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The Role of Dynamical Synapses in Retinal Surprise Coding

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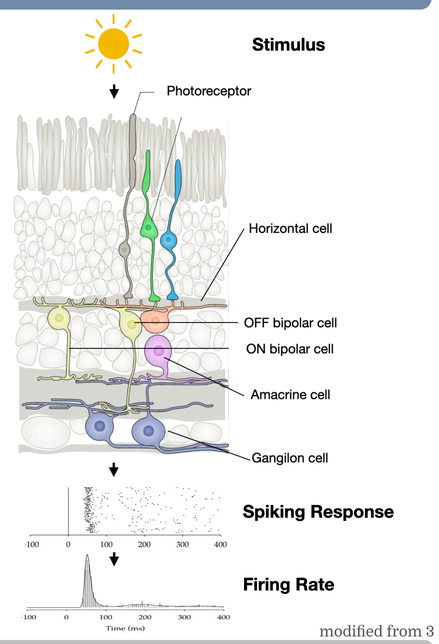
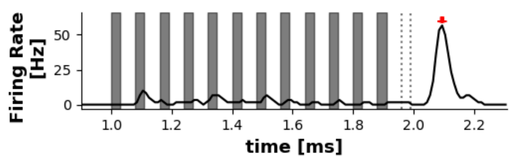
1 Background

- The Retina transforms visual information into spike trains transmitted to the rest of the brain.
- It processes information in **parallel pathways** selectively responding to specific features of the visual input:
  - The ON pathway responds to bright light,
  - The OFF pathway responds to dark stimuli.
- The retina also contains **predictions** of its future input and detects **violation of its expectation** with high precision.
- An example of this 'surprise signal' is the **Omitted Stimulus Response** (box 1).

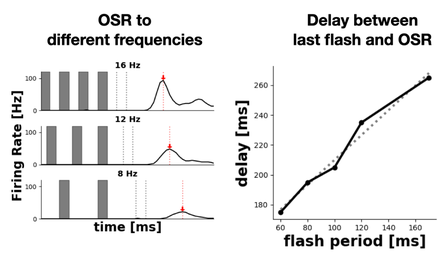


modified from 3

Box 1: Omitted Stimulus Response (OSR)



- periodic flash sequence
- omitted flash
- pulse of activity signaling the missing stimulus



Peak time **adapts to frequency** of the presented flash sequence

*

2 Motivation

The Retina can recognize patterns and signal its 'surprise' when these patterns are violated, with a high level of precision.

How can a local circuit such perform complex computations to detect 'surprise' and which cellular mechanisms enable these computations ?

We combine **electrophysiological experiments** in which we pharmacologically **inactivate specific cell types** in the retina, to identity key components to produce a dynamic response to changes, with **computational modelling** to investigate the potential role and location of **short-term plasticity.**

3 Experiments

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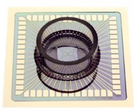
Methodology

1. Microelectrode Array Recordings:

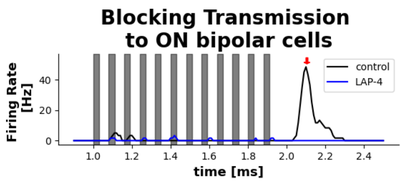


- Stimulation a dissected retina with a sequence of periodic dark flashes
- Extracellular spike recordings.

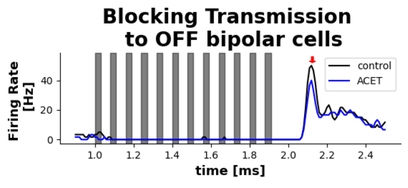
2. Identification of necessary components via pharmacological inhibition of synaptic transmission onto :

- ON bipolar cells via mGluR6 receptor antagonist LAP-4.
- OFF bipolar cells via AMPA receptor antagonist ACET.

Results



ON BC inhibition **cancels** the OSR.



OFF BC inhibition has **no direct effect** on the OSR.

Conclusions

- The ON pathway is required for the OSR to dark flashes[1] whereas the OFF pathway is not directly required, but could receive lateral input posterior to photoreceptor transmission
- This asymmetric contribution of ON and OFF pathway could be caused by :

A) a network effect **via directed lateral connections** (amacrine cells),

B) an **intrinsic mechanism** specific to ON bipolar cells.

4 Modeling surprise coding in the Retina

Existing Models

Gao et al., 2007, Computation in Neural Systems

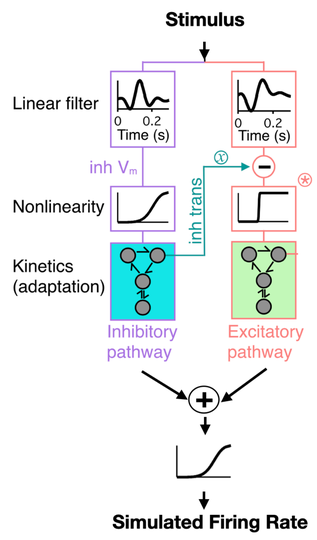
- Existing Models explained the OSR via two antagonistic (ON-OFF) parallel pathways organization and a resonance mechanism in ON bipolar cells;
- This mechanism could not be experimentally verified and cannot account fully for the predictive timing to flash frequency (box 1).

We will test a model of synaptic adaptation *in silico* to explore the hypothesis that **dynamical synapses cause the rapid frequency adaptation**.

Linear-Nonlinear-Kinetic (LNK) Model

Kastner et al., 2017, Current Biology

- Two parallel pathways that together provide input to one ganglion cell,
- Directed lateral connection before summation,
- Short-term plasticity in bipolar cell and amacrine cell synapses.



Processing Steps:

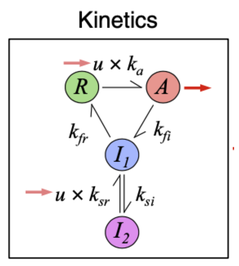
- **Step 1:** Convolution of stimulus and a temporal kernel simulates the integration of the stimulus into bipolar cell voltage.
- **Step 2:** Applying a nonlinearity simulates rectification within bipolar cells.

$$u(t) = N_{LNK}\left(\int F_{LNK}(t-\tau)s(\tau)d\tau\right). \quad (1)$$

- **Step 3:** Kinetics of **synaptic vesicle release** are simulated as a dynamical system of Markov type (box 2).
- **Step 4:** Summation and second nonlinearity simulates transformation of the response into a ganglion cell output firing rate .

Box 2: Short-term plasticity (STP)

- Synaptic vesicles can occupy 1 out of **4 different States** :
  - R : readily releasable
  - A : active (released)
  - I1 : inactive (empty)
  - I2 : inactive (refilled)
- P = (P_R P_A P_{I1} P_{I2}) are **probabilities** to occupy each state



- **Transitions** between states are controlled by **rate constants:**
  - k_a : vesicle activation
  - k_{fi}, k_{si} : fast/slow inactivation
  - k_{fr},k_{sr} : fast/slow recovery
- fixed or **vary in time**, scaled by bipolar cell voltage u(t) (1).

$$\frac{dP^T(t)}{dt} = P^T(t) * \begin{pmatrix} -u(t)*k_a & u(t)*k_a & 0 & 0 \\ 0 & -k_{fi} & -k_{fi} & 0 \\ k_{fr} & 0 & -(k_{fr}+k_{si}) & k_{si} \\ 0 & 0 & u(t)*k_{sr} & -u(t)*k_{sr} \end{pmatrix}$$

The change in probability is described by a set of first-order **differential equations**

The **output** of the synapse will be determined by the Probability of the active state, $P_{A(t)}$

5 Perspectives

Can the Omitted Stimulus Response with its predictive latency be explained via the model of STP ?

Can a similar mechanism, embedded in a **large scale network** account for **more complex pattern recognition**, such as motion reversal ?

We aim to build new hypothesis at the limits of biological experiments & understand computational paradigms at work.

In future we will experimentally test if:

- A lateral amacrine connection is involved in the OSR
- The OFF pathway contributes indirectly to the OSR

6 Acknowledgements

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* All experiments were performed in the team of Olivier Marre at Institut de la Vision.

6 References

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