**Neuron, Volume *99***

## Supplemental Information

# Internally Generated Predictions Enhance Neural and Behavioral Detection of Sensory Stimuli in an Electric Fish

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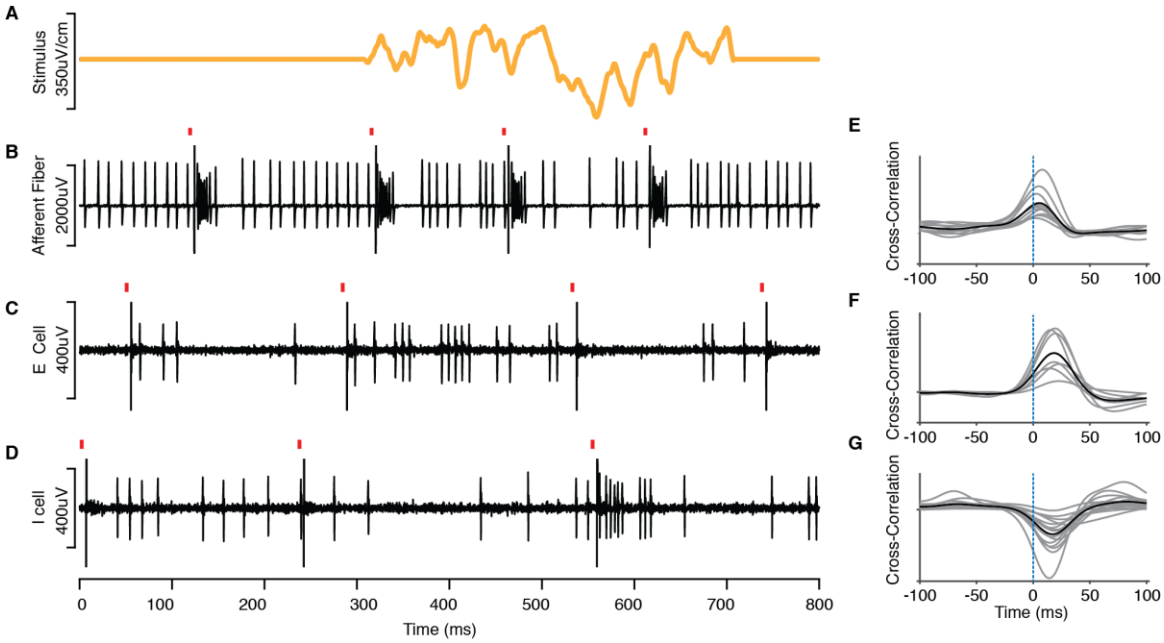


**Figure S1. Basic properties of electroreceptor afferents, E cells, and I cells, Related to Figure 2** (A) Prey-like stimulus waveform. (B) Sample voltage trace from an electroreceptor afferent recording. Red tics indicate the time of the EOD command and are followed by a stimulus artifact resulting from the delivery of the EOD mimic. Note the prominent bi-phasic response to the EOD mimic, a burst followed by a pause. Upstrokes and downstrokes in the prey-like stimulus evoke firing rate increases and decreases, respectively. (C) Sample voltage trace from an E cell recording. Note the minimal response to the EOD mimic, consistent with cancellation. Polarity of response to the prey-like stimulus is the same as for the electroreceptor afferent. (D) Sample voltage trace from an I cell recording. Note the minimal response to the EOD mimic, consistent with cancellation. Polarity of response to the prey-like stimulus is opposite that of the electroreceptor afferent and the E cell. (E-G) Gray lines, cross-correlations between the prey-like stimulus waveform and the firing rate for all the afferents (E), E cells (F), and I cells (G) included in the analysis for **Figure 2**. Black lines, average cross-correlation for each group.

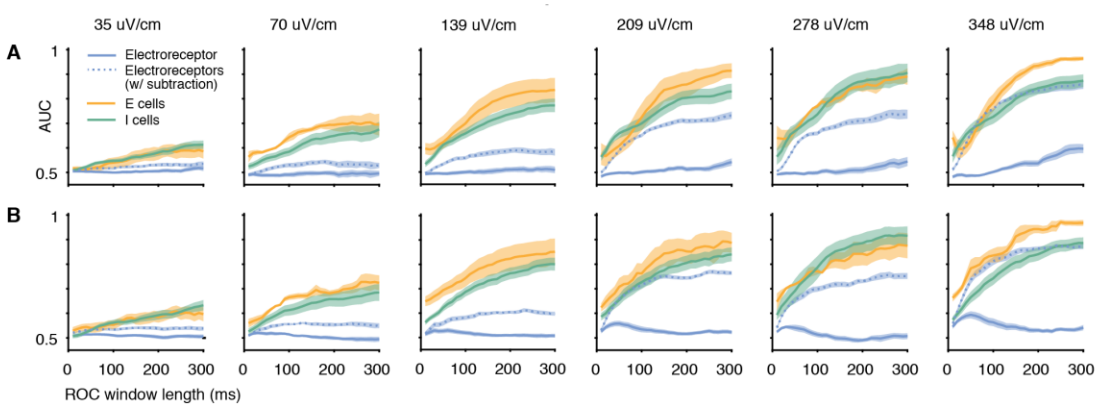


**Figure S2. Superior detection in ELL principal cells versus electroreceptor afferents does not depend on ROC analysis window size, Related to Figure 2** (A) AUC values as a function of the length of the analysis window (10-300 ms), with the start of the window aligned to the time of the EOD. Rows show the same analysis for different prey-like stimulus amplitudes. Lines are averages and ribbons are SEM. Data are the same as for **Figure 2**. A value of 100 ms was used for the analysis in Figure 2. (B) Same as A, but for sliding analysis windows taken independent of the times of the EOD.

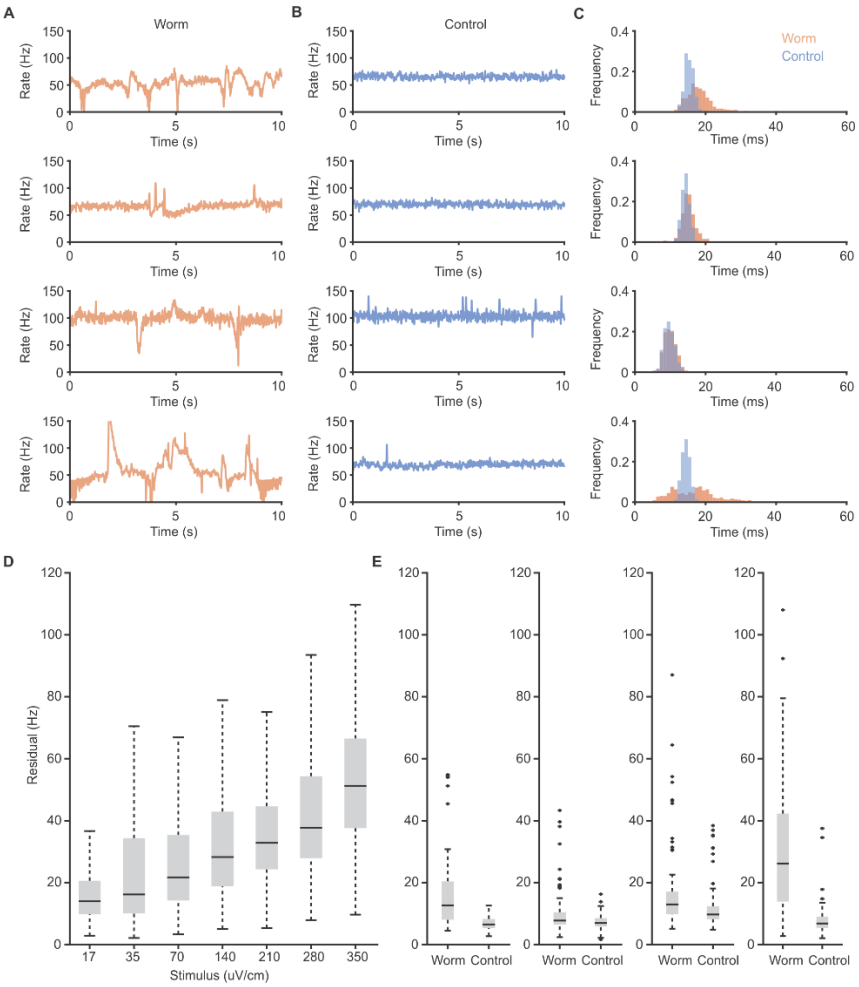


**Figure S3. Electroreceptor responses to actual prey versus artificial prey-like stimuli, Related to Figure 2 (A)** Firing rate modulations due to blackworms in 4 electroreceptor afferents recorded in the VLZ. For the top 3 examples a live worm was attached to a glass pipette and positioned near the electroreceptor pore of the recorded afferent. The exact location of the worm relative to the fish depended on the movements and configuration of the wriggling worms, which were 1-1.5 cm in length. The bottom example shows the response to moving the cut tip of a worm glued to a pipette near the skin with a manipulator (distance < 5 mm). **(B)** Firing rates of the same afferents as in **A** but in the absence of worms. In the bottom example a glass pipette was moved near the pore but without a worm attached. **(C)** Inter-spike interval histograms in the presence (orange) and the absence (blue) of worms for the electroreceptor afferent recordings in **A**. **(D)** Firing rate residuals calculated as maximum deviations from the mean firing rate over sliding 100 ms windows for all electroreceptor afferents used in **Figure 2**. Box represents 25th-75th percentile, whiskers extend to 1.5*interquartile range. Outliers not plotted. **(E)** Firing rate residuals for responses of electroreceptor afferents to worms, as in **D**. Black dots represent data points > 2 SD from the mean. These data points likely come from periods when spontaneous movements of the worm brought it near the electroreceptor pore innervated by the recorded afferent. These results suggest that natural prey are capable of driving firing rate modulations as large or larger than the artificial prey-like stimuli used in this study.

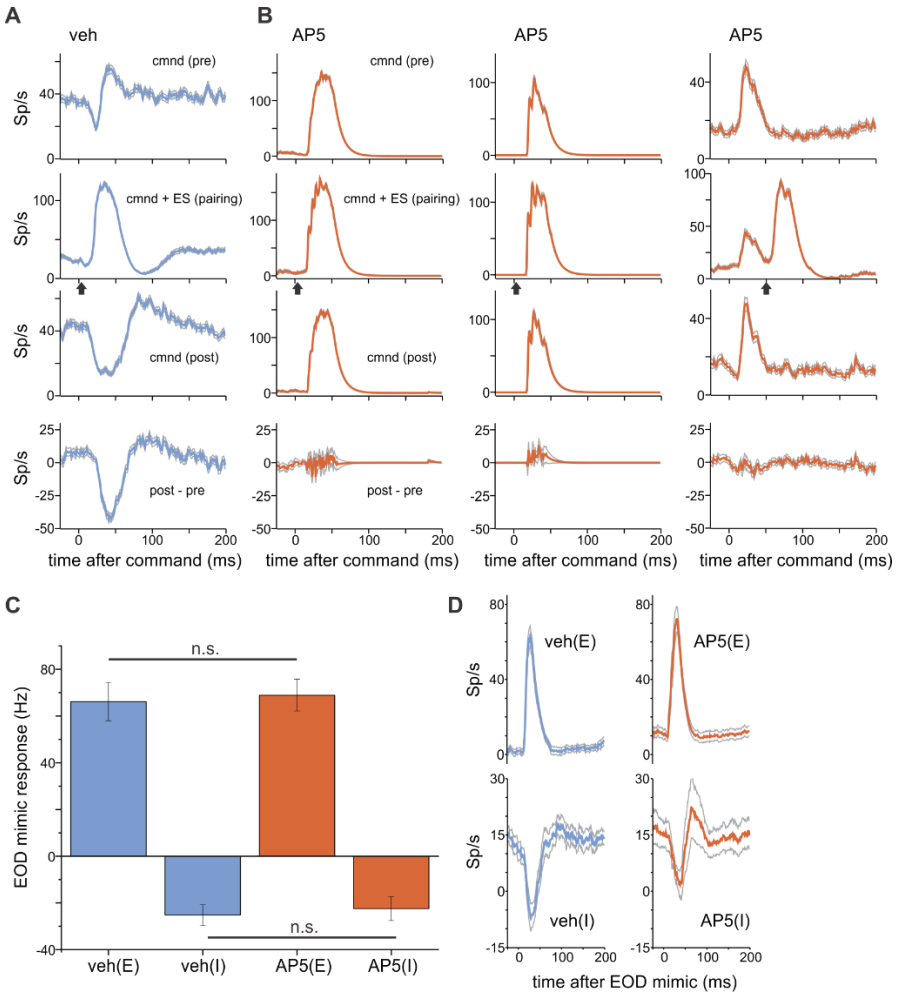


**Figure S4. Effects of NMDA receptor blockade on negative image formation and responses to the EOD mimic in ELL neurons, Related to Figure 7** (A) Example cell from the vehicle condition showing the formation of a negative image (3rd and 4th rows) after 4 minutes of pairing the command with an EOD mimic (-25 uA, arrow). The difference in the command response after pairing (post-pre, bottom row) is temporally matched and opposite in polarity to the response during pairing (2nd row). Gray outlines are SEM. (B) Three cells from the AP5 condition showing the failure of pairing to induce negative images. Conditions for pairing are the same as for the veh condition. Note the prominent responses to the EOD command alone (see main text for explanation). (C) Average peak or trough firing rate responses evoked by global EOD mimics (±25 uA) in E and I cells in vehicle treated versus AP5 treated fish. Neurons were recorded >15 minutes after application of vehicle (fish Ringer's solution or 0.9% NaCl) or AP5 (300 uM-1 mM) directly onto the exposed surface of the VLZ molecular layer. Both excitatory (E) and inhibitory (I) effects on firing rate were evoked for both E and I cells by switching the polarity of the EOD mimic and cells were pooled according to response polarity. AP5 treatment did not alter responses to the EOD mimic (E responses: $P = 0.797$, Student's t-test, n= 15 (veh), n = 16 (AP5); I responses: $P = 0.688$, Student's t-test, n= 15 (veh), n = 11 (AP5). Error bars are SEM. (D) Average traces showing the timing and polarity of responses to the EOD mimics for all of the cells included in C.

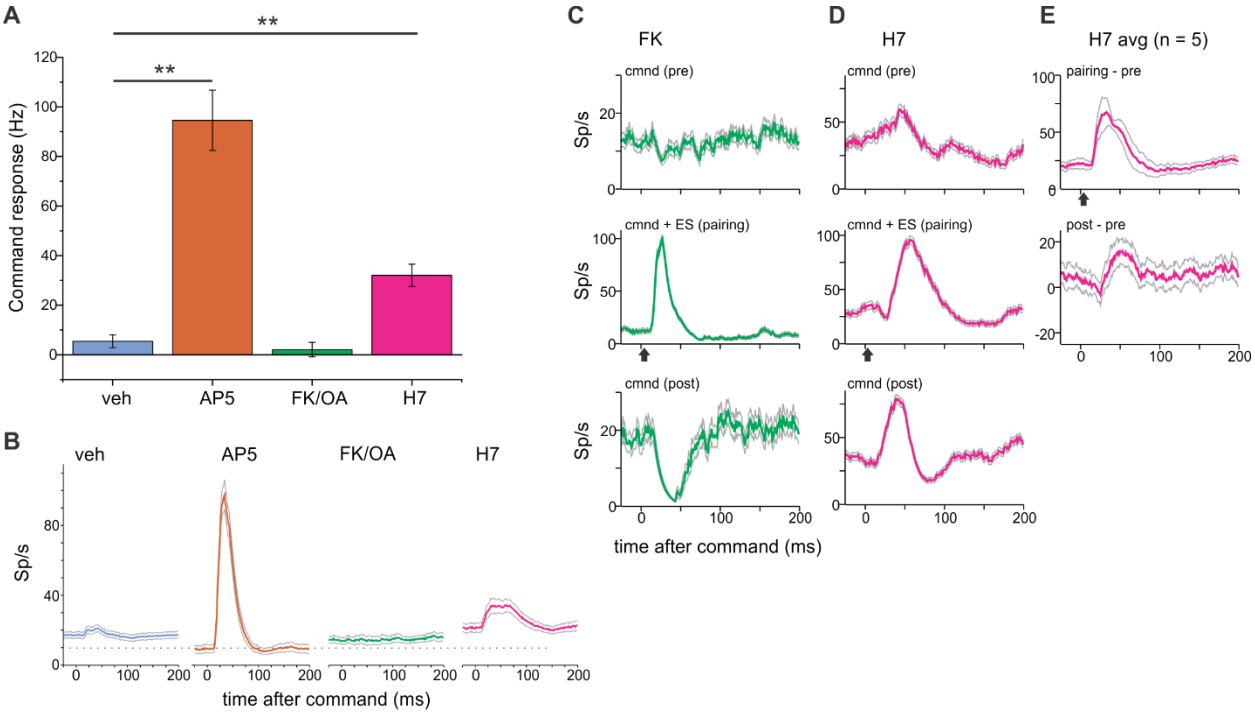


**Figure S5. Effects of kinase and phosphatase inhibitors on command responses and negative image formation**

**Related to Figure 7** (A) Average peak or trough firing rate responses to the EOD in E and I cells in vehicle treated versus drug treated fish. Neurons were recorded >15 minutes after application of either a vehicle solution (n = 27), AP5 (300 uM-1 mM) (n = 27), FK506 (1 mM) (n = 6), Okadaic acid (1 mM) (n = 3), or the kinase inhibitor H7 (0.5-2 mM) (n = 32) directly onto the exposed surface of the VLZ molecular layer. Command responses were increased relative to the vehicle condition following AP5 or H7 treatment ($P < 0.0001$, Student's t-test), although the magnitude of the increase for AP5 was larger than for H7. Error bars are SEM. (B) Average traces showing temporal profiles of command-evoked firing rates for all of the cells and conditions summarized in A. (C) Example cell from the FK506 (phosphatase inhibitor) condition showing the formation of a negative image (bottom panels) after 4 minutes of pairing the command with an EOD mimic (-25 uA, arrow). (D) Example cell from the H7 (kinase inhibitor) condition showing a failure of negative image under the same pairing conditions as used in C. (E) Average of 5 cells tested for negative images after H7 treatment. Note, the difference in the command response after pairing (post-pre) is not a negative image of the response to the stimulus (pairing-pre). Gray outlines in B-E indicate SEM.

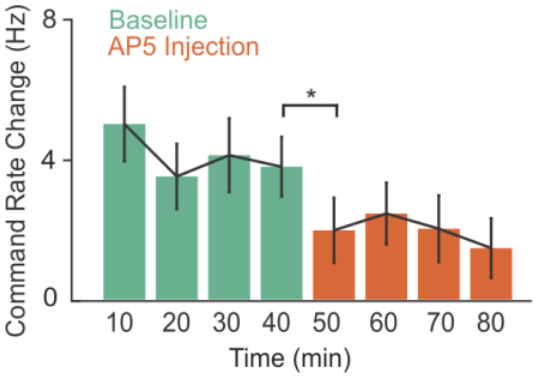


**Figure S6. Effects of NMDA receptor blockade on behavioral NRs evoked by prey-like stimuli, Related to Figure 7** Command rate changes evoked by a prey-like stimulus during a baseline condition (green) and following micropressure injections of AP5 (red) into the ELL molecular layer. AP5 injections reduced command rate changes evoked by a prey-like stimulus ($P < 0.001$, Friedman's non-parametric test, n = 6 repetitions of the experiment in 6 fish). Error bars indicate SEM.