead to new ways to resolve several major debates in the study of replay.

## Results and Discussions

### Modeling framework

Consider an experiment where the animal is navigating on a one-dimensional track (Fig. 1A), which is a commonly used behavioral paradigm in studying replays. During SWRs, hippocampal activity encodes sequence of locations on the track. Classic replay detection methods assume that these locations change at a constant speed (as if the animal is running on the track at a constant speed). We generalize this idea by allowing more flexible transition dynamics between replay states.

Specifically, we assume that the temporal transition dynamics of replayed locations was characterized by a drift-diffusion process (Fig. 1B):

$$dz = \lambda dt + \sigma dW \quad (1)$$

where  $\lambda$  and  $\sigma$  are the drift and diffusion parameters.  $dW$  denotes the standard Brownian motion process. We further assume that given the latent state, the activity of individual neurons follows an independent Poisson process. Practically, we discretize time into small bins (e.g., 10ms), in which case the dynamics can be approximated using transitional probability between the different states for adjacent time steps (i.e., a first-order Markov process). While we will focus on modeling replay in 1-D environment, the approach can be generalized to more complex environments. Several special cases of our model worth pointing out (Fig. 1C):

- **Brownian motion** When drift= 0, and the diffusion parameter is non-zero, the latent trajectory is sampled from 1-d Brownian motion. Brownian motion is recently proposed to describe replay dynamics in 2-D open arena (Stella, Baracskay, O'Neill, & Csicsvari, 2019).
- **Stationary events** When both the drift and diffusion parameters are zero, the trajectory is stationary, a scenario which is emphasized recently in (Denovellis et al., 2021).
- **Pure drift** When diffusion= 0, and drift is non-zero, the latent trajectory will drift toward one direction with a constant speed. Intuitively, this corresponds to a "perfect replay" event according to the classic notion of replay events.

### Model fitting and validation

The drift-diffusion model is formalized as a hidden Markov model (HMM). The observed variables consist of the spike activity recorded from a population of place cells, while the hidden variables correspond to the spatial locations represented during replay events. To fit this model, we use a MLE approach applied to each replay event. Specifically, we utilize the forward-pass algorithm of the HMM to calculate the log-likelihood, which is the sum of natural logarithm of the forward probabilities at each time step. We validated the model with recovery analysis suggesting that parameters can be well recovered with sufficient number of spikes (not shown).

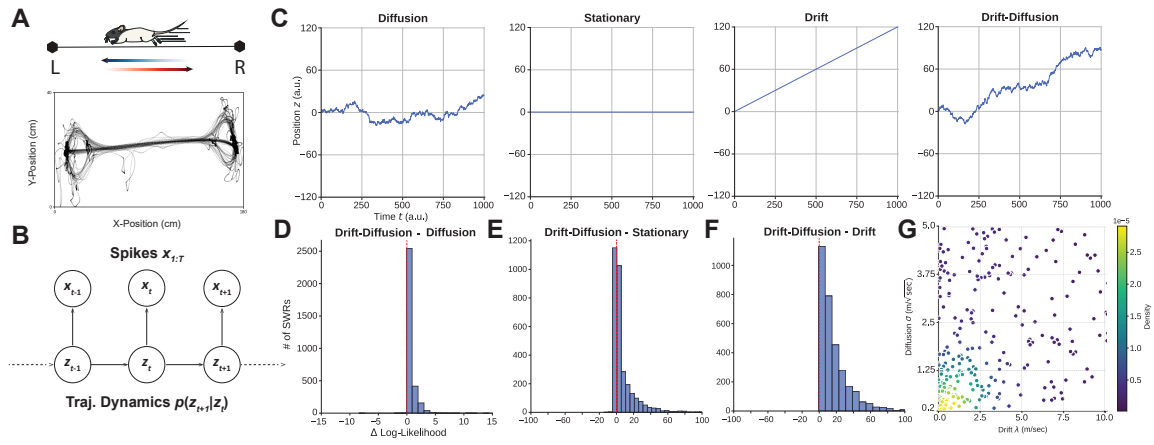


Figure 1: **A.** Top, rat runs back and forth in a 1.8 m linear track to receive rewards shown alternatively at two ends. Bottom, location tracking of the rat during a recording session. The two ends are slightly elongated to place food rewards. **B.** The graph of the hidden Markov models. **C.** Categories of trajectory dynamics considered in the study. **D-F.** Decoding likelihood comparison of stationary, drift, diffusion, and drift-diffusion dynamics. The difference of log-likelihood is calculated between two dynamics for every replay event, with drift-diffusion being the reference. **G.** The distribution of the decoded drift-diffusion parameters for SWRs before running experience ( $n = 544$ ). Each dot is color-coded based on the estimated density from decoded parameter pairs of all pre-run SWRs.

## Applications

We have preliminarily applied our framework to investigate several open questions in the study of replay. We analyze the data from (Pfeiffer & Foster, 2015) by fitting our model to individual SWRs events ( $n = 3185$ ). In these experiments, the rats were navigating on a 1-dimensional track (Fig. 1A).

**Question 1: Does hippocampus replay follow Brownian motion?** A recent study suggests that replays in 2-D open arena resembled Brownian motion (Stella et al., 2019). It is presently unclear whether similar results hold in 1-D. We investigate this question by comparing whether the SWRs events are better explained by drift-diffusion model or a Brownian motion model (i.e., pure diffusion, equivalent to setting the drift parameter to 0). We find that most SWRs events are well explained by the diffusion model (Fig. 1D). Meanwhile, a fraction of the events are slightly better explained by the drift-diffusion model, thus has a non-zero drift speed. These preliminary results suggest that on linear tracks, the majority, but not all, of SWRs events do not exhibit a substantial drift.

**Question 2: Does a large fraction of hippocampus replay stationary?** Recent work argued that a substantial portion of SWR events were stationary events (Denovellis et al., 2021). Our framework offers a natural way to further investigate this question by studying the inferred drift and diffusion parameters from data. Stationary events have zero drift and zero diffusion. Fitting our model to the data, we find a fraction of portion of events with low inferred drift parameter values. To test it further, we constrain the drift and diffusion parameters to be both 0, and fit this model to the data. Comparing the fitted log-likelihood, we find that a significant portion of SWRs are consistent with stationary dynamics (Fig. 1E). However, models based on stationary dynamics perform poorly in a substantial fraction of SWRs (745/3185,  $\sim 23\%$ , have log-likelihood difference  $> 10$ ), thus can not explain all SWRs events.

## Question 3: Is there evidence for preplays during SWR?

It has been suggested that the hippocampus “preplay” sequences of neural activity before the animal has any experience in a given environment (Dragoi & Tonegawa, 2011). While preplays potentially have important implications in the function of replays, the existence and prevalence of preplays remain debated (Silva, Feng, & Foster, 2015), mainly due to the difficulty in characterizing replay events. As our method provides a more general approach to characterize replays, we set to test whether there is evidence for the replay. Applying our method to the data in the sleep phase before running experience (Pfeiffer & Foster, 2015), we observed that a small fraction of the SWRs exhibit sequential structure before the behavioral experience (60 out of 544 SWRs with  $\lambda > 2$  m/s and  $\sigma < 1$  m/ $\sqrt{s}$ ), larger than the fraction obtained from temporally reshuffled data (33 out of 544; p-value = 0.002, one-side test; 90% C.I for difference in proportion: [2.2%, 7.7%]). These preliminary results suggest that (i) hippocampus activity before spatial experiences contain certain sequential structures that is unlikely due to chance; (ii) preplay, if existed, would be generally rare.

## Discussions and future directions

We have developed a drift-diffusion framework to model the replays. A recent study (Krause & Drugowitsch, 2022) uses second-order HMM to model replay. In contrast, we use first-order HMMs that characterize a wide range of dynamics with only a few parameters. We will seek to understand the relationship between our inferred parameters and those from previous template matching-based methods. It should be possible to extend our method to 2-D, incorporating jumping dynamics (Denovellis et al., 2021) and super-diffusive dynamics (McNamee et al., 2021). We expect that a flexible and efficient statistical framework will enable a deeper understanding of the dynamics of replays in the brain.

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