Hydra’s Neural Symphony : Tuning into the Rhythms and Connections of cnidarians

Sarah Gaubi | Pasteur Institute, Paris

Authors : Gaubi Sarah, Manich Maria, Olivo-Marin Jean-Christophe and Lagache Thibault
Affiliations : Biological Image Analysis Unit, CNRS UMR 3691, Institut Pasteur and Sorbonne Université, Paris, France.

ABSTRACT :

Hydra vulgaris is a freshwater organism from the cnidarian family, representing a prototype of one of the earliest nervous systems while exhibiting a wide repertoire of behaviors. Since 1964, electrophysiological recordings by Passano and McCullough have revealed that Hydra vulgaris possesses identifiable neuronal ensembles that generate rhythmic patterns [1]. These biologically organized rhythmic neural circuits, known as Central Pattern Generators (CPGs), are responsible for producing stereotyped motor actions in humans and animals, particularly insects. Among its diverse behaviors, Hydra demonstrates somersaulting, a swaying locomotion composed of six steps related to sequential activation of specific neuronal ensembles and muscle. The use of the calcium indicator GCaMP in specific transgenic lines (Figure 1), has enabled visualization of Hydra’s entire nervous system [2]. Such studies reveal that Hydra’s nervous system consists of non-overlapping nerve nets organized into distinct neuronal ensembles. Imaging during somersaulting has identified two key ensembles: contraction bursts (CB) and rhythmic potentials (RP1) that form a half-center oscillator regulated by neuropeptides associated with each neuronal group [3].
To uncover the fundamental neuroscience principles underlying this primitive CPG, we developed a multiscale mathematical model that connects neuronal activity and neuropeptide signaling to somersaulting behavior. First, using single-cell RNA sequencing data [4] and a set of selected ionic channels, we modeled the excitability of neurons within each CB and RP1 ensembles involved in somersaulting. We calibrated the primary ionic conductances in standard Hodgkin-Huxley models using [5] and successfully reproduced the observed neuronal rhythms, including the alternation between rhythmic RP1 firing and CB bursts, as well as the increase in RP1 tonic spiking

frequency preceding somersaulting (Figure 2). Furthermore, leveraging the neuronal clustering t-SNE map from [4], we conducted a rapid gene expression analysis for hyperpolarization-activated ion channels (HCN channels) across neuronal groups suggesting that pacemaker neurons, characterized by the presence of HCN channels, belong to the CB ensemble only.

Then, using high-speed calcium imaging (~50 Hz), together with an image-based simulation framework for neuron population placement and neurite connectivity (Figure 3), we found that synaptic connections should play a crucial role in integrating spatial information, highly impacting on the temporal excitability of the system.

Finally, to address the challenge of neuropeptide modulation, we proposed an integrated approach to enhance the coupled oscillator model. Specifically, we extended the previous Hodgkin-Huxley conductance-based framework by coupling it with a reaction-diffusion model to account for neuropeptide secretion and transport across Hydra's body.

The model successfully reproduces the neuronal activity of both neuronal ensembles during the distinct steps of the somersaulting behavior. It allowed us to propose various plausible scenarios, offering insights into the cellular pathways and basic neuroscience principle underlying a prototype of CPG.

References

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