A Neuronal Model for Visually Evoked Startle Responses in Schooling Fish

Master thesis

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Abstract

Many aspects of fish school behavior can be explained qualitatively by self-propelled agent models with social interaction forces that are based on either metric or topological neighborhoods. Recently, startling of fish has been analyzed in its dependence of the network structure (Rosenthal et al., 2015) but a mechanistic model and its influence on the collective behavior is missing. Here we couple a model for collective behavior with a neuronal model that receives looming visual stimulus input to initiate a startle response, inspired by the neurobiologically well-studied Mauthner cell system. First, we analyzed the basic properties of the startle behavior of a single fish as a reaction to a looming stimulus. On the group level, we looked at startling frequency as well as group cohesion and polarization depending on neuronal and collective behavior parameters via simulations of the combined model. Our results indicate that the startling frequency strongly depends on the dynamics of the group structure, e.g. when the group approaches a boundary of the arena. In summary, we took first steps towards a biologically plausible model for startle response initiation in the context of collective motion.

1 Introduction

A common interpretation of the function of the nervous system in animals is to use the sensory input in order to make appropriate actions. One situation where this would be useful for the animal is the sudden appearance of a predator. The quick response to such a sudden, unexpected stimulus is called startle response and can be observed in many species (Eaton, 1984). In fish, the startle response can take the form of freezing, where the fish stops moving entirely, or the form of an escape response, where it quickly accelerates and moves away within less than a second. Escape responses in fish, also called fast starts, can be divided into the three stages 1) first body bend, 2) second body bend and a third, variable stage where the fish either goes into continuous swimming, coasting or braking (Domenici, 2011). Due to the body shape at the end of the first stage escape responses are also called C-start or S-start (Domenici, 2011)[1]. This thesis will focus on the C-start behavior of fish.
The C-start behavior in fish has been extensively studied and one of the main reasons for this is that a pair of neurons that play a major role in the initiation of the C-start, have large soma and axons and are therefore relatively easy to find in experiments. They are called Mauthner cells (M-cells), named after Ludwig Mauthner who first found and described their axons (Mauthner, 1859).
Before going into the details of the M-cell circuit I will give a brief overview of the nervous system of fish to provide some context. Since I will later focus on visually evoked C-starts I will go into more detail when it comes to the visual pathways in the brain. The overall structure of the nervous system of fish is very similar to mammals. Starting at the caudal end there is the spinal cord with descending motor pathways and the ascending sensory pathways. The spinal cord goes over into the hindbrain region with the medulla and the cerebellum. This is followed by the midbrain which comprises the rostral part of the brainstem and a roof region, the tectum **?**. The remaining forebrain consists of the diencephalon and the telencephalon. In terms of sensory organs fish are equipped with the same senses as mammals and additionally have the lateral line organ that senses lower frequency signals around the body such as e.g. water flow and in some cases organs that can sense electrical fields.
Going from outside to inside, the eyes, again similar to mammals, consist of the cornea, the lens surrounded by the iris and the retina followed by the photoreceptors which build the most inside layer. In contrast to mammals the pupils of fish are not responsive to the amount of light in the environment. Fish mostly have rods and three different cones although across species there are up to seven different types of cones. The retina has different types of neurons that build different layers. The output neurons of the retina are the ganglion cells which show different kinds of tuning and whose axons build the optic nerve when the exit the eye. Although most fish don't have a fovea as we know it from humans there are retinal areas of higher ganglion cell and photoreceptor densities (Pita et al., 2015). Most of the ganglion cell axons cross sides and end up in the optic tectum which is the equivalent to the mammalian superior colliculus. While in humans much of the visual information goes further to the primary visual cortex in fish the optic tectum is the main site of processing of visual information. Similar to cortical areas it is comprised of different layers, also receiving input from other senses and other brain areas such as the telencephalon. The output of the optic tectum goes, among other regions, to the reticular nuclei in the hindbrain where we also find the Mauthner cell and can thus come the M-cell circuit.
The M-cell is located in the hindbrain and has two major dendritic branches, the ventral dendrite and the lateral dendrite. It receives multisensory input which is divided between the two dendritic branches. The lateral dendrite receives auditory and lateral line input whereas the ventral dendrite receives visual input via the optic tectum as described before. While this means that the visual input is highly processed by the networks in retina and optic tectum before it arrives at the M-cell the auditory input comes directly from the auditory nerve. This might be one of the reasons why the physiology of the auditory input has been studied

[1] It should be noted here that not all C-starts are escape responses because the can also be involved in e.g. prey capture but we will ignore other roles in the following.

in more detail than the visual part. I will therefore continue to describe the properties of the auditory processing and will have to assume that they also hold for the processing of the visual input. The synapses between auditory nerve and lateral dendrite are called club endings and transmit auditory signals via electrical as well as chemical mechanisms which leads to Excitatory Post-Synaptic Potentials (EPSPs) that consist of a fast and a slow component (Korn and Faber, 2005). At the same time the auditory nerve excites an interneuron which itself inhibits the M-cell. One interpretation of this feed-forward inhibition (FFI) is to increase the threshold for initiating the startle response. But this is not the only function of these interneurons because they also inhibit the contralateral M-cell as well as their contralateral counterparts (Koyama et al., 2016).

This microcircuit is probably responsible for the decision of which direction to escape to. To illustrate why this connectivity makes sense in this decision-making context, let us consider an auditory stimulus coming from the left side: It will inhibit the M-cell on the right side, inhibit the interneurons on the right side and excite the M-cell on the left side. Effectively, we have an increased inhibition of the right M-cell, decreased inhibition of the left M-cell and increased excitation of the left M-cell. Because the axons of the M-cells cross sides, an action potential of the M-cell on the left side will lead to a contraction of muscles on the right side, resulting in movements of head and tail away from the stimulus on the left side.

There are further properties that seem to make the M-cell specialized for initiating the C-start. Additional to the feed-forward inhibition the big size of the some of the M-cell leads to a high input resistance which again increases the threshold for incoming currents to initiate an action potential. The axon of the M-cell is unusually big as well which results in a fast signal transmission when an action potential is initiated. The axon is also connected to interneurons that provide feedback inhibition to both M-cells. This is thought to prevent repetitive firing of the M-cell that fired in the first place and also to prevent the contralateral M-cell to fire shortly after. Apart from this feedback inhibition the axon goes through the whole spinal chord with colaterals that go to the motor neurons on the contralateral side. And also at this level we have again interneurons that putatively have the role of inhibiting a different set of motor neurons that are responsible for steady swimming movements (Song et al., 2015).

The exact role of the M-cells and the surrounding circuit in the C-start behavior are still a subject of study. The current state of research seems to suggest the M-cell is sufficient and necessary to evoke the first phase of short-latency C-starts. Nevertheless, if the M-cell is ablated the fish are still able to perform long-latency C-starts. Furthermore, there is another population of neurons, that, if ablated, increase the latency of C-starts in a similar manner as the ablation of the M-cell does.

In the first part of this thesis I will make first steps towards a mechanistic understanding of functional role of the M-cell circuit for the C-start behavior. For this, I will greatly simplify the physiological properties of the M-cell and use a Leaky Integrate-and-Fire (LIF) model to capture the relevant dynamics. I didn't choose the more realistic Hodgkin-Huxley like model type that takes into account different ion currents because I was not interested in the action potential shape but rather in the action potential timing dependent on the input. The simpler LIF model also allowed for more efficient simulation which was also useful for the integration of the neuronal model in the collective behavior model in the second part. For the input of the M-cell I will assume that the visual input, coming from the optic tectum, is the result of a feature extraction of the visual scene. Taken together, this will allow me to link parameters of the neuronal model to behavioral response properties and to compare and fit this to experimental data.

While the first part of the thesis is concerned with the behavior of single fish, for many fish species the natural environment is rather that of being in a large group of fish. Such groups of fish that move around together are called shoals if they are rather uncoordinated and schools if they move in a highly ordered manner. This collective behavior is not well understood yet and in the second part of this thesis I want to analyze how the startle response interacts with it. In more detail, I was interested in the following questions: Can the startle response be evoked spontaneously in the fish school e.g. when neighboring fish come too close too fast? Does the startling of a single fish spread in the school? How do these effects depend on the properties of the school?

In order to address these questions I will use an agent-based model that describes the interactions between fish by so-called social forces. Typically, there are the three forces

repulsion, alignment and attraction and they can work either on neighbors within a specific range (metric interaction) or only on topological neighbors (topological interaction). An example for a topological type of interaction would be to only consider the neighboring cells of the Voronoi tessellation of the group of fish. Using such an agent-based collective behavior model with metric interaction Couzin et al. (2002) could show that the simulated fish school shows different modes of behavior dependent on the parameters of the social forces. While in one mode the collective would be uncoordinated but stay loosely together, it would move highly polarized and cohesive in another parameter regime or show a kind of milling behavior in a third mode.

2 Single Mauthner Cell - Theory

2.1 Neuronal model

$$I(t) = f(\theta(t)) \tag{2.1}$$

$$\theta(t) = 2 \cdot \arctan(\frac{L/2}{distance}) \tag{2.2}$$

$$\tau_\rho \frac{d\rho}{dt} = -(\rho(t) - \rho_0) + c_\rho I(t) + \eta_\rho(t) \tag{2.3}$$

$$\tau_m \frac{dV_m}{dt} = -(V(t) - E_L) + R_m I(t) - \rho(t) + \eta_m(t) \tag{2.4}$$

2.2 Adiabatic approximation

We assume that the timescale of the Input is much higher than the timescale of the dynamics of the inhibitory population so that we have a the following stationary process:

$$\hat{V}_m(t) = E_L + I_{tot}(t) + noise \tag{2.5}$$

where

$$I_{tot}(t) = R_m I(t) - \hat{\rho}(t) \tag{2.6}$$

$$\hat{\rho}(t) = c_\rho 10^7 I(t) + \rho_0 \tag{2.7}$$

$$I(t) = 10^{-11} c_{exc} f(\theta(t)) = 10^{-11} c_{exc}(m \cdot \theta(t) + b) \tag{2.8}$$

We set all noise to zero and want to find the input at which the membrane potential reaches the threshold $V_t = -61$ mV:

$$\hat{V}_m(t) \stackrel{!}{=} V_t \tag{2.9}$$

$$\Leftrightarrow E_L + R_m I(t) - c_\rho I(t) - \rho_0 \stackrel{!}{=} V_t \tag{2.10}$$

Inserting values for the fixed parameters $E_L = -79$ mV, $R_m = 10$ MΩ and $V_t = -61$ mV:

$$-0.079 + 10^7 I(t) - c_\rho 10^7 I(t) - \rho_0 \stackrel{!}{=} -0.061 \tag{2.11}$$

$$\Leftrightarrow 10^7 I(t) - c_\rho 10^7 I(t) - \rho_0 \stackrel{!}{=} 0.018 \tag{2.12}$$

$$\Leftrightarrow 10^{-4} c_{exc} f(\theta(t))(1 - c_\rho) - \rho_0 \stackrel{!}{=} 0.018 \tag{2.13}$$

$$\Leftrightarrow f(\theta(t)) \stackrel{!}{=} \frac{180 + \rho_0 10^4}{c_{exc}(1 - c_\rho)} \tag{2.14}$$

$$\Leftrightarrow \theta(t) \stackrel{!}{=} \frac{180 + \rho_0 10^4}{m \cdot c_{exc}(1 - c_\rho)} - \frac{b}{m} \tag{2.15}$$

2.2.1 Further points

- first paragraph

3 Single Mauthner Cell - Numerical experiments

3.1 Response properties of a single LIF neuron

As a first step we presented a single LIF neuron with the visual angle θ over time as input current. In order to compare our results with experimental work (see e.g. Bhattacharyya et al. (2017), Temizer et al. (2015), Dunn et al. (2016)) we analyzed the angle, distance, latency and time-to-collision of the response. The response onset was defined as the time of the first spike of the LIF neuron. We ignore further processing time after the spike of the Mauthner cell because it is in the order of milliseconds (Preuss and Faber (2003)) and thus irrelevant with respect to the overall response time which is in the order of at least hundreds of milliseconds for visual stimuli (Preuss et al., 2006).
In the model, we used the basic electrophysiological parameters that were measured in larval zebrafish 4 days post-fertilization (Koyama et al., 2016) and kept them fixed for all simulations. We analyzed the effects of parameters of a linear transformation of the input, i.e. the slope and offset and furthermore the effects of noise on the input, on the initial condition, and on the spiking threshold. All parameters are listed in table 3.1.
effects:

- effects of increasing m:
  - mean response distance: mean increases linearly independent of threshold noise (only for high threshold noise slightly sub-linear)
  - variance of response distance: increases linearly for small threshold noise (except for a high lv value and low threshold noise, this is due to a very low mean and outliers that distort the standard deviation estimate), increases sub-linearly for medium threshold noise, slightly decreases for high threshold noise
  - mean response angle: decreases exponentially independent of threshold noise
  - variance of response angle: slightly decreases independent of threshold noise
  - mean time to collision: absolute value increases linearly independent of threshold noise, decreases more strongly for higher L/V values
  - variance of time to collision: very small increases for L/V values smaller than 0.9, for L/V values above 0.9 the variance is in general higher, for small threshold noise it is smallest for medium m-values and for higher threshold noise it also increases with m
  - mean response time: very similar to TTC
- effects of increasing threshold noise:
  - mean response distance:
- Effect of input transformation
- Effect of different noise sources
- Effect of input type

3.1.1 Input

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Parameter	Value (unit)	Comment
E_L	-79 mV	Resting potential
R_M	10 MOhm	Membrane resistance
τ_m	23 ms	Membrane time constant
V_t	-61 mV	Mean spiking threshold
dt	0.001 s	Integration time step
T	5 s	Total time
sd_{thr}	1 mV	Standard deviation of spiking threshold noise
sd_I	5 mV	Standard deviation of input noise
sd_{init}	1 mV	Standard deviation of initial condition noise
m	1 °/s	Slope of linear transformation
b	0 °	Offset of linear transformation

Table 3.1 – Parameters of the single LIF neuron model with a looming stimulus input. Parameters that were explored are indicated either by a value range such as e.g. for μ_s or by a set with all explored values inside of curly brackets such as e.g. for σ_s.

3.1.2 Feedforward inhibition

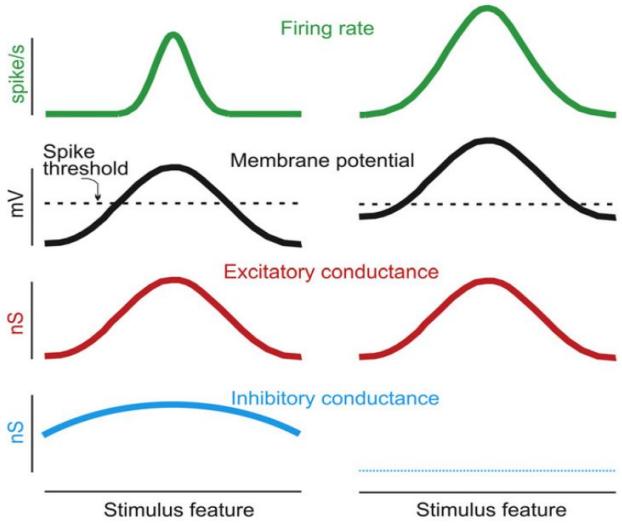

Figure 4. Inhibition Sharpens Stimulus Selective Spike Output via the "Iceberg Effect"
Schematic illustrates hypothetical tuning curves for firing rate (green), membrane potential (black), excitatory (red), and inhibitory (blue) conductances of a cortical neuron to stimulus features (e.g., orientation). Action potential firing occurs only when membrane potential exceeds a fixed spike threshold (dotted line). Responses are shown in the presence (left) and absence (right) of a weakly tuned inhibitory conductance. Inhibition leads to more narrowly tuned spike output by allowing only the strongest (preferred) excitatory stimuli to drive the membrane potential above spike threshold.

Figure 3.1 – how input sharpens tuning. From Isaacson and Scanziani (2011)

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3.1.3 Cross-inhibition

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3.1.4 Feedback inhibition

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4 Two Mauthner Cells Model

5 Coupling of Neuronal Model and Collective Dynamics

6 Discussion

- we focus here on the experimental results from Bhattacharyya et al. (2017) but one should keep in mind that their results might be specific to properties of experiment such as fish handling, fish age, species, arena, environment, stimulus setup (projection on screen)
- we took the fitted parameters from Koyama et al. (2016) but those are fitted for their specific context which might vary in other experimental conditions and certainly in other species
- furthermore the LIF model makes strong assumptions about the processing power of the neuron which are likely not true. see for example Koch and Segev (2000), and specifically for the M-cell Medan et al. (2017)

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.1 Appendix