

Neuroscientists release state-of-the-art spikesorting software

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Spike detection and feature extraction. **a**, Schematic of the pipeline for detecting spikes and extracting spike features. **b**, Short segment of preprocessed data over 70 channels and 1,000 time points (data from elsewhere¹⁶). Insets show an expanded section with multiple overlapping spikes. **c**, Example simple templates centered at a single position on the probe. Templates are repeated at 1,536



positions for a Neuropixels probe. **d**, Example learned templates centered at different positions on the probe. **e**, Reconstruction of the data in **b** based on the inferred templates and spike times. **f**, Residual after subtracting the reconstruction from the data. **g**–**i**, *t*-SNE visualization of spike features from a 40-µm segment of the probe. Spike features were extracted using either simple templates (**g**) or learned templates without (**h**) or with (**i**) background subtraction. **j**, Spatial distribution of a subset of the final extracted spikes colored by their template norm. Credit: *Nature Methods* (2024). DOI: 10.1038/s41592-024-02232-7

How do researchers make sense of the mountains of data collected from recording the simultaneous activity of hundreds of neurons? Neuroscientists all over the world rely on <u>Kilosort</u>, software that enables them to tease apart spikes from individual neurons to understand how the brain's cells and circuits work together to process information.

Now, researchers at HHMI's Janelia Research Campus, led by Group Leader Marius Pachitariu, have <u>released Kilosort4</u>, an updated version of the popular spike-sorting software that has improved processing, requires less manual work, and is more accurate and easier to use than previous versions.

"Over the past eight years, I've been refining the algorithm to make it more and more human-independent so people can use it out of the box," Pachitariu says.

Kilosort has become indispensable for many neuroscientists, but it may never have been developed if Pachitariu hadn't decided he wanted to try something new.



Pachitariu's Ph.D. work was in <u>computational neuroscience</u> and <u>machine</u> <u>learning</u>, but he yearned to work on more <u>real-world applications</u>, and he almost left academia for industry after he completed his Ph.D. Instead, Pachitariu opted for a postdoc in the joint lab of Kenneth Harris and Matteo Carandini at University College London, where he could do more experimental neuroscience.

The lab was then part of a consortium testing a probe called <u>Neuropixels</u>, developed at HHMI's Janelia Research Campus. Pachitariu had no idea how to use the probes, which record activity from hundreds of neurons simultaneously, but he knew how to develop algorithms to keep up with the enormous amount of data his labmates were generating.

In the first year of his postdoc, Pachitariu developed the initial version of Kilosort. The software, which was 50 times faster than previous approaches, allowed researchers to process the millions of data points generated by the Neuropixels probes. Eight years later, the probes and the software are staples in neuroscience labs worldwide, allowing researchers to identify and classify the spikes of individual neurons.

In 2017, Pachitariu became a group leader at Janelia, where he and his team seek to understand how thousands of neurons work together to enable animals to think, decide, and act. These days, Pachitariu spends most of his time doing experiments and analyzing data, but he still finds time to work on improving Kilosort. The newly released Kilosort4 is the best in its class, outperforming other algorithms and correctly identifying even hard-to-detect neurons, according to the researchers.

Pachitariu says it is much easier to squeeze in work on projects like Kilosort at Janelia than at other institutions where he would have to spend time writing grants and teaching.

"Every now and then, I can put a few months into spearheading a new



version and writing new code," he says.

Pachitariu says he also enjoys refining Kilosort, which allows him to use the core set of skills he developed during his Ph.D. work.

"I enjoy doing it, and I know it is useful to other people so that always helps in motivating me," he says.

The paper is published in the journal Nature Methods.

More information: Marius Pachitariu et al, Spike sorting with Kilosort4, *Nature Methods* (2024). DOI: 10.1038/s41592-024-02232-7

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