Title: Real-Time Temporal Code-driven Stimulation using Victor-Purpura Distance for Studying Spike Sequences in Neural Systems

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Introduction (750 characters)

Most neural systems encode information through sequences of action potentials (spikes) [1-3], associated with specific functions and have a stereotyped temporal structure [4]. However, intrinsic variability in neuronal systems introduces temporal variations in spike sequences. In this context, ~~we use~~ the validated closed-loop stimulation protocol [5-8]~~. It allows~~ for the exploration of the underlying meaning of these sequences through its controlled detection, and subsequent stimulation, evaluating whether the administered stimulus elicits comparable responses. We applied it to detect a specific dynamic state in the activity of the Hindmarsh-Rose (HR) neural model [9] and, stimulate it to drive its activity toward a target dynamic state.

Methods (750 characters)

The protocol is based on the Temporal Code-Driven Stimulation [10-12] algorithm, which acquires a neural signal in real-time, binarizes it, and delivers stimulation upon detecting a specific spike sequence (target code). It computes the Victor-Purpura distance [13] between the detected neural codes and the target code, triggering stimulation when the distance is below a defined threshold. The protocol's performance was analyzed for real-time application. Furthermore, two proof-of-concept experiments were conducted: i) the protocol detected bursting activity in the HR model and delivered stimulation to generate brief bursts of spikes, and ii) the protocol regularized chaotic bursting HR model activity.

Results (750 characters)

The real-time performance tests indicated that the protocol can operate at frequencies of up to 20 kHz and detect codes of up to 50 bits for a fixed frequency of 10 kHz, fulfilling the temporal requirements for studying temporal coding in neural systems. The two proof-of-concept experiments validated the protocol's ability to detect a specific dynamic state in the activity of the HR model and drive it toward a target state. Finally, the protocol outperformed an open-loop approach, in which no specific code conditions the stimulation, in conditioning the activity of the HR model.

Discussion (750 characters)

The real-time closed-loop stimulation protocol studied in this work enables the study of temporal coding in neural systems while accounting for their intrinsic variability in encoding information. The protocol was validated for real-time use. Additionally, the two proof-of-concept experiments demonstrated that the protocol can detect specific dynamic states with variability and drive neural activity toward a target state through activity-dependent stimulation. This allows for the study of neural codes that could have the same functional meaning if stimulation following their detection generates equivalent responses.

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