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Can Linear-Nonlinear Models capture simple forms of retinal adaptation?

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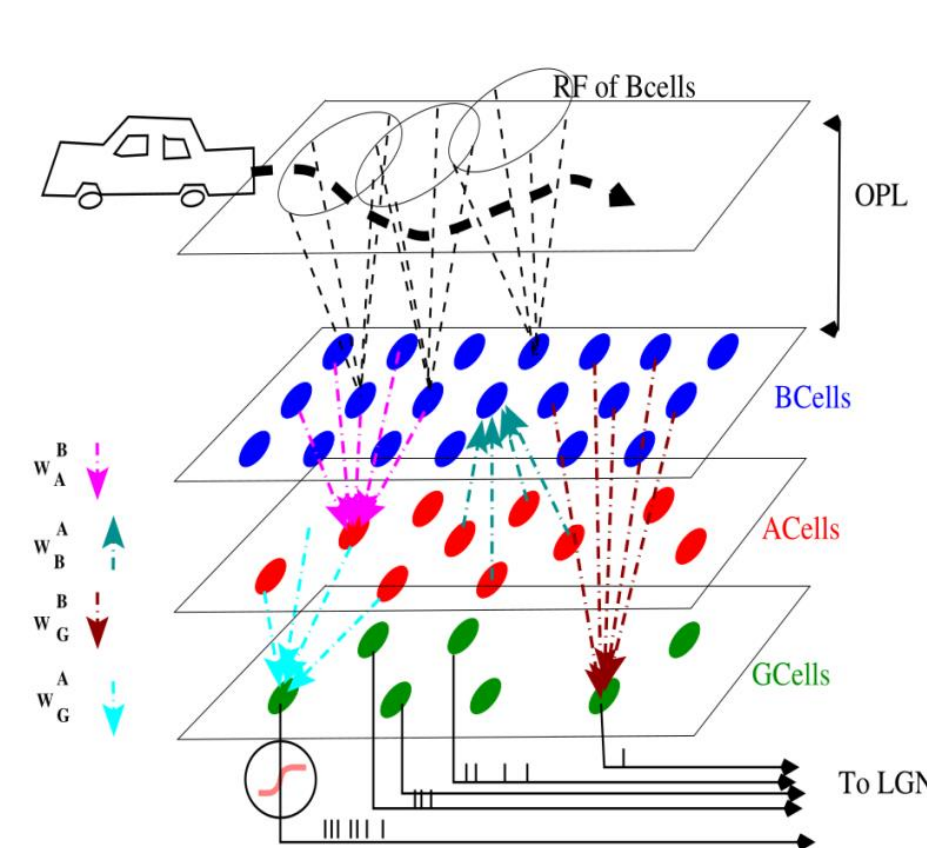
Abstract

The retina is a tissue situated in the inner part of the eyes of vertebrates. It is responsible for transforming the light of the visual field into action potentials, forwarded to the visual cortex through the optic nerve. **Short-term Plasticity (STP)**, the strengthening or weakening of synapses in reaction to the past pre- and post-synaptic activity, plays an important role in this network's ability to encode an ever-changing visual environment, for example, across different levels of luminosity and contrast. While the retina's activity in response to static or uncorrelated inputs is commonly described through **Linear-Nonlinear (LN) Models** [1], these models often fail to capture responses to dynamic stimuli with spatiotemporal correlations such as natural movies [2].

In this project, we apply different versions of the classical LN model to **Retinal Ganglion Cells** – the output stream of the retina – and test its performance on their responses to a simple stimulus protocol designed to measure STP: a sequence of repeated light flashes (see Figure 2). We show that these models fail as well to reproduce STP as captured in experiments.

The retinal network

- Visual stimuli travel from the photoreceptors through the layers of the retina's neuronal network and are converted to spiketrains by the Retinal Ganglion Cells (RGC).



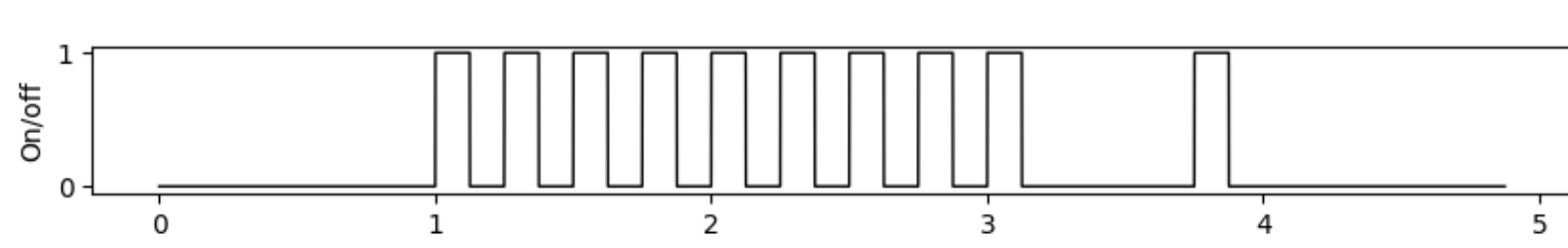
- RGCs possess a **receptive field**: this can serve as **convolution kernel** (in the following: **filter**) for a retinal model.

(Fig. 1) Connectivity of the retina's cell types^[3]: Bipolar (B), Amacrine (A) and Ganglion (G) cells. A-cells and B-cells have recurrent projectio90ns.

Measuring short-term plasticity

- Adaptation and prediction in the retina are due to STP.
- The STP flash stimulus protocol compares firing rate responses to repetitions of the same stimulus.

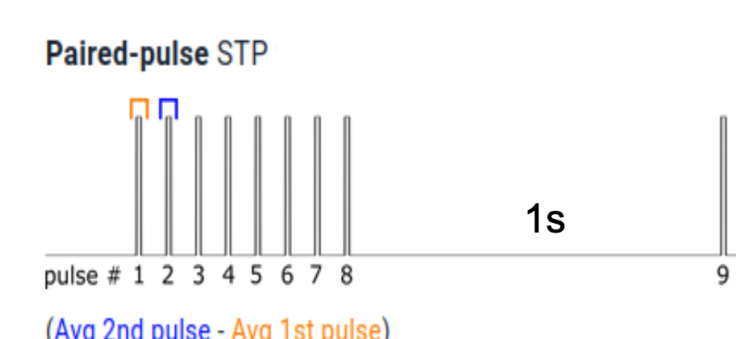
Stimulus used:



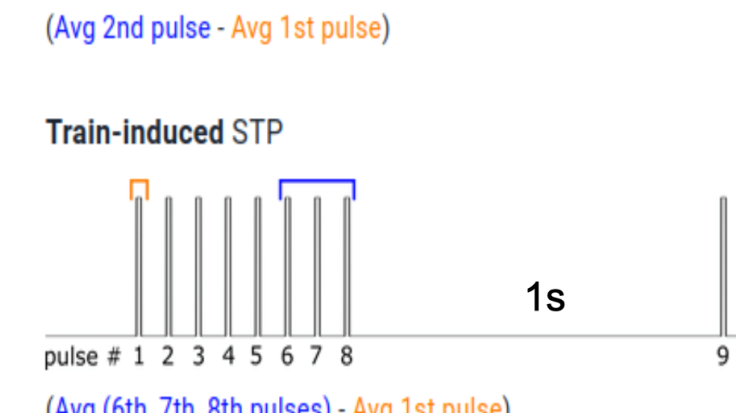
(Fig. 2) 9 identical bright, full-field flashes (spaced at 4 Hz frequency) followed by a pause, then another flash.

Plasticity measures^[4]:

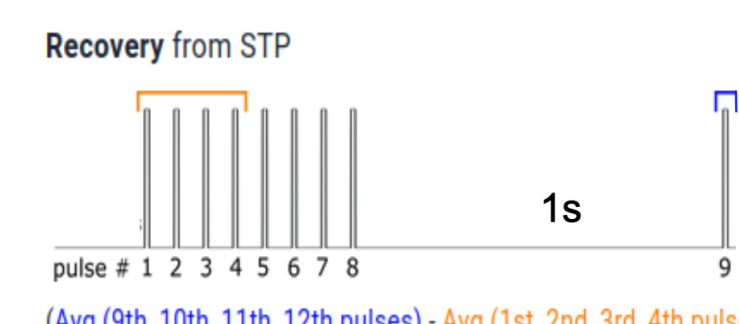
Paired-pulse STP: Response comparison between the first two flashes.



Train-induced STP: Response comparison between the first flash and the last flashes before the pause.

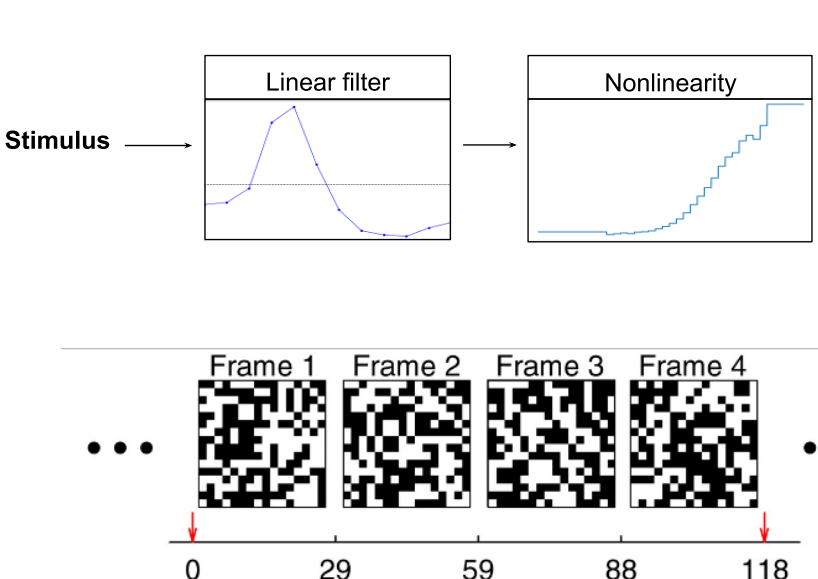


Recovery: Response comparison between the first flashes and the flash after the pause.



The Linear-Nonlinear Model

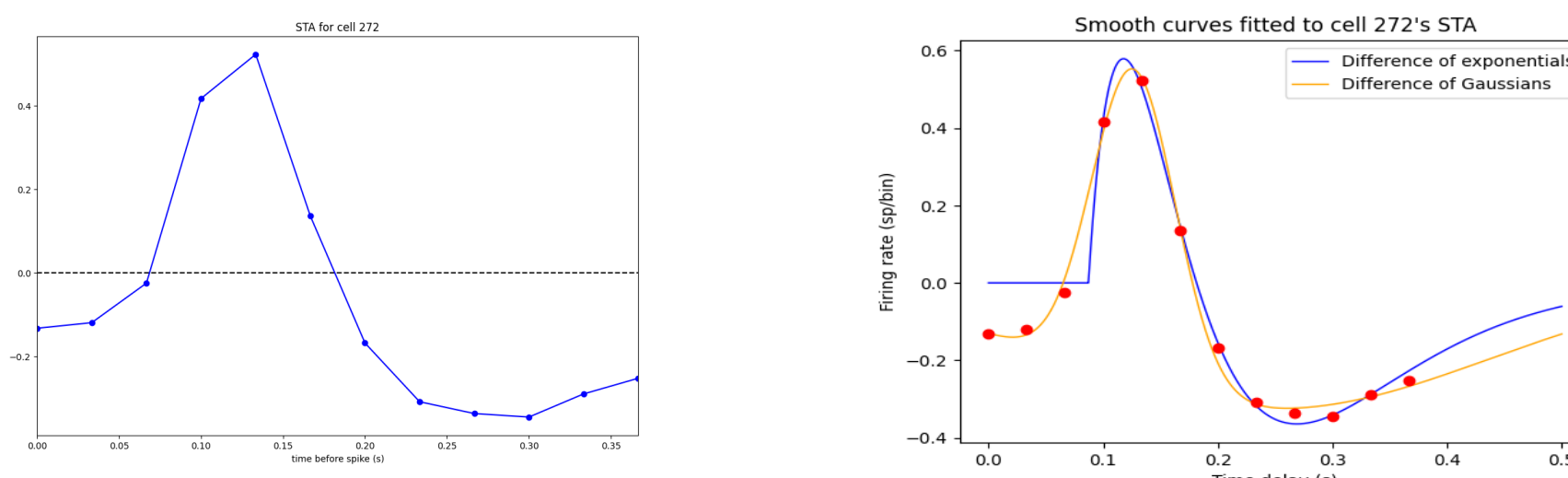
- A **static model** that simulates the given RGC's firing rate from a **stimulus** (represented as a function showing intensity in time; see: Fig. 2).
- The LN Model has two steps:
 - Convolution** of the stimulus with a **linear filter**.
 - Scaling** of the filter output with a nonlinear function (**nonlinearity**).
- Both components (filter and nonlinearity) can be obtained from the same RGCs' responses to a **tuning stimulus**, the white noise checkerboard stimulus.



(Fig. 3) Steps of the Linear-Nonlinear Model (above). White noise checkerboard stim., a movie consisting of random black-and-white grids (below).

Linear filters

- The **nonparametric version** of the filter for the LN Model is obtained from the **spike-triggered average (STA)** and is an estimate of the **temporal receptive field** of the cell (the filters obtained and shown here are only temporal since the STP flash stimulus is uniform in space).
- The **parametric version** is a curve fitted to the STA.



(Fig. 4) Nonparametric filter ie. STA (left), curve fits for the parametric filter (right) with Biphasic Alpha (blue) and Difference of Gaussians (orange) curves. Both images refer to Cell 272.

Equations of the parametric curves (f_1 : Biphasic Alpha; f_2 : Difference of Gaussians) and parameters of f_1 fitted to Cell 272 (H denotes the Heaviside step function):

t_0	0.0871421 s
τ_1	0.0561836 s
τ_2	0.0621376 s
w	1.04142

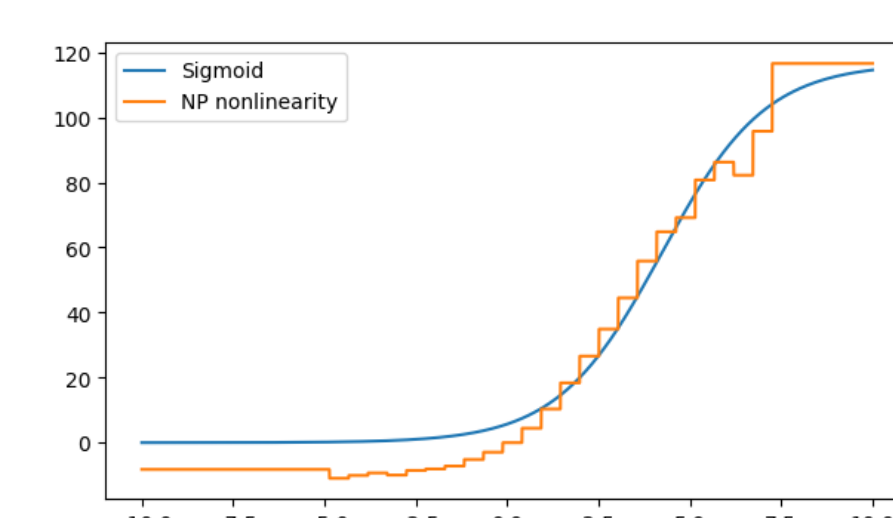
$$f_1(t) = \frac{t - t_0}{\tau_1} e^{-\frac{t - t_0}{\tau_1}} H(t - t_0) - w \frac{t - t_0}{\tau_2} e^{-\frac{t - t_0}{\tau_2}} H(t - t_0)$$

$$f_2(t) = a_1 e^{-\frac{(t - t_0)^2}{2\sigma_1^2}} H(t - t_0) - a_2 e^{-\frac{(t - t_0)^2}{2\sigma_2^2}} H(t - t_0) + \varepsilon g(t, \alpha, \beta)$$

$$g(t, \alpha, \beta) := \beta(t - \alpha)H(t)H(\alpha - t)$$

Nonlinearities

- The **nonparametric nonlinearity** is a piecewise constant function. Each step's height is obtained by sorting the filter's output in a preset number of bins and counting the proportion of white noise spike responses that fall into each.
- The **parametric version** fits a sigmoid curve to the bin centres.



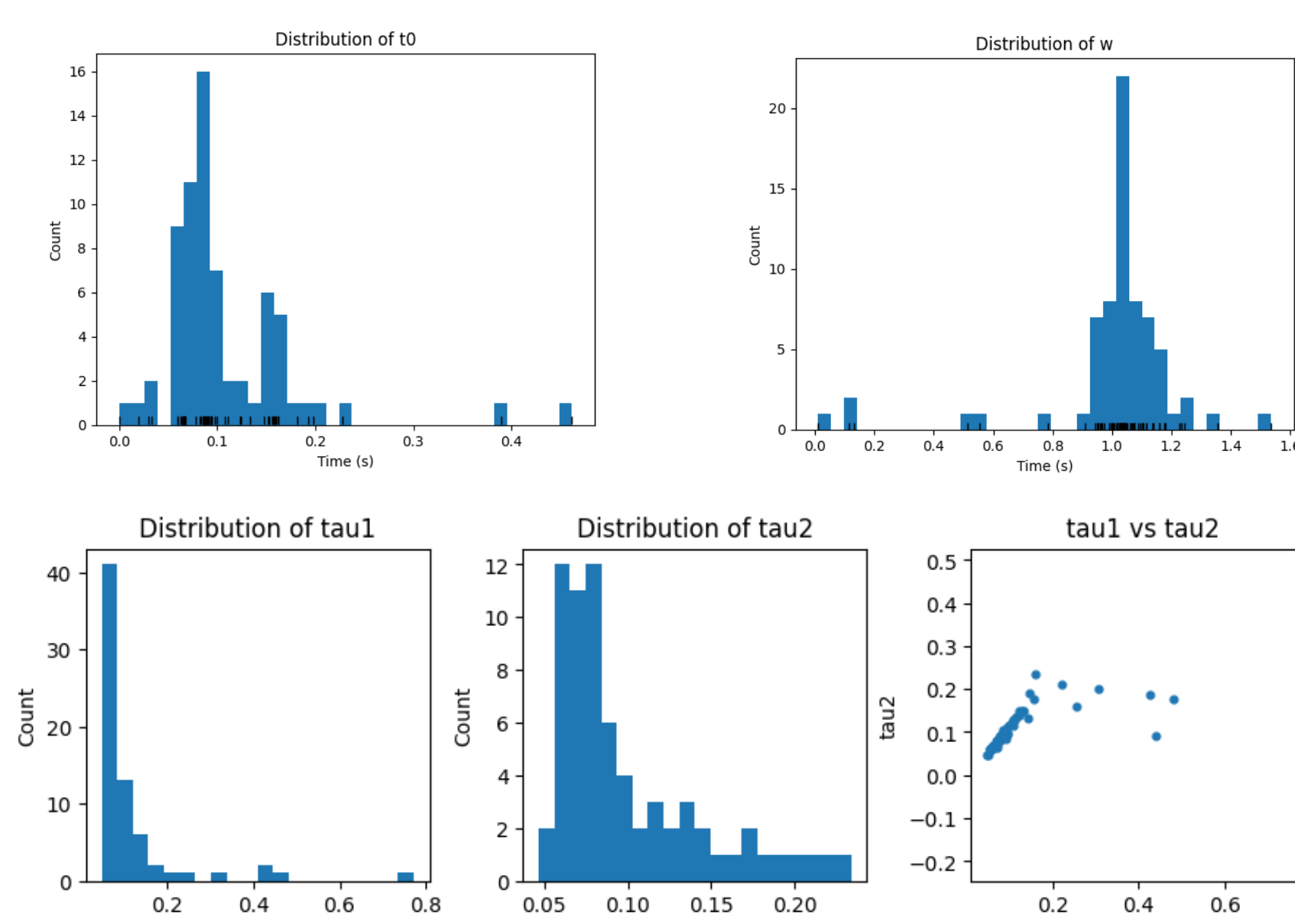
Equation of the sigmoid curve:

$$\text{sig}(x) = \frac{v_{\max}}{1 + e^{-m_{\text{slope}}(x - v_{\text{threshold}})}}$$

(Fig. 5) Nonparametric nonlinearity (orange) and parametric sigmoid curve fitted to it (blue).

Parameter statistics from fitted filters

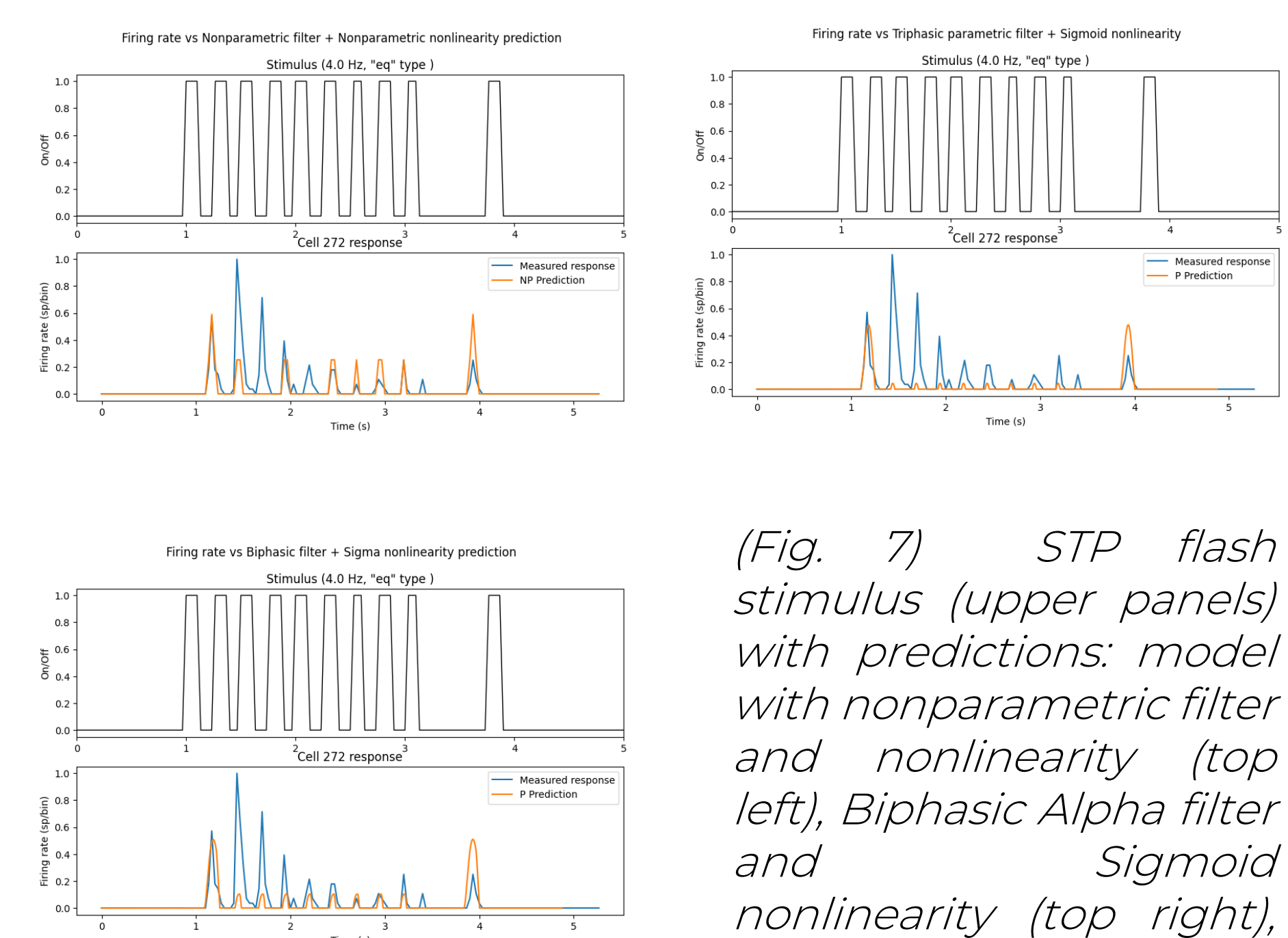
- Statistics were obtained by fitting the Biphasic Alpha curve to **87 retinal ganglion cells**.
- The cells used were chosen from those categorized as **ON cells** based on responses to a **Chirp stimulus**, meaning that their firing rate increases in reaction to an increase in luminance.



(Fig. 6) Fitted parameters of the Biphasic Alpha filters: initial time delay t_0 (top left), weight proportion of the two phases (top right), time constants of the positive (bottom left) and negative (bottom middle) phases, τ_1 and τ_2 . When plotted together (bottom right), the time constants show high correlation in the <200 ms regime.

Model predictions

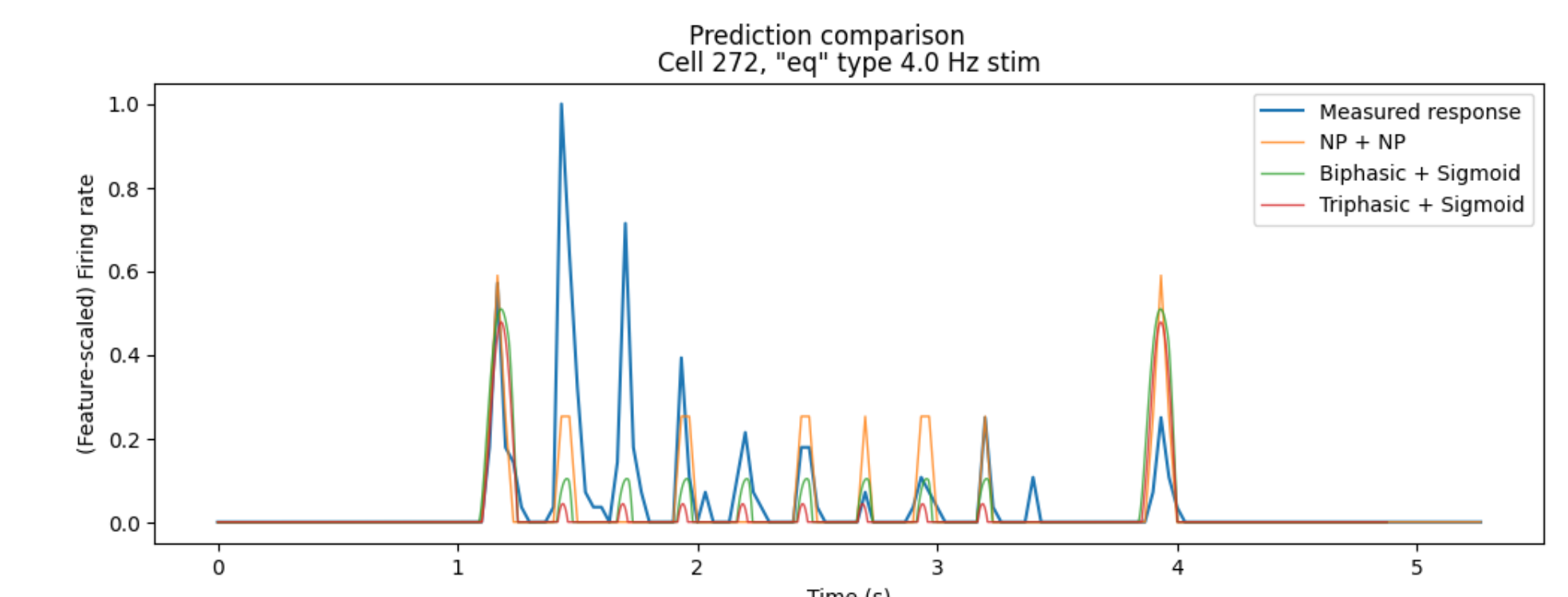
- Three variants of the model were tested:
 - Nonparametric (STA) filter + nonparametric (piecewise constant) nonlinearity**
 - Biphasic Alpha parametric filter + Sigmoid nonlinearity**
 - Difference of Gaussians filter + Sigmoid nonlinearity**
- Predictions were made by applying the models (tuned to Cell 272) to the STP flash stimulus shown in Figure 2.



(Fig. 7) STP flash stimulus (upper panels) with predictions: model with nonparametric filter and nonlinearity (top left), Biphasic Alpha filter and Sigmoid nonlinearity (top right), Difference of Gaussians filter with Sigmoid nonlinearity (bottom).

The lower panels show the average firing rate from the actual cell recordings (blue) and the one predicted by the models (orange).

Comparison of all model predictions:



- For **paired-pulse STP**, the cell's response shows **facilitation**, with an increase of firing rate between the first and the second flash. **The models fail to reproduce this.**
- The cell's firing rate decreases towards the end of the flash train, indicating **depression** for train-induced STP. **This is present in the model predictions as well.**
- Both the response and the predictions show a **recovery** of the firing rate after the pause but the models produce a **higher amplitude than expected.**
- Predictions also neglect the **Omitted Stimulus Response**^[5] which can be seen in the responses as an additional peak after the flashes end.

Conclusion

Retinal ganglion cells are the output neurons of the retinal neuronal network. A simple way to model their firing rate in response to stimulation presented in the visual field is the Linear-nonlinear (LN) model, which includes a linear filter and a nonlinear function. We constructed one nonparametric and two parametric LN models based on responses to a white noise stimulation. By applying the former to spike responses to a stimulus meant to measure short-term plasticity (STP), we found that not all aspects of the network's synaptic dynamics can be reproduced with this method. In particular, LN model predictions exhibit train-induced plasticity but not paired-pulse plasticity. Further research is necessary to construct either a dynamic version of the model with variables for vesicle dynamics^[5] or response feedback, or one with parallel LN models.

Acknowledgements

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[1] Chichilnisky E. J. (2001). A simple white noise analysis of neuronal light responses. *Network* (Bristol, England), 12(2), 199-213.
[2] Vystrčilová M., Sridhar S., Burg M. F., Gollisch T., Ecker A. S. (2024) Convolutional neural network models of the primate retina reveal adaptation to natural stimulus statistics. *bioRxiv* 2024.03.06.583740; doi: <https://doi.org/10.1101/2024.03.06.583740>
[3] Cessac, Bruno (Jan. 2022). "Retinal Processing: Insights from Mathematical Modelling". In: *Journal of Imaging* 8 (1), p. 14. ISSN: 2313-433X. DOI: 10.3390/jimaging8010014.
[4] Allen Brain Institute. Allen brain map: Synaptic physiology methods: Experimental stimuli.
[5] Simone Ebert (Dec. 2023). *Dynamical Synapses in the Retinal Network*. Theses, Université Côte d'Azur.