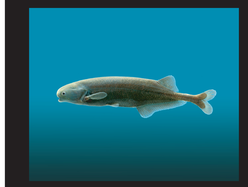

A re-analysis of the delay line anti-coincidence model for communication signal encoding in the electric fish brainstem

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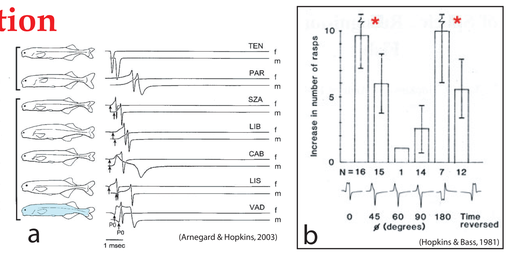
Introduction

1 The temporal features of an EOD are used for social recognition

Weakly-electric African mormyrid fishes use the timing information in an electric organ dishcharge waveform (EOD) to identify sex and species of other mormyrids. EODs of Gabon *Brienomyrus* are both sex- and species-specific (a). Male *B. vadamans* sing to female EODs but not phase-shifted EODs (b).



(Arnegard & Hopkins, 2003)

(Hopkins & Bass, 1981)

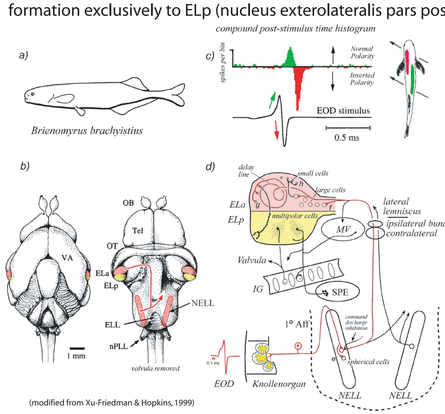
2 Timing of EOD waveforms, encoded by Knollenorgan electroreceptors, is re-encoded by small cells in midbrain nucleus, ELa

Knollenorgan electroreceptors phase-lock to an EOD

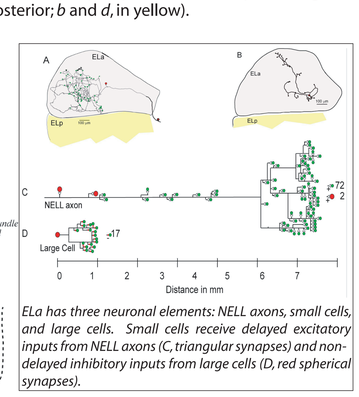
Knollenorgan electroreceptors (KOs) in the skin of *B. brachyistius* (below, *a*) are responsive to the positive-going voltage transient of an EOD (*c*), therefore, sensory inputs from different areas of the body are required to encode the entire EOD waveform.

Temporal processing in the brainstem

KOs project to a dedicated time-coding pathway in the brainstem (below, *b* and *d*). Midbrain toral nucleus exterolateralis pars anterior (ELa; *b* and *d*, in pink) is the proposed site of EOD waveform temporal analysis, where 'small cells' compare arrival times of spikes coming from the periphery. Small cells output timing information exclusively to ELp (nucleus exterolateralis pars posterior; *b* and *d*, in yellow).



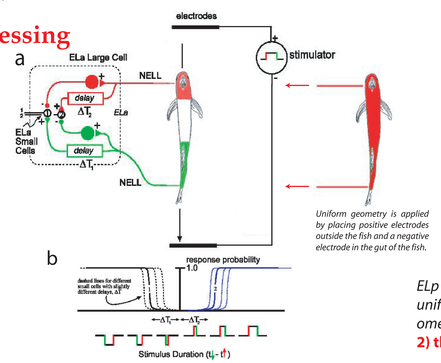
(modified from Xu-Friedman & Hopkins, 1999)



ELa has three neuronal elements: NELL axons, small cells, and large cells. Small cells receive delayed excitatory inputs from NELL axons (C, triangular synapses) and non-delayed inhibitory inputs from large cells (D, red spherical synapses).

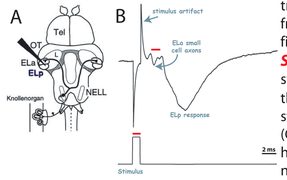
3 Model of EOD waveform processing in ELa

We tested the hypothesis that ELa small cells act as delay line anti-coincidence detectors (Mugnaini & Maler, 1987; Friedman & Hopkins, 1998). Stimulus-evoked spikes from two different regions of the body (e.g., head and tail) arrive at small cells, both through a delayed excitatory pathway and a non-delayed inhibitory path (at right, a). Stimulus durations exceeding axonal delays should be able to excite small cells (b; that is, excitation at the pulse onset gets through the axonal delay and arrives at the small cell before inhibition from the pulse offset; e.g., small cell '2'). We predict that uniform geometry stimulation should activate inhibitory inputs in advance of excitation, preventing ELa small cells from firing.



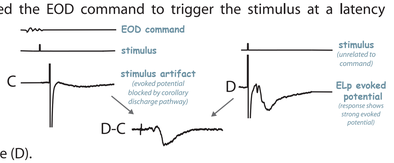
Uniform geometry is applied by placing positive electrodes outside the fish and a negative electrode in the gut of the fish.

Experiments



ELp evoked field potentials Small cell size and large presynaptic terminals precludes intracellular recording, so we tested the model by recording evoked local field potentials (B) from ELp (A) - the exclusive recipient of ELa small cell projections - under different electric field geometries (uniform, differential) and polarities, and amplitudes and durations.

Stimulus artifact subtraction To eliminate contamination by the stimulus artifact at high stimulus amplitudes, we used the EOD command to trigger the stimulus at a latency that would prevent the stimulus from reaching ELa (C), accomplished by the inhibitory blanking mechanism of the electric organ corollary discharge pathway. Then, we subtracted the artifact from the ELp response (D).

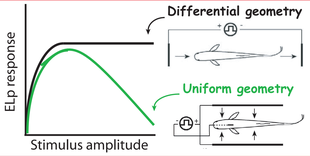


Prediction of the model

If all KOs are stimulated simultaneously (i.e., uniform field geometry), small cells will be inhibited via the non-delayed pathway and, subsequently, there will be no response in ELa and, therefore, ELp

ELp response functions

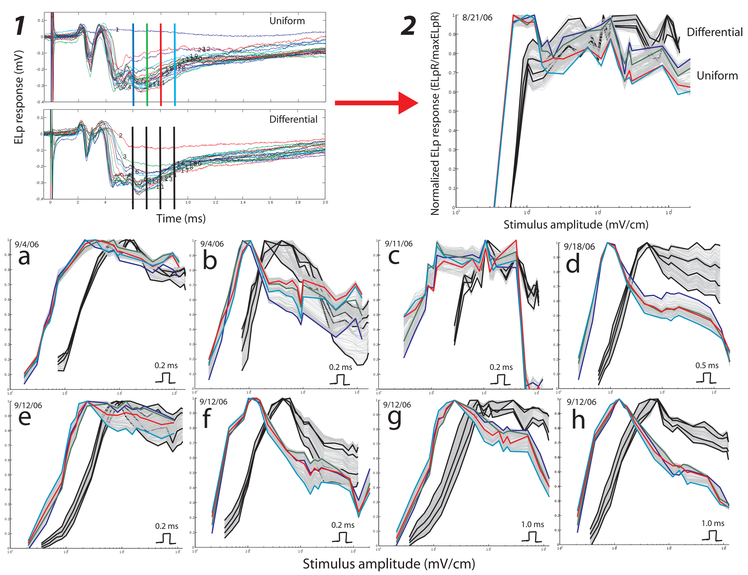
As stimulus amplitude increases, excitation in ELp under differential electric field geometry will increase rapidly to a maximum level. However, under uniform geometry, inhibition to small cells will increase as all KOs are stimulated simultaneously, thus, excitation in ELp will decrease at high stimulus ampltudes.



Results

4 ELp evoked response magnitude varies with location at high stimulus amplitude under uniform field geometry

ELp response functions To quantify the change in the ELp evoked response (ELpR) as a function of increasing stimulus strength, we selected a range of times during which the bulk of the ELpR occurs. For each time point, ELpR of every stimulus amplitude was normalized to the maximum ELpR for that time slice (*1*). Then, normalized data for both geometries were plotted against stimulus amplitude (*2*).



ELp response functions were used to compare uniform and differential geometries. At high stimulus amplitudes, ELpR was inhibited in uniform relative to differential field geometry in some cases (c, d,g,h); however, ELpR did not differ between uniform and differential geometries in other cases (a,b,e). Therefore, we conclude that **1) inhibition does not precede excitation for every small cell**, *and that* **2) the part of the model predicting the role of inhibition in EOD waveform analysis must be revised.**

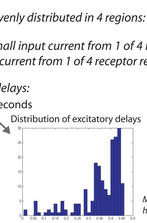
5 Computer modelling of ELa small cell responses

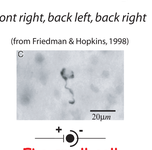
The complex nature of inputs to ELa's time-comparator small cells lead us to utilize a simulation of certain neural elements in the KO pathway. The program simulated receptors from four regions of the body, output spike trains to the small cells, and calculated the summed ELa small cell response as a function of stimulus amplitude. Simulated ELp response functions were generated for ***n*** fish to see the effects of inhibitory delay and stimulus duration. The simulation included the following steps:

1) *Simulation of receptor potentials from 100 electroreceptors, evenly distributed in 4 regions: front left, front right, back left, back right*

2) *For each small cell, randomly pick an excitatory input with small input current from 1 of 4 receptor regions, and randomly pick an inhibitory input with large input current from 1 of 4 receptor regions*

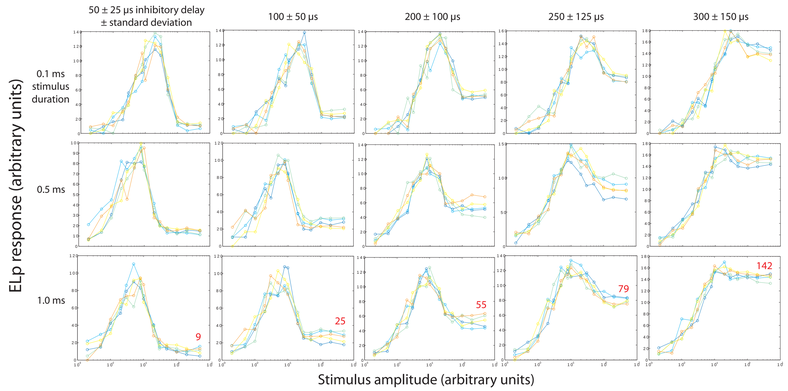
3) *Pass each excitation and inhibition through the appropriate delays:*
   - NELL axon excitatory delay = mean of about 300 microseconds with variance forming a left-skewed distribution
   - large cell inhibitory delay = **user-specified**





More information available at:
http://www.nbb.cornell.edu/neurobio/land/PROJECTS/ELAhopkins/index.html

4) *Simulated ELa small cell outputs (approximates ELp response function) for 800 small cells to increasing stimulus amplitude for 5 different inhibitory delays at 3 different stimulus durations applied to n=5 'fish' in uniform geometry:*



At simulated high stimulus amplitudes, ELa small cell outputs did not differ across stimulus durations; however, they did differ across increasing inhibitory delays (see red values in 1.0 ms-duration). This variation in ELa output matches variations in uniform geometry ELp response functions in the experimental data (see part 4). For example, compare 4c to simulations with 50 ± 25 µs, 4f to simulations with 200 ± 100 µs, and 4a,e to those with 300 ± 150 µs inhibitory delays.

Conclusions

Comparisons of ELp response functions (indirect measures of ELa small cell activity) between uniform and differential electric field geometry indicate that ***a partial revision of the delay line anti-coincidence model of encoding EOD waveforms is necessary.***

- At high stimulus amplitudes (*i.e.,* where it is probable that all KOs are being driven), larger-than-predicted levels of excitation from ELa small cells were recorded in ELp for some locations. From this, we conclude that ***excitation arrives ahead of inhibition for a certain population of small cells, that inhibitory delays are longer than excitatory delay lines for some cells.***
- Interestingly, by varying the length of the inhibitory delay in ***computer simulations*** of ELa small cell response, we were able to roughly match several experimentally-derived ELp response functions in uniform geometry. According to these simulations, ***variation in ELp response functions may reflect a distribution of inhibitory delays in ELa.***

The implications of inbibitory delays which exceed excitatory delays as regards the processing EOD waveform durations are not known at this time. It may be instructive to look for comparisons between the KO pathway and sound localization circuits in birds and mammals and to consider the role of inhibition, generally, in time-coding circuits.

Acknowledgements

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