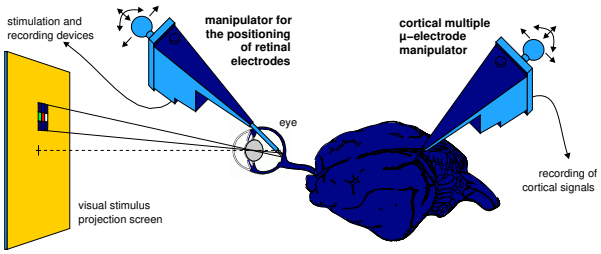
Introduction

1. **Goal.**
   Specific electrical stimulation of retinal ganglion cells for the development of a retina implant for blind humans with damaged photoreceptors. Basic visual perception may be provided even with few electrodes if spatial and temporal stimulation patterns are optimized such that the evoked cortical activity reflects as much visual information as possible.

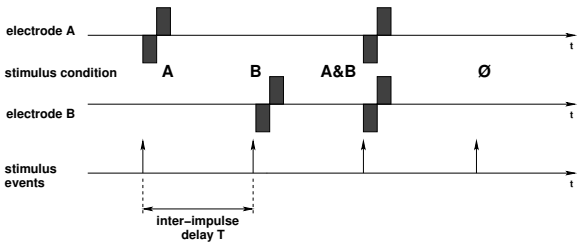
2. **Experimental methods.**
   Retinal ganglion cells of anesthetized cats were electrically stimulated by epiretinally placed micro electrodes ① with biphasic current impulses ②. Single-unit spike trains and population activities were simultaneously recorded via multiple micro electrodes from area 17 and 18 ③,④.

3. **Analysis algorithms.**
   Cortical spikes were sorted using a threshold criterion ③ or form analysis (PCA) ⑤ to assess potential selective activation. After estimation of the conditional probabilities ⑥ information theory ⑦ was applied to analyze the relationship between stimulus conditions and response measures.

1 Experimental Setup

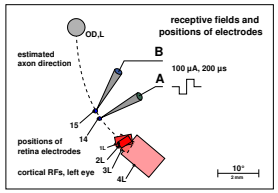


2 Sequences of Spatio–temporal Stimuli



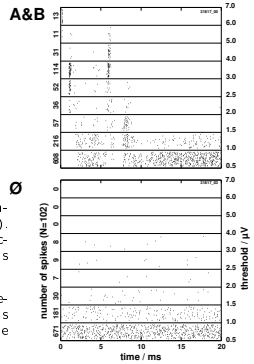
Precise stimulus events were used to trigger the electrodes' current sources. Here, only two electrodes (A and B) are displayed allowing the four stimulus conditions A, B, A&B and Ø. Different inter-impulse delays and current impulse amplitudes ranging from 30 to 100 μA were applied. Current impulses were charge-balanced and biphasic with 200 μs phase duration.

3 Evoked Spike Responses

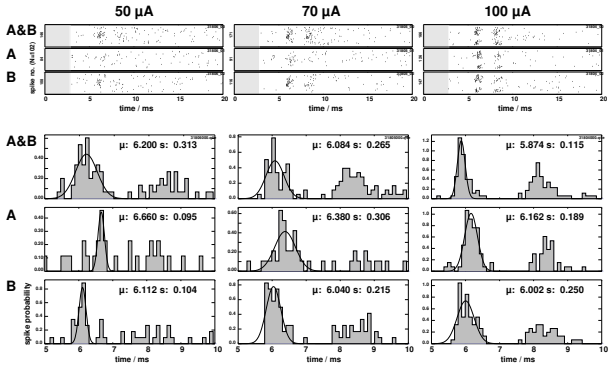


The receptive field plot explains the examined stimulus conditions A&B, A, B and Ø (zero stimulus). Stimuli were applied from electrode A and B, respectively. The spatio-temporal course of the stimulus currents is schematicly shown in ②.

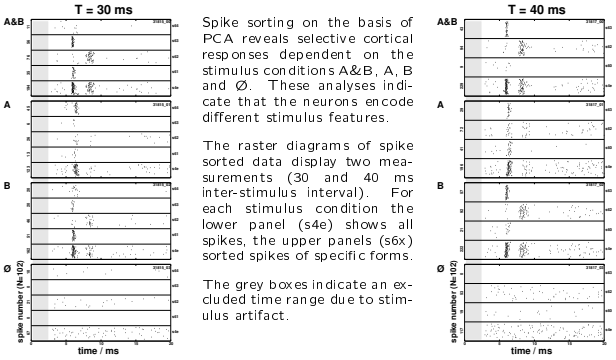
The diagrams on the right show the evoked responses for stimulus conditions A&B (synchronous stimulation) and Ø with respect to the size of the recorded action potentials.



4 Responses Depend on Stimulus Conditions



5 Assessing Selective Cortical Activation

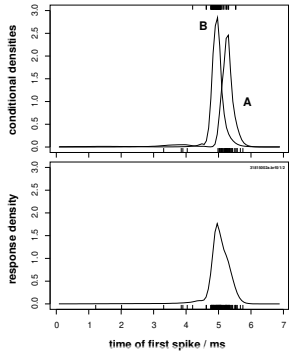


Spike sorting on the basis of PCA reveals selective cortical responses dependent on the stimulus conditions A&B, A, B and Ø. These analyses indicate that the neurons encode different stimulus features.

The raster diagrams of spike sorted data display two measurements (30 and 40 ms inter-stimulus interval). For each stimulus condition the lower panel (s4e) shows all spikes, the upper panels (s6x) sorted spikes of specific forms.

The grey boxes indicate an excluded time range due to stimulus artifact.

6 Estimation of Conditional Probabilities



To assess the mutual information between stimulus and response, the following steps were performed:

1. **Stimulus and response measures.**
   The stimuli to discriminate between are applied currents by two retinal electrode positions A and B ③. As response measure the time of the first spike was chosen.

2. **Density estimation.**
   The conditional and a priori response densities were estimated using the Locfit algorithm (see C. L. Loader, Locfit: An Introduction, Statistical Computing and Graphics Newsletter, April 1987).

7 Calculation of Transmitted Information

The evoked cortical responses depended strongly on the stimulus conditions, being reflected in the conditional probabilities ⑥. Thus, evoked action potentials provide information about the preceding stimulus. However, the less the conditional probabilities overlap, the more information can be transmitted.

The time of the first occurring spike after stimulation has been chosen as the information carrying signal. Times of following spikes might also transmit information about the stimulus, but were not analyzed in detail, here.

Let $p_{t/s}(t)$ be the probability density for evoked spikes at time t under the condition of the preceding stimulus s_i. With the discrete a priori probabilities $p_s(s_i)$ of the stimuli and the response density $p_t(t)$, the mutual information is calculated as

$$\mathcal{H}(S;T) = \sum_{i=1}^{N_s} p_s(s_i) \int_{-\infty}^{\infty} p_{t/s}(t) \log_2 \frac{p_{t/s}(t)}{p_t(t)}\, dt.$$

With the estimated densities in ⑥ the mutual information for stimulus conditions A and B results in $\mathcal{H}(S;T) = 0.5$ bits per spike.

Results and Conclusions

1. Electrical stimulation of ganglion cells can evoke precisely timed cortical responses. The mean delay between stimulus and first spike ranged from 5 to 7 ms, the standard deviation from 100 to 300 μs. The responses were temporally structured and consisted of two distinct distributions. The relatively sharp early response was followed by a flatter response at 8 to 9 ms delay.

2. The structure of the responses depended on the stimulus current. At higher currents the responses occurred slightly earlier and were more precise. Spike sorting revealed that the cortical neurons responded selectively to different stimulus conditions.

3. According to their timing precision the action potentials transmitted information about the time point of the stimulus. Two electrodes (A and B) 300 μm apart evoked responses with a relative delay of about 200 μs. Each spike carried 0.2 to 0.6 bit of information about the stimulus.

4. A fundamental requirement for transmitting visual information to the cortex using a retina implant, is a precise and selective cortical activation. Hence, future work has to concentrate on optimizing spatio-temporal current patterns for information maximization.

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