Testing burst coding models of working memory with spike trains from primate prefrontal cortex

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Abstract

Working memory (WM) requires the brain’s ability to convert a brief stimulus-driven signal into an internal representation that can then be maintained across a mnemonic delay of several seconds. In prefrontal cortex (PFC), a neuronal correlate of WM is stimulus-selective persistent activity during the delay. This hallmark persistent activity is typically measured by the elevated mean firing rate, averaged across trials for a stimulus condition, and therefore may obscure more complex patterns of spiking on individual trials. It was recently proposed that observed persistent activity in WM may be an artifact of trial averaging, and that WM is instead subserved by sparse intermittent bursts of neural activity (Lundqvist et al. (2016)). However, that study was done with local field potential (LFP) data, while the predictions of this alternative burst-coding WM proposal for single neuron spiking activity have not been characterized or tested.

To investigate this debated issue, we applied the theory of stochastic processes and analysis of single-neuron recordings from PFC during WM tasks, focusing on measures of across-trial variability such as Fano factor (FF). We first mathematically formalized the burst-coding proposal through a doubly-stochastic inhomogeneous Poisson process model, in which the underlying firing rate transitions follow a two-level telegraph process (Figure 1). This model admits an analytical expression for the FF. We demonstrated that under the burst-coding model, as opposed to the persistent-activity model, elevated WM activity should exhibit an increase in FF. These conclusions are robust under the introduction of refractoriness.

Based on these model predictions, we next tested the plausibility of the burst coding mechanism by analyzing spike train data of many single neurons in monkey PFC during two classic WM tasks used in primate electrophysiology: the oculomotor delayed response task (Constantinidis, Franowicz, and Goldman-Rakic (2001)) and the vibrotactile delayed discrimination task (Romo, Brody, Hernández, and Lemus (1999)). We found that among neurons with selective mean WM delay activity, the majority of cells do not exhibit the variability signatures predicted by the burst-coding model, although a small number do exhibit some burstiness. We also found that globally there tends to be a reduction in FF during the stimulus presentation and WM delay relative to the foreperiod, consistent with prior studies and inconsistent with predictions from the burst-coding model.

We finally analyzed simulated data generated from circuit models. For persistent activity, we used the ring model with strong recurrent excitation proposed by Compte, Brunel, Goldman-Rakic, and Wang (2000). To obtain bursting, we added spike-frequency adaptation and short-term facilitation to a discrete decision making model introduced in Brunel and Wang (2001) and Wang (2002). We showed that FF well differentiated these two divergent mechanisms, with persistent activity showing a decrease in trial-to-trial variability and bursting model showing an increase during the delay. These results demonstrate that these variability analyses can dissociate distinct circuit mechanisms proposed for WM coding.
Taken together, our findings suggest that for these WM tasks, single-neuron spiking activity does not exhibit hallmarks of WM coding by sparse intermittent bursting. Our mathematical and computational framework can be further used to characterize candidate models of WM representations.

**Keywords:** Bursting; Circuit models; Fano factor; Persistent activity; Working memory

**References**


