Large-scale spike sorting for the analysis of electrical stimulation

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Summary

Overarching goal:

- To develop methods for the analysis of large-scale electrophysiological recordings in MEAs with electrical stimulation, a potentially powerful tool for closed-loop feedback control and perturbation of neural networks.

Context: retina

- Interest in understanding how retinal ganglion cells (RGC) respond to electricity.
- Useful for the development of high-resolution prostheses [1].
- Despite the context specificity, developed methods should extend to other settings.

Challenge

- Electrical stimulation induces transient distortions, or artifacts, on the recordings. Their magnitude is much greater than of spikes, making separation difficult [2].
- Existing artifact subtraction methods cannot handle with short latency or low time variability in spikes, the norm in our context. Human labeling does not scale!

Strategy

- We propose a probabilist generative model: data is made up by the superposition of spikes, artifact and noise. The artifact is highly structured and we represent this structure by imposing a Gaussian Process (GP) prior, enabling a fast and scalable implementation [3].

Results

- We developed an algorithm that achieves an accuracy greater than 99% on a large-scale dataset (512 electrodes, $\sim$ 1.000.000 spikes and around 15 retinal preparations). This algorithm admits a simplification that is easier to code and faster, but with lower accuracy guarantees.
- We illustrate how to apply the algorithm to infer quantities relevant for closed-loop experiments.

Important!!

- The corresponding manuscript is currently under review, and the pre-print is available in the bioRxiv/Neuroscience under the title Electrical Stimulus Artifact Cancellation and Neural Spike Detection on Large Multi-Electrode Arrays

Experimental Setup

- Experimental design: stimulation is available for a series of stimulus of increasing magnitude. Some repetitions are available for the same stimulus.
- Visual stimulation allows to infer action potentials.

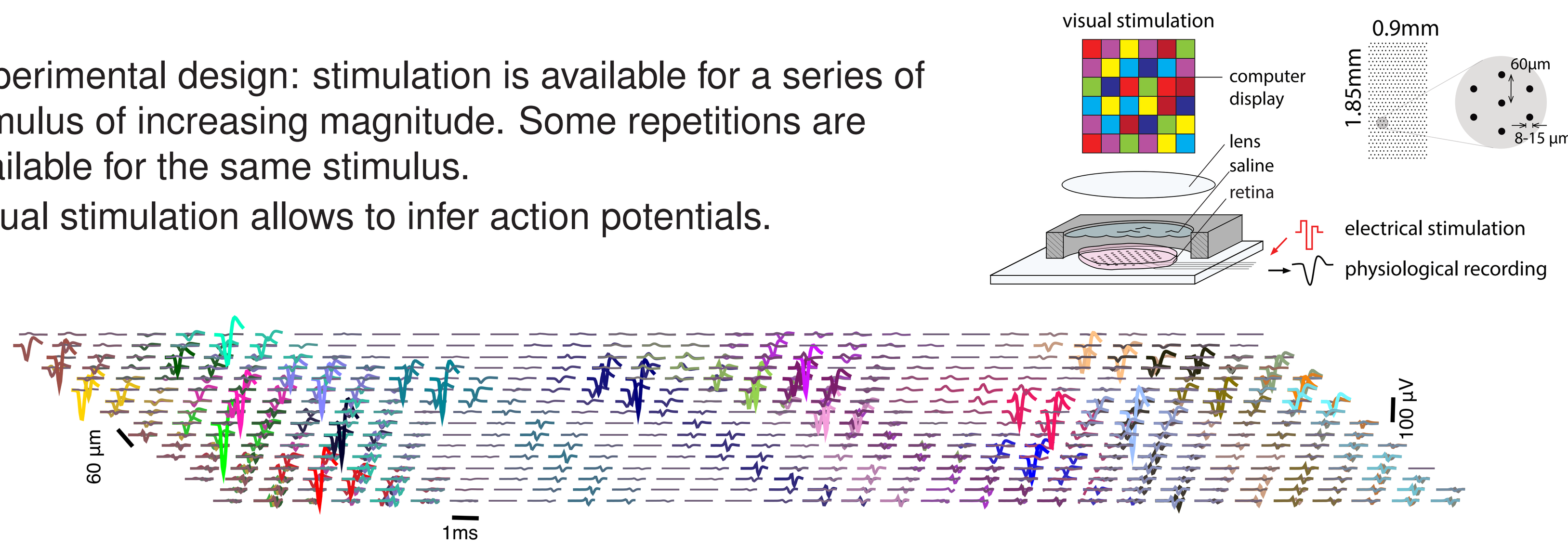


Figure: **Action potential templates or Electrical Images of many cells obtained after visual stimulation.**

Why spike sorting can be hard here?

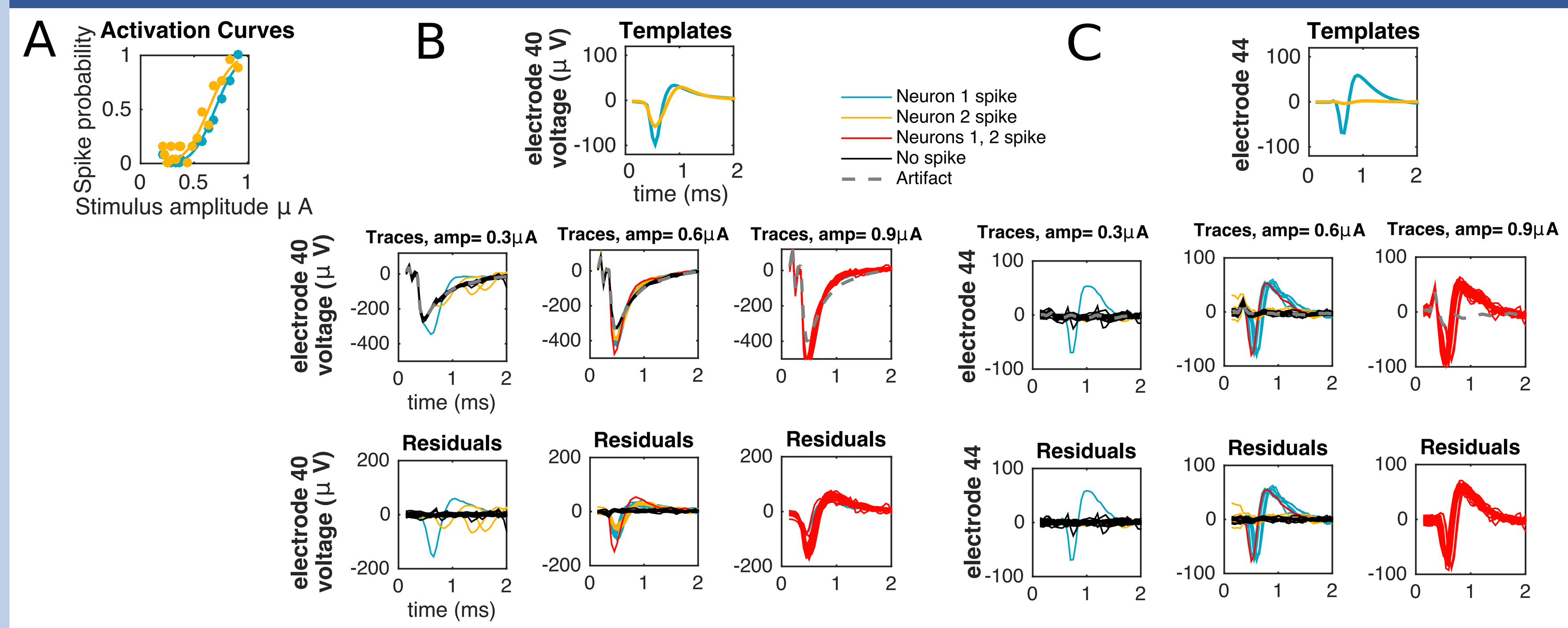


Figure: **Inferring the activity of two neurons can be hard. A Activation curves. B a stimulating electrode: templates (top), raw traces (center) and artifact-subtracted traces (or residuals, bottom) for different repetitions of three increasing stimulus. C same as B but on a different, non-stimulating electrode.**

Stimulus Artifact

- Artifacts, although unknown, are highly structured in time, space and magnitude of stimulation

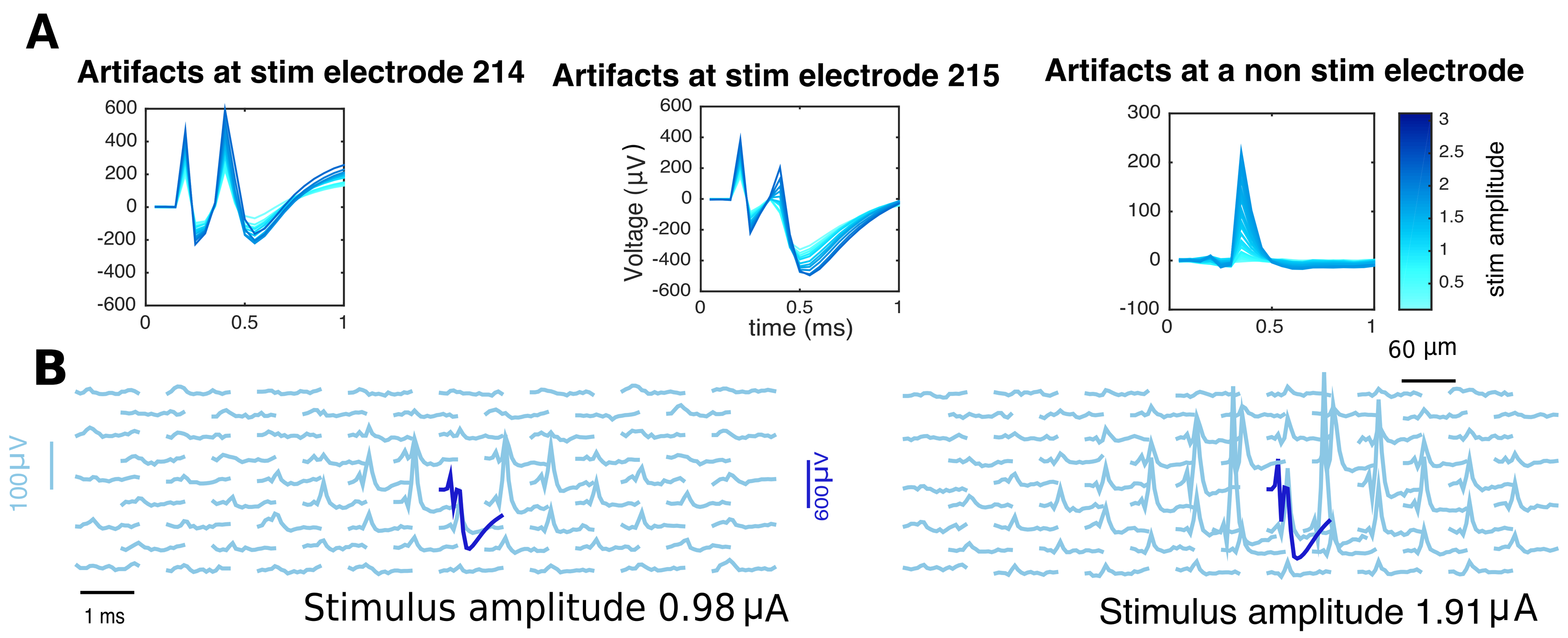


Figure: **TTX experiments. A electrode-wise, artifact magnitude increases with stimulus strength and it it oscilates more wildly in stimulating(s) electrode(s). B artifact has a characteristic spatio-temporal decay in the non-stimulating electrodes.**

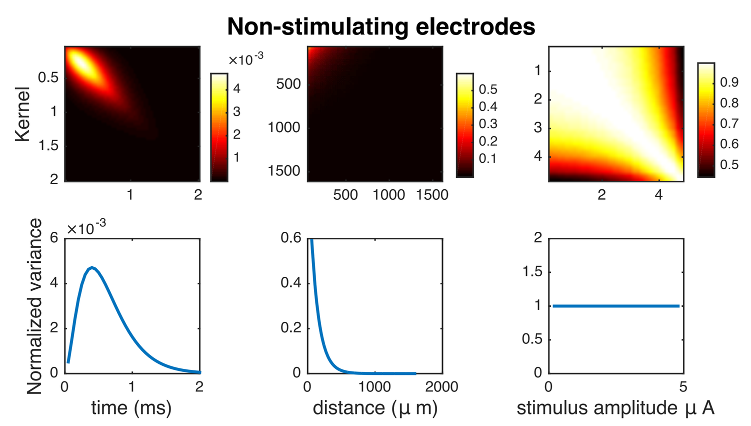
Math and algorithm details

- Recorded traces $Y = (Y)_{t,e,j,i}$ are stacks of movies (t=times, e= space, j =stimulus magnitude and i= stimulus repetition).
- Linear decomposition: $Y = A + s + \epsilon$, i.e., $Y_{t,e,j,i} = A_{t,e,j} + s_{t,e,j,i} + \epsilon_{t,e,j}$
- Neural activity s decomposes into individual activities $s = \sum_i^n s_n$, each expressed as a time-shifted Electrical Image.
- Prior on artifact $p(A) \sim GP(0, K)$ with $K = \rho K_t \otimes K_e \otimes K_j + \phi^2 I$ acts as a (structured) regularization term to further constrain the problem.
- The Kronecker product $\otimes$ leads to tractable computations. Each kernel is expressed as a smoothing kernel (e.g. Matérn) times a gamma envelope.

Algorithm Summary

- **Input:** Traces $Y = (Y_j)_{j=1,\dots,J}$ and Electrical images of the n targeted neurons.
- Step 0: Estimation of Kernel Hyperparams: translates into maximizing a likelihood.
- Step 1: For each of the J stimuli:
  - Construct an estimate of the artifact by extrapolating from previous stimulus (using a GP extrapolation formula).
  - Alternate between estimation of the artifact (using the GP filtering formula) and estimation of neural activity (template matching [4]) until no further changes are observed.
- **Output:** Estimates of artifact $\hat{A}$ and neural activity $\hat{s}^n$ for each neuron.

Figure: **Inferred Kernels (top) and their corresponding diagonals (bottom).**



Results

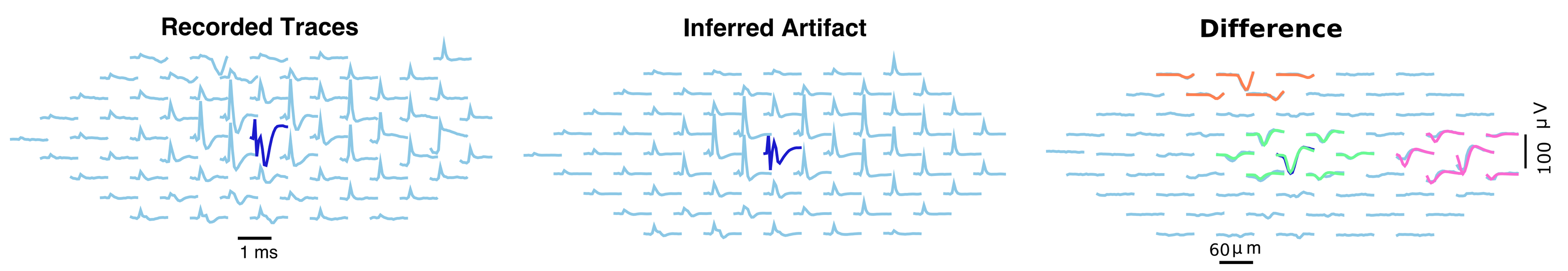


Figure: **Example of the (correct) inference of an artifact and three spikes.**

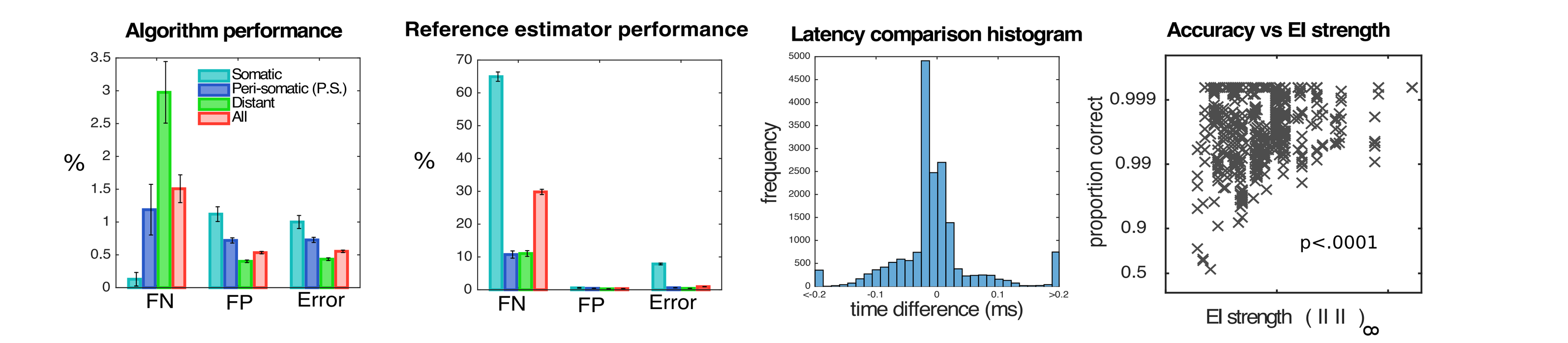


Figure: **By comparison to human annotated data, we establish very low error rates, unlike a reference estimator**

Application I: local analysis

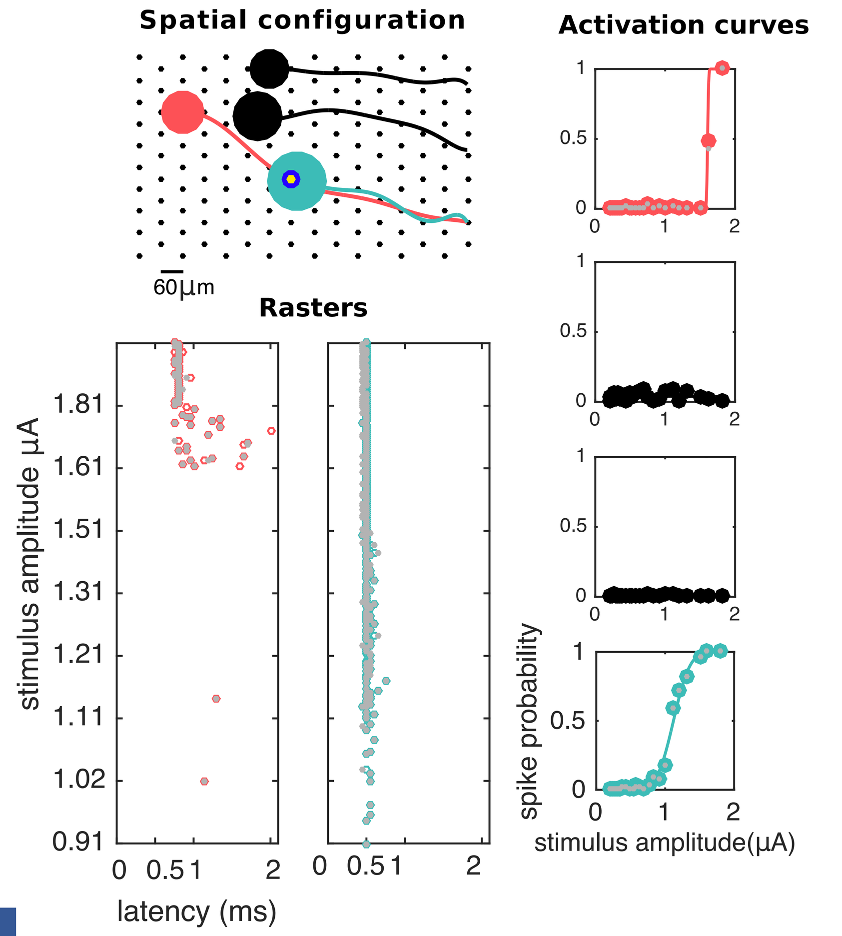


Figure: **Analysis of responses of neurons in a neighborhood of the stimulating electrode. Grey dots indicate results of human analysis.**

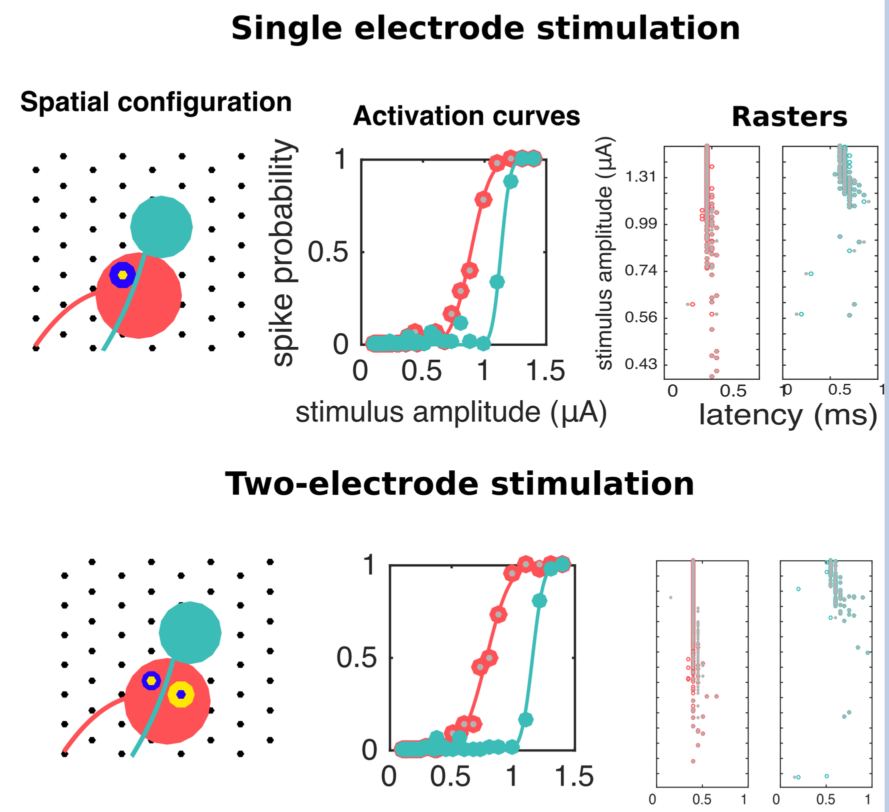


Figure: **Analysis of differential responses to single and two-electrode stimulation.**

Application II: large-scale analysis

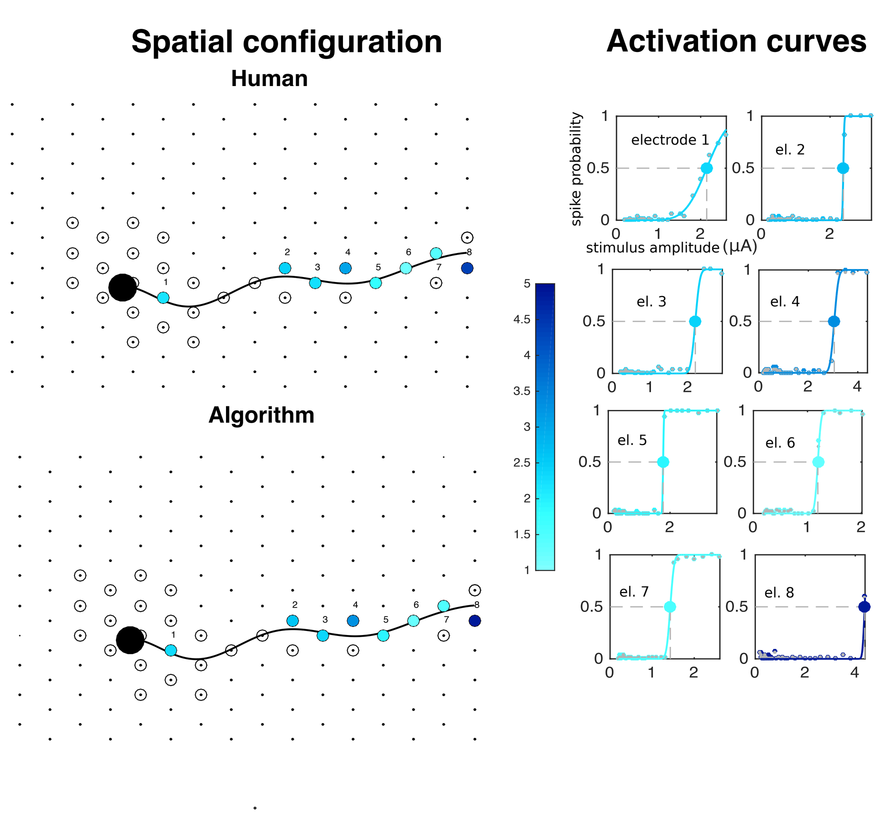


Figure: **Electrical receptive field of a neuron to stimulation at different sites.**

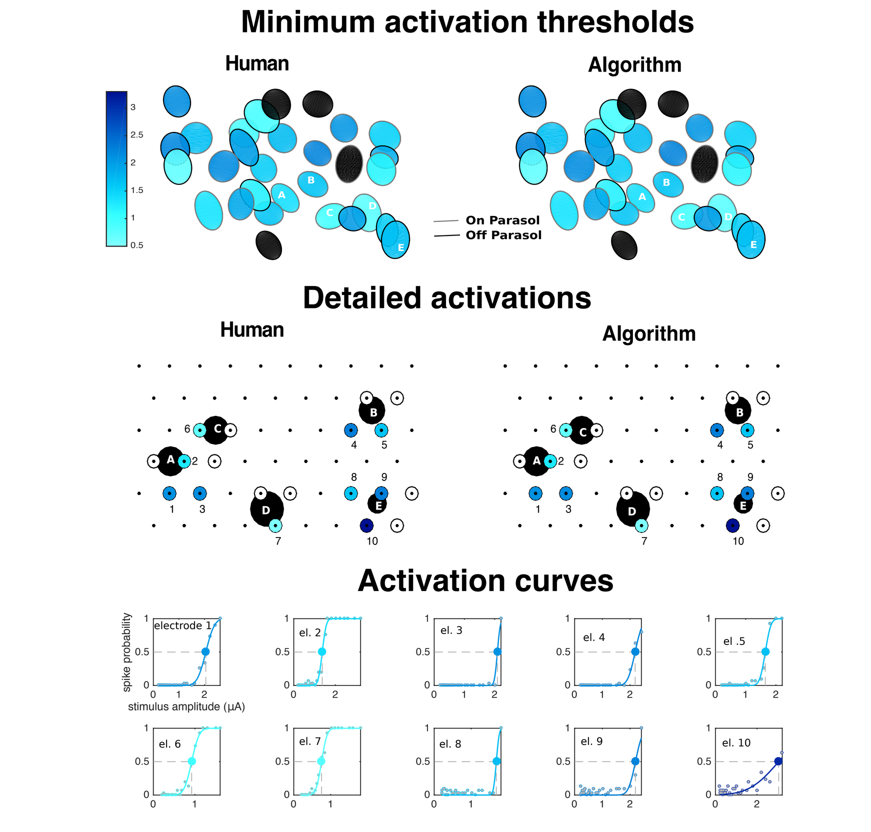


Figure: **Large-scale analysis of the stimulation of a population of parasol cells.**

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