Neuromechanical Simulation of Zebrafish OMR

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1 Introduction

Zebrafish larvae, a vertebrate model, have increasingly gained attention in neuroscience due to their optical accessibility and readily quantifiable behaviors [1]. Scientists have elucidated some of the neural mechanisms underlying a variety of visually driven behaviors, such as prey-, escape-, optokinetic-, and optomotor responses (**OMR, a behavior to describe that a fish swims by following its surrounding visual motion**). Whereas few studies have explored a constructive approach using neuromechanical simulations, i.e., neuromechanical simulations of both the visuomotor circuits and the body, to investigate how sensory-driven behavior depends on neural circuits.

Recent advances in the understanding of the neural function and new simulation technologies have made this a feasible goal. **We constructed neuromechanical simulations that reproduce body, water interactions, neural circuits, displays to provide visual stimulation, and closed-loop visual environments replicating the experimental settings for live zebrafish behavioral recordings (Figure 1a, b, c, and d). This simulation platform allows for systematical evaluation of the effects induced by the components (e.g., neural components) in the body.**

2 Neural Mechanisms

Through an iterative strategy combining simulations, and monitoring of behavioral, and neural activity, we reached to construct a neural model (shown in Figure 1e) that can faithfully reproduce zebrafish OMR behaviors. Our model integrates circuit elements that have been independently described in previous studies [2]–[4], to compile a complete neural model underlying the OMR. For neural mechanisms that have not been experimentally verified, we iterate between testing hypothesized connections and comparison with animal experiments. Our simulation aims to integrate all published data, providing a framework to test different models. In the model, the sensory input is represented as simplified direction-selective ganglion cells (DSGCs) in the retina. DSGCs on the lower-temporal retina detect the visual motion and project to monocular direction-selective (DS) cells in the early pretectum (PT)[2], [5], which drive diverse responses in downstream PT neurons [3], [6]. In general, PT represents sensory information lateralized, with the left and right PT preferentially responding to respective leftward and rightward motion [3]. To generate swimming behaviors, the PT population projects to a midbrain premotor region, thought to control bout frequency (the nucleus of the medial longitudinal fasciculus, nMLF [3]). To modulate turning behaviors, the PT population projects first to the anterior hindbrain (aHB [3]) and then to ventral spinal projections neurons (vSPNs) which

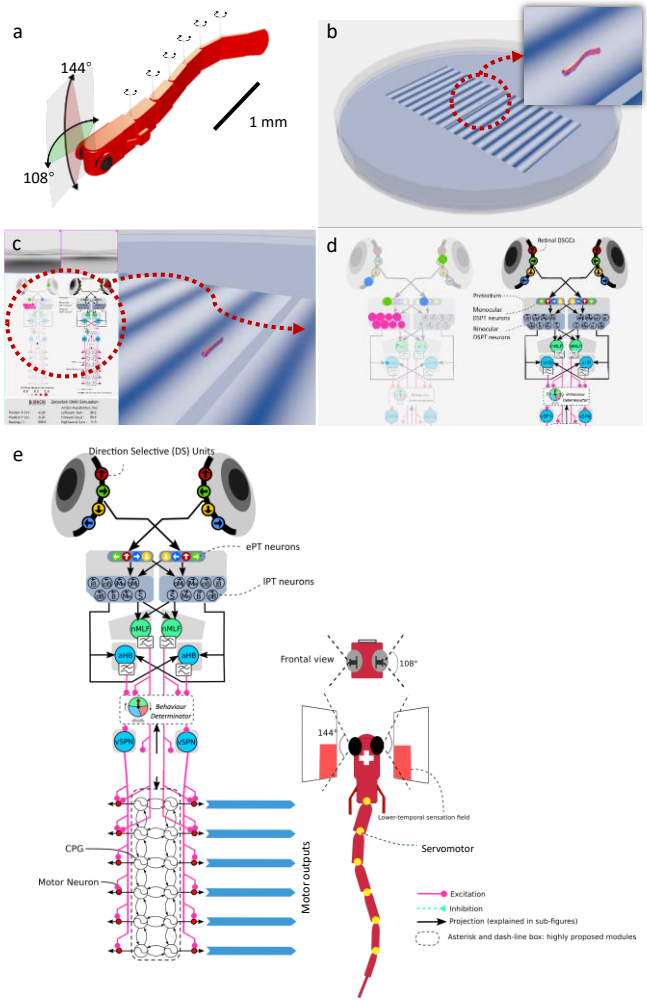

Figure 1: a, simulated zebrafish body, the body contains two cameras (with a field of view of 144*108 degrees) and six degree-of-freedoms actuated by servomotors. B, simulated OMR experimental environment. The environment contains 5-mm thick of water on a petri dish. Two displays on the bottom present visual stimulation to the simulated zebrafish. c and d, this platform provides a view into the internal states such as the camera views and neuronal activation in the body. e, embedded OMR neural model in the simulation.

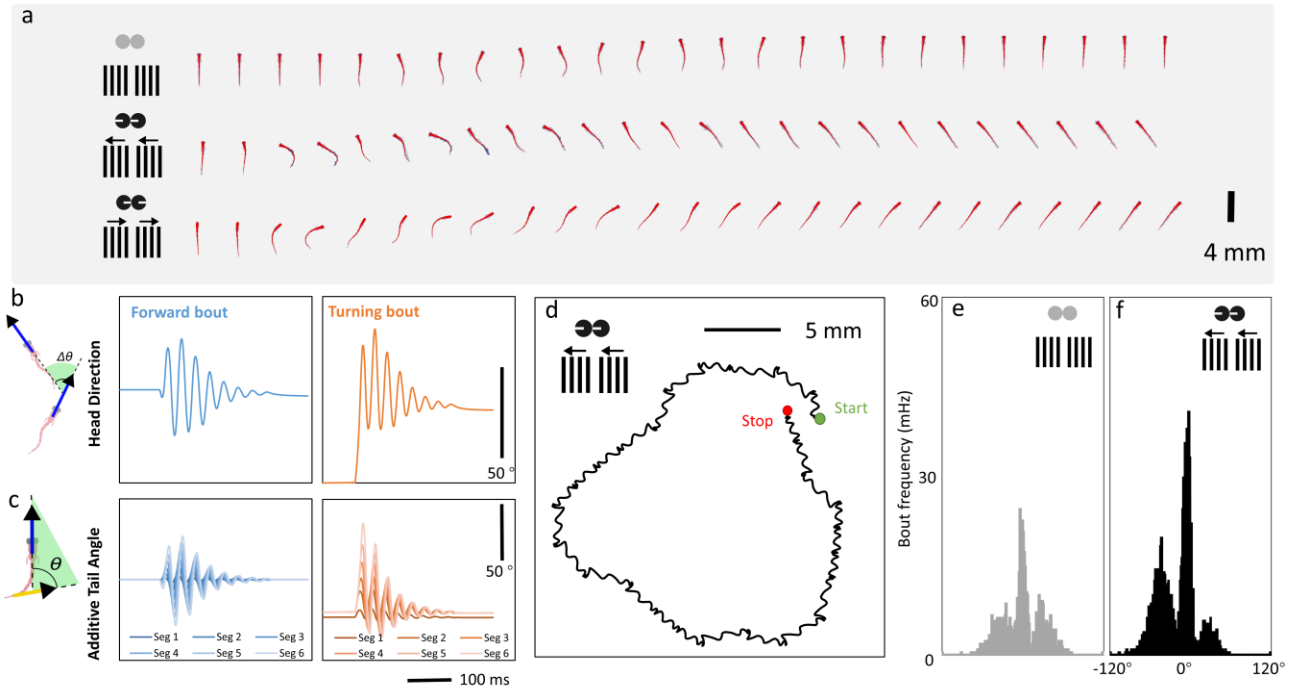

Figure 2: Swimming behavior of the neuromechanical simulation replicates real zebrafish swimming and turning maneuvers. a, Frames of the robotic simulation during a forward swim bout, a leftward turning bout, and a rightward turning bout, induced by full-field motion. b and c, Head direction and additive tail angle of a forward bout and a turning bout for each tail segment. d, Recording of the x, y trajectory of swimming for 25 seconds in response to binocular leftward stimulation. e and f, Histogram of frequencies of swimming bout angle (2000 second trial for each type of stimulation, bin size: 1°) in response to a static and leftward motion.

modulate turn amplitude. As experimental data shows that nMLF and aHB neurons possess cumulative and delayed response dynamics, we added low-pass filters to the output of the two types of modules [7], [8]. Together nMLF and vSPNs drive a set of bilateral central pattern generators (CPGs) which in turn activate motor neurons with ultimately drive undulating tail movements. **By constructing the neural model, we confirm the necessary components that drive OMRs, as well as reveal the unknown mechanisms that need to be studied in the future (e.g. the mechanism to generate swimming bout).**

3 Results

With the embodiment of the neural model, in the simulation, the zebrafish can behave similarly compared to real zebrafish in various aspects. For example, the simulated zebrafish can perform bout and gliding swimming (several cycles of tail-beating followed by a gliding movement with a straight body posture) that is similar to zebrafishes (see the zebrafish recording in [9]), when measuring the frames, head direction, tail angle, and trajectory (shown in Figure 2a, b, c, and d). With the presentation of a static pattern on the displays on the bottom, a 2000-second recording of the zebrafish head direction of each bout shows three clusters of the turning angle of bouts (shown in Figure 2e). With the presentation of the binocular leftward motion, the simulated fish behaves increased frequency of leftward bouts, increased frequency of forward bouts, and decreased frequency of rightward bouts (shown in Figure 2f). This animal-like behavior demonstrates that our neural model can faithfully reproduce zebrafish OMR behaviors (see the zebrafish recording in [3]).

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