P267 Real-time closed-loop perturbation of electrically coupled neurons to characterize sequential dynamics in CPG circuits

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Introduction

Dynamical invariants in the form of robust cycle-by-cycle relationships between intervals that build robust neural sequences have been observed recently in central pattern generators circuits (CPGs) [1]. In this study, we analyze the effect of different closed- loop perturbations on electrically coupled neurons that are part of a CPG to determine the associated modulation of sequence interval variability, synchronization and dynamical invariants.

Methods

This research was performed in the pyloric CPG involving both voltage recordings and current injection in the PD neurons, which are electrically coupled cells in this circuit. Additionally, we recorded extracellularly from the LP neuron to quantify the LPPD delay, an interval that builds a dynamical invariant with the cycle-by-cycle period. We implemented an active electrical compensation procedure [2] on RTXi real-time software, which prevents the recording artifact using a single electrode. Three closed-loop perturbations were delivered on the PD neurons: 1. A Hindmarsh-Rose (HR) model neuron electrically coupled to a PD neuron, thus building a biohybrid circuit. 2. A square pulse current injection during the PD burst. 3. An additional artificial electrical synapse between the two PD neurons.

Results

The electrical coupling with a negative artificial bidirectional synapse did not change the existing invariant relation between the LPPD delay and the period but increased the rhythm variability and increased the Victor-Purpura distance, i.e., reduced the PD synchronization level. The squared pulse perturbation decreased the variability and thus the LPPD delay linear relationship was reduced. The level of synchronization between both PDs was also reduced with the pulse perturbation with respect to the control. The biohybrid circuit built by adding an additional electrical coupling to an artificial HR neuron also reduced the variability but changed the intercept of the linear relationship i.e., for the same LPPD delays the PD period was sorter.

Discussion

In this study, we effectively disrupted the dynamics of two electrically coupled neurons with three different perturbations by injecting current into the neurons that modulated the synchronization level. This not only modified the dynamics of these neurons but also the whole circuit variability and the associated dynamical invariants. All protocols have been proven e ffective to study the relationship of electrical coupling and sequential dynamics with the help of real-time closed-loop neurotechnologies.

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P268 Modelling Nitric Oxide Diffusion and Plasticity Modulation in Cerebellar Learning

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Introduction

Nitric Oxide (NO) is an important molecule in processes such as synaptic plasticity and memory formation [1]. In the cerebellum, NO is produced by neural NO Synthase expressed in Granule Cells and Molecular Layer Interneurons [2]. NO diffuses freely in tissues beyond synaptic

connections, functioning as a volume neurotransmitter. At parallel fiber-Purkinje Cell (pf-PC) synapses [4][5], NO is necessary but not sufficient for both Long Term Potentiation and Depression [6][7]. This study investigates NO role in cerebellar learning mechanisms using a biologically realistic Spiking Neural Network, implementing a NO-dependent plasticity model and testing it with an Eye-Blink Classical Conditioning (EBCC) protocol [8][9].

Methods

We developed the NO Diffusion Simulator (NODS), a Python module modeling NO production and diffusion within a Spiking Neural Network. The model represents the chemical cascade triggered by calcium influx during spikes, leading to NO production [10]. NO diffusion is modeled using the heat diffusion equation and an inactivation term, solved with Green's function [11]. We implemented a NO-dependent supervised Spike-Timing Dependent Plasticity [12] where a term weights synaptic updates based on NO concentration. The model was tested using the EBCC protocol, where the cerebellum learns to associate a Conditioned Stimulus (CS) with an Unconditioned Stimulus (US), generating anticipatory Conditioned Responses (CR) (Fig. 1).

Results

We first validated the equation in NODS with the single source production of NO performed with NEURON simulator [13]. Then we investigated the effect of NO in cerebellar learning trough the addition of different background noises. In principle, the incoming CS and US stimuli should exert a depression only at the pf-PC synapses active right before the US stimuli. By adding an increasing noise these learning processes result directly impaired. When including NO-dependent plasticity, we can highlight a different behavior of during a CS and 4 Hz simulation. Here, only the pf-PC synapses receiving the CS stimuli have sufficient NO for plasticity, while the ones randomly activated by noise remain under threshold.

Discussion

The results demonstrate that NO interaction significantly affects synaptic plasticity, dynamically adjusting learning rates based on synaptic activity patterns. This mechanism enhances the cerebellum's capacity to prioritize relevant inputs and mitigate learning interference selectively modulating synaptic efficacy. Our results prove that NO could act as a noise filter, thus focusing learning in the cerebellum only on the relevant inputs for the ongoing task. The NODS implementation connects the molecular processes and large spiking neural network-level learning. This work underscores the critical role of NO in cerebellar function and offers a robust framework for exploring NO-dependent plasticity in computational neuroscience.

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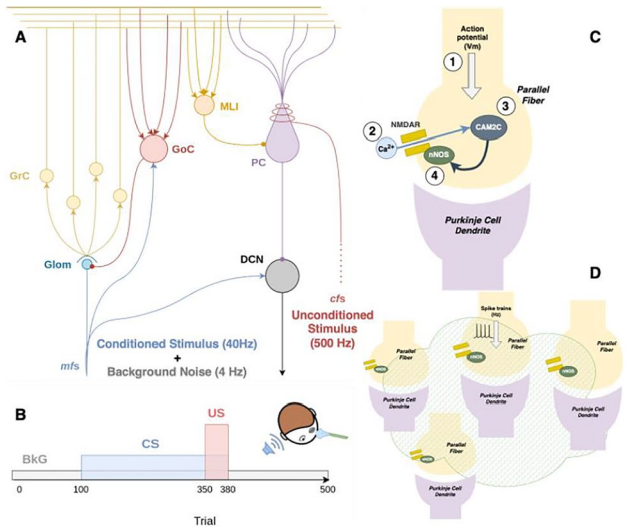

Figure 1: Spiking neural network with NODS mechanism. (A) SNN of the cerebellum microcircuit, with the different populations and detail of CS, US and Background Noise stimuli. (B) One trial of the EBCC protocol with timing of the stimuli. (C) The NO production mechanism at a single synapse. (D) NO as volume transmitter at different pf-PC synapses.

P269 Modeling Calcium-Mediated Spike-Timing Dependent Plasticity in Spiking Neural Networks

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Introduction

Calcium dynamics serve as bridge between neuronal activity and synaptic plasticity, orchestrating the biochemical cascades that determine synaptic strengthening (LTP) or weakening (LTD) [1]. Extending the work of Graupner and Brunel [2], Chindemi and colleagues recently introduced a data-constrained model of plasticity based on postsynaptic calcium dynamics in the neocortex [3]. Th e model has been developed for NEURON simulations capturing diverse plasticity dynamics with a single parameter set across pyramidal cell-types. In this work, we translated Chindemi' s model to a spiking neural network by implementing a point neuron model and a unified synapse, testing it across various calcium-concentration scenarios.

Methods

We developed our model using NESTML [4], an open-source language integrated with NEST [5] simulator, enabling the application of our models to diverse neural networks. The implemented neuron was built upon the existing Hill-Tononi (HT) model, which already incorporates detailed NMDA and AMPA conductance dynamics [6]. As in Chindemi, the synapse was instead based on the Tsodyks -Markram (TM) stochastic synapse model [7], allowing to manipulate vesicle release probability. Following paired pre-and post-synaptic activity calcium-dependent processes influence synaptic efficacy at both sides. Our implementation extends these established components to create a comprehensive framework that captures the relationship between calcium dynamics and synaptic plasticity while maintaining computational efficiency for network-scale simulations.

Results

We first validated our model for the TM stochastic synapse paired with HT modifications to account for calcium currents postsynaptic neuron. Then, we connected two neurons