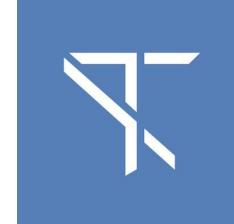




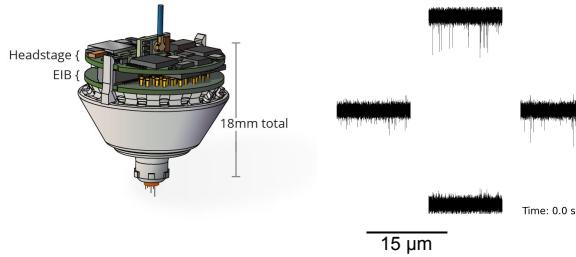
# SpikeInterface, a unified framework for spike sorting

Alessio Buccino\*, Cole Hurwitz\*, Samuel Garcia, Jeremy Magland,  
Joshua Siegle, Roger Hurwitz, Matthias Hennig

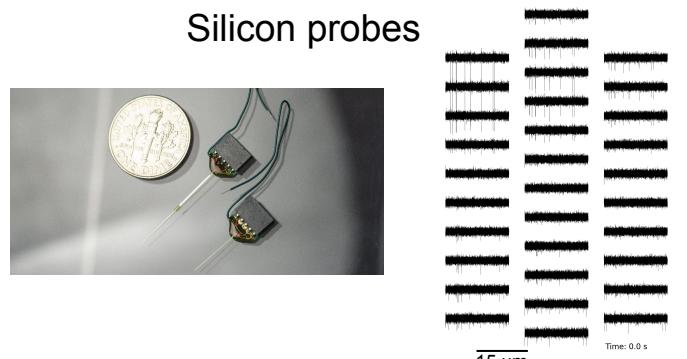


# Extracellular electrophysiology is the most widely used technique to probe neural activity

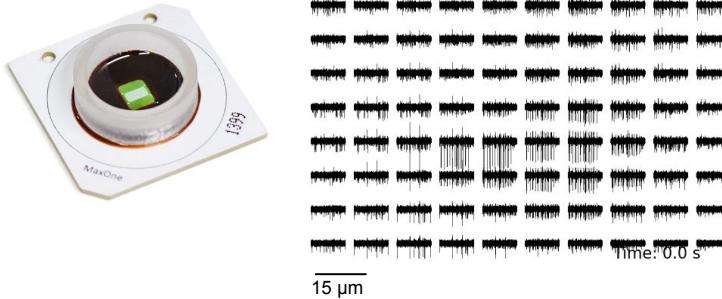
Tetrodes



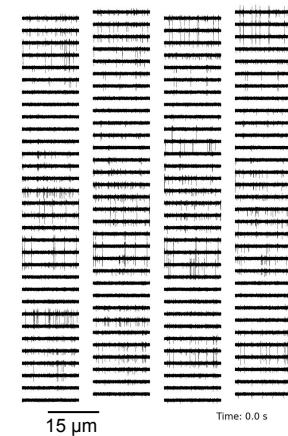
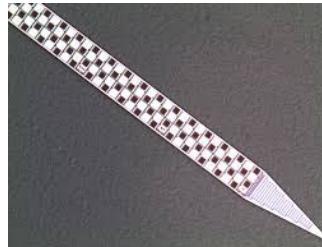
Silicon probes



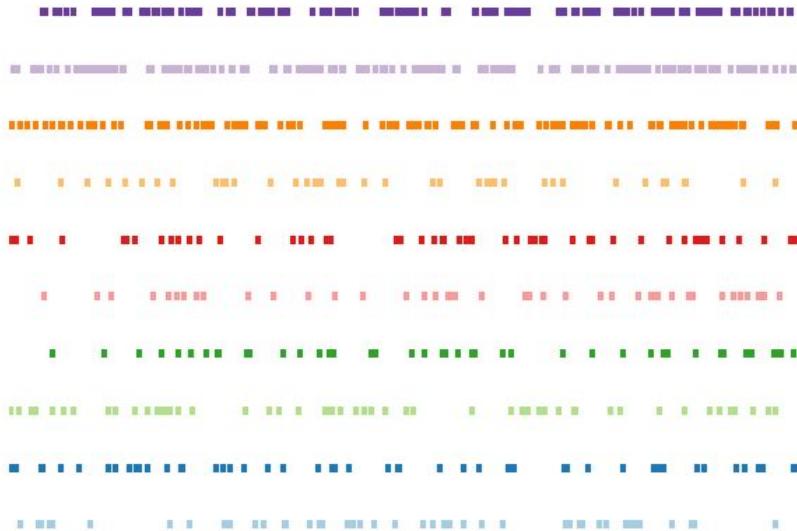
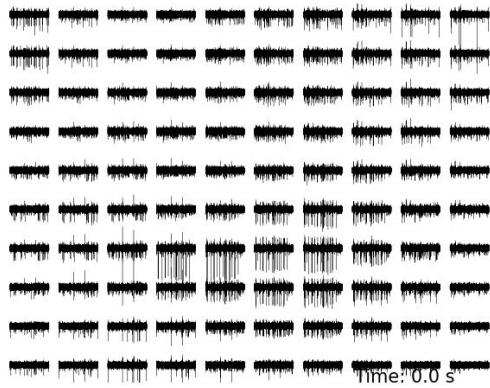
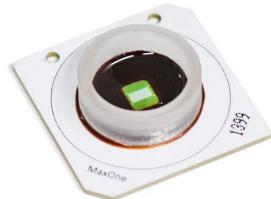
Planar HD-MEA  
*In vitro*



Shank HD-MEA  
*In vivo*



*Spike sorting* is the process to extract single unit spike trains from the mixture of recordings



It is an **essential** step in extracellular electrophysiology to study neural activity at single-cell resolution

Out there, there is a jungle of spike sorting tools...

Klusta



SPYKING  
CIRCUS

Wave clus

JRCLUST

Hherding Spikes 2



YASS: Yet Another Spike Sorter

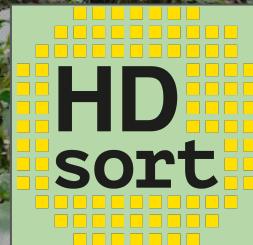
KiloSort

Kilosort2

Kilosort2.5

Kilosort3

MountainSort4



IronClust



Tridesclous

...and you might feel a little lost!

Klusta



SPYKING  
CIRCUS

Hherding S



YASS: Yet Another Spike Sorter



KiloSort

Kilosort2

Kilosort2.5

Kilosort3



IronClust



Tridescuous

# Some unaddressed challenges of spike sorting

- 1. Extracellular file format incompatibilities.**
  - a. Sharing/reusing data stored in different formats is challenging.
  - b. Building software to accommodate all formats is a difficult task.
- 2. Hard to run and compare many spike sorting algorithms simultaneously.**
  - a. Many underlying languages (e.g. C, C++, MATLAB, and Python).
  - b. Large variety of specific configuration files/parameters
  - c. There exists little rigorous benchmarking of current algorithms.
- 3. Lack of data provenance and reproducibility**
  - a. A lack of provenance can lead to a lack of reproducibility.
  - b. Reproducing analysis pipelines of other labs is essential for health of the field but is currently challenging.

# **SpikeInterface** is a Python package...

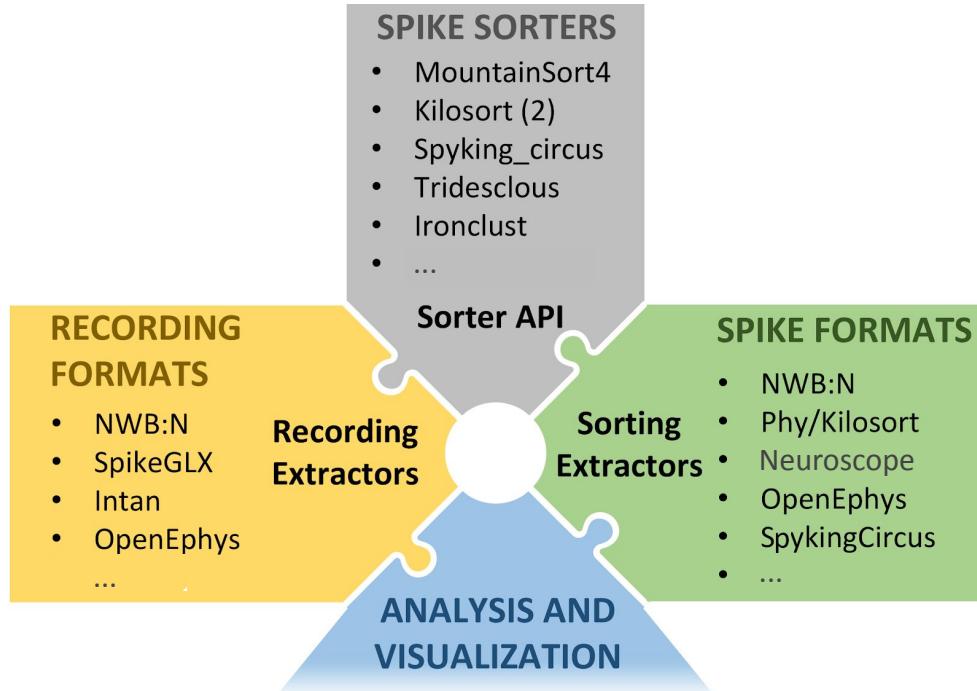
...to run multiple sorters on the same data.

...that bundles functionality for  
pre- and post-processing,  
including validation and curation.

...has tools for spike sorting  
comparison.

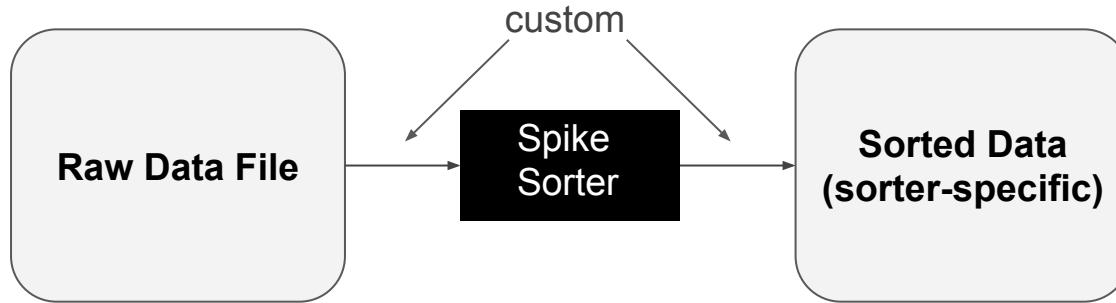
...offers data visualization.

...enables fully reproducible  
analysis workflows.



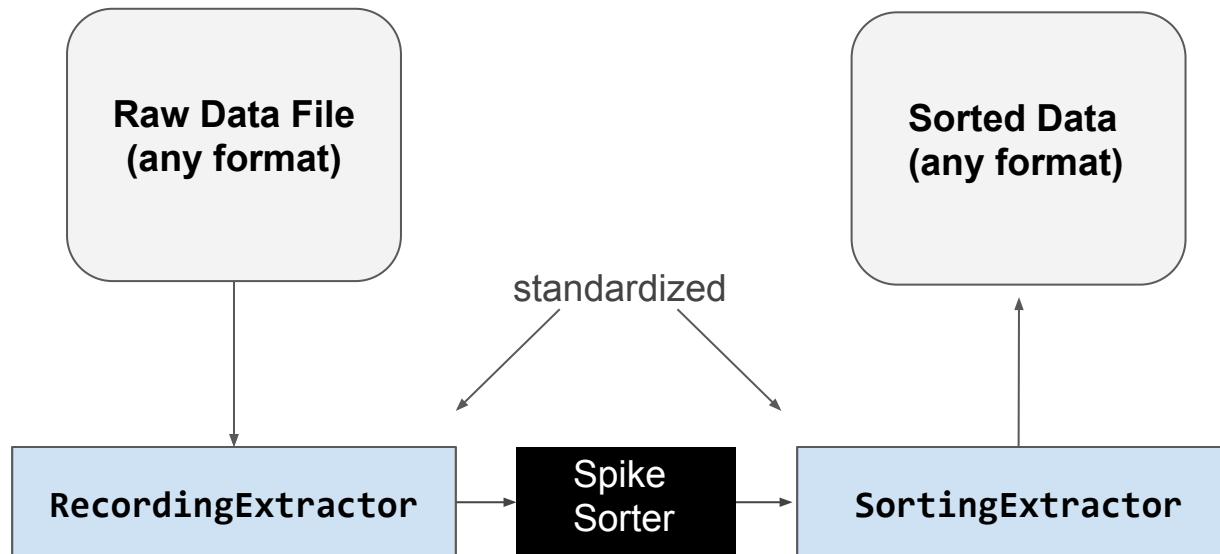
Thanks Ben Dichter for the graphic

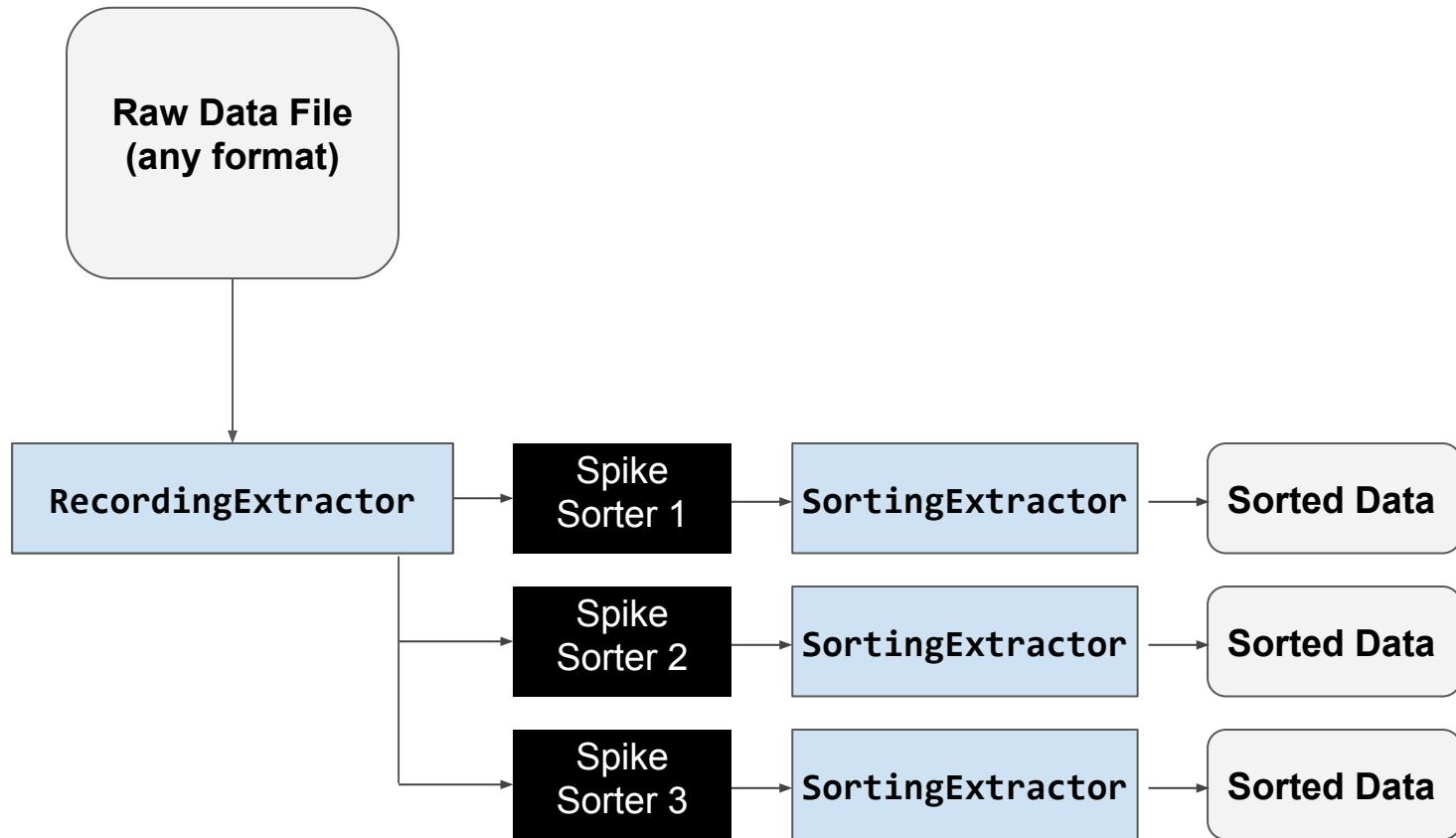
## Manual workflow



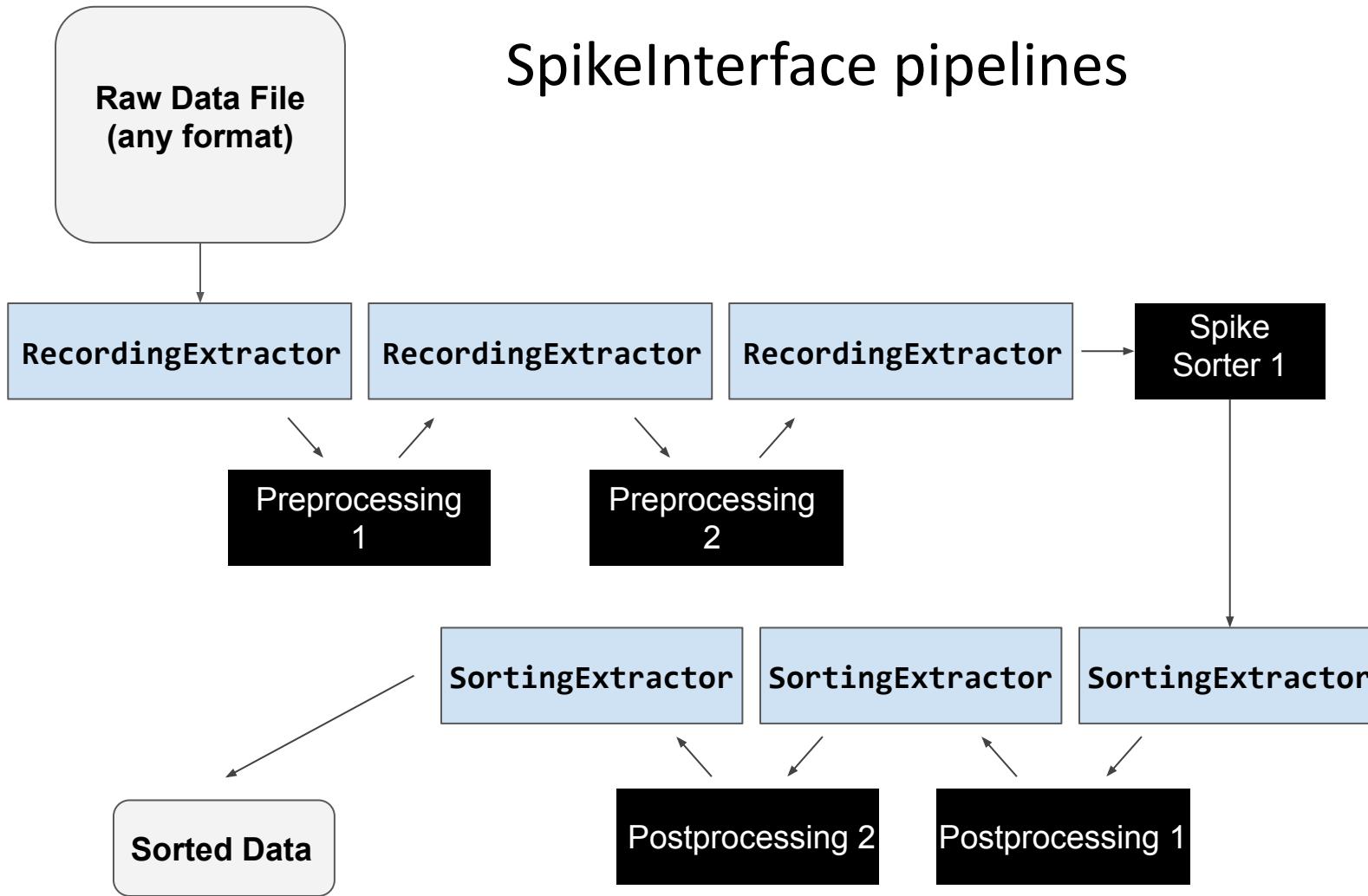
---

## SpikeInterface





# SpikeInterface pipelines



# Supported technologies

## RecordingExtractor

- Binary
- Biocam (3Brain)
- Blackrock
- CED
- Exdir
- Intan
- Klusta
- MaxOne/MaxTwo (Maxwell)
- MCS system
- MDA (Mountainsort)
- MEArec
- NIX
- NWB
- Neuroscope
- Neuralynx
- Open Ephys
- Phy
- Plexon
- Shybird
- SpikeGLX
- Spyking Circus

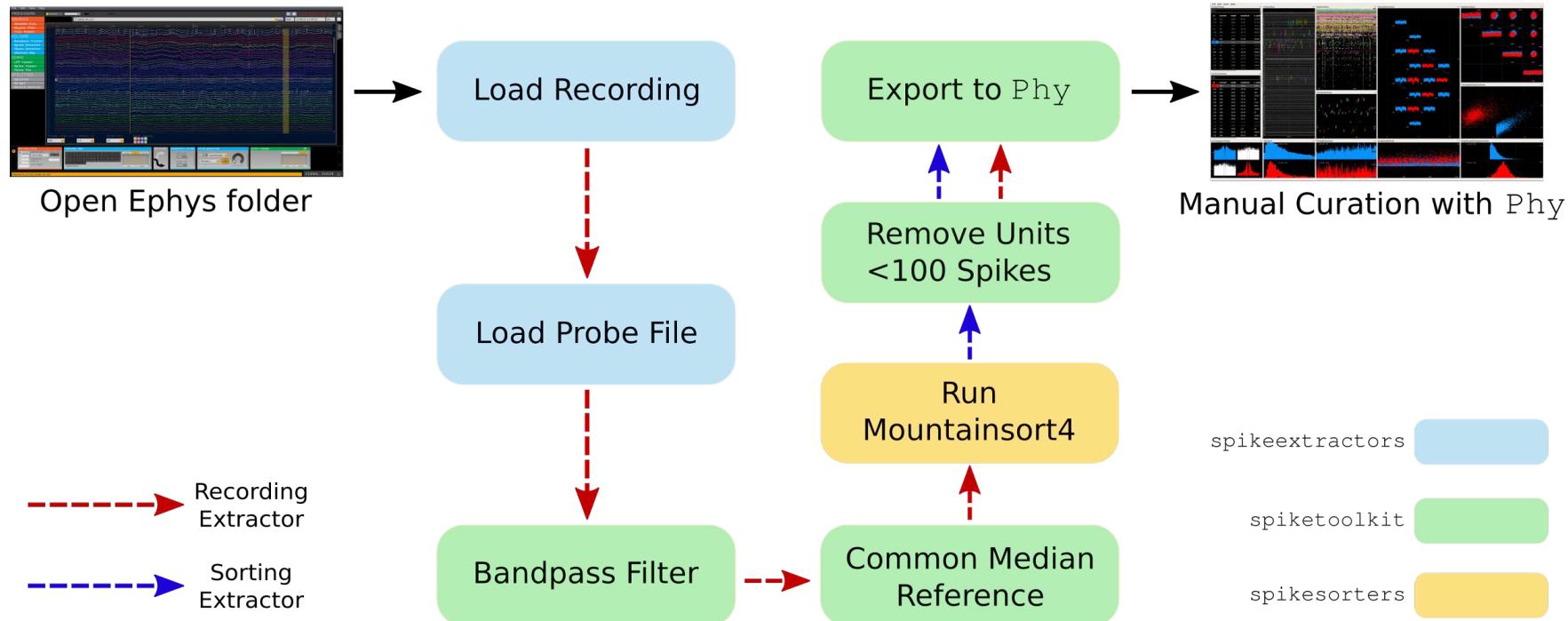
## Sorter

- Combinato
- HDSort
- Herding Spikes
- Ironclust
- Kilosort 1, 2, 2.5, 3
- Klusta
- Mountainsort4
- Spyking Circus
- Tridesclouds
- Waveclus
- YASS

## SortingExtractor

- ALF
- Blackrock
- CellExplorer
- Combinato
- Exdir
- HDSort
- Herding Spikes
- JRClust
- Kilosort
- Klusta
- MaxOne/MaxTwo
- MDA (Mountainsort)
- MEArec
- Neuralynx
- NIX
- NWB
- Neuroscope
- NPZ (created by SpikeInterface)
- Open Ephys
- Phy
- Plexon
- Shybird
- Spyking Circus
- Tridesclouds
- Waveclus
- YASS

# SpikeInterface pipelines: a concrete example.



# The 7 steps of the pipeline translate into 7 lines of Python code!

```
import spikeinterface.extractors as se
import spikeinterface.toolkit as st
import spikeinterface.sorters as sorters

recording = se.OpenEphysRecordingExtractor('path-to-open-ephys-folder')
recording = recording.load_probe_file('path-to-probe.prb')
recording = st.preprocessing.bandpass_filter(recording, freq_min=300, freq_max=6000)
recording = st.preprocessing.common_reference(recording, reference='median')
sorting_MS4 = sorters.run_mountainsort4(recording)
sorting_curated = st.curation.threshold_num_spikes(sorting_MS4, min_num_spike_threshold=100)
st.postprocessing.export_to_phy(recording, sorting_curated, output_folder='phy_output')
```

# Meta-analysis and benchmark of spike sorting tools

Klusta



SPYKING  
CIRCUS

Hherding Spikes 2

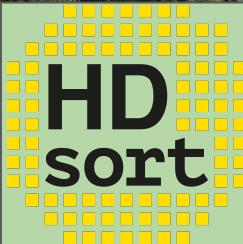


YASS: Yet Another Spike Sorter

Wave clus

JRCLUST

MountainSort4



KiloSort

Kilosort2

Kilosort2.5

Kilosort3

IronClust

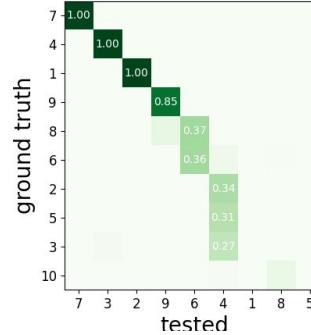


Tridesclous

# Spike sorting comparison

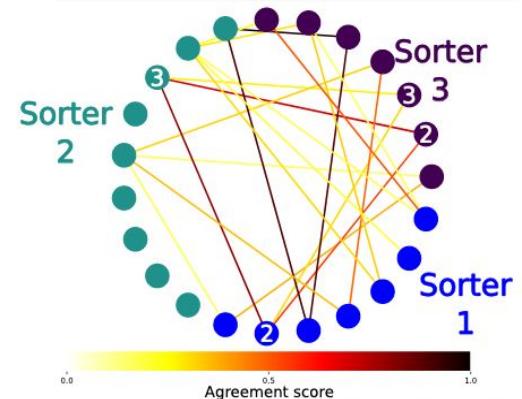
Ground truth analysis:

- Agreement score for each pair of spike trains
- Best-match assignment
- Computes various performance metrics (precision, recall, accuracy)
- Classifies units as true/false positives, redundant or overmerged



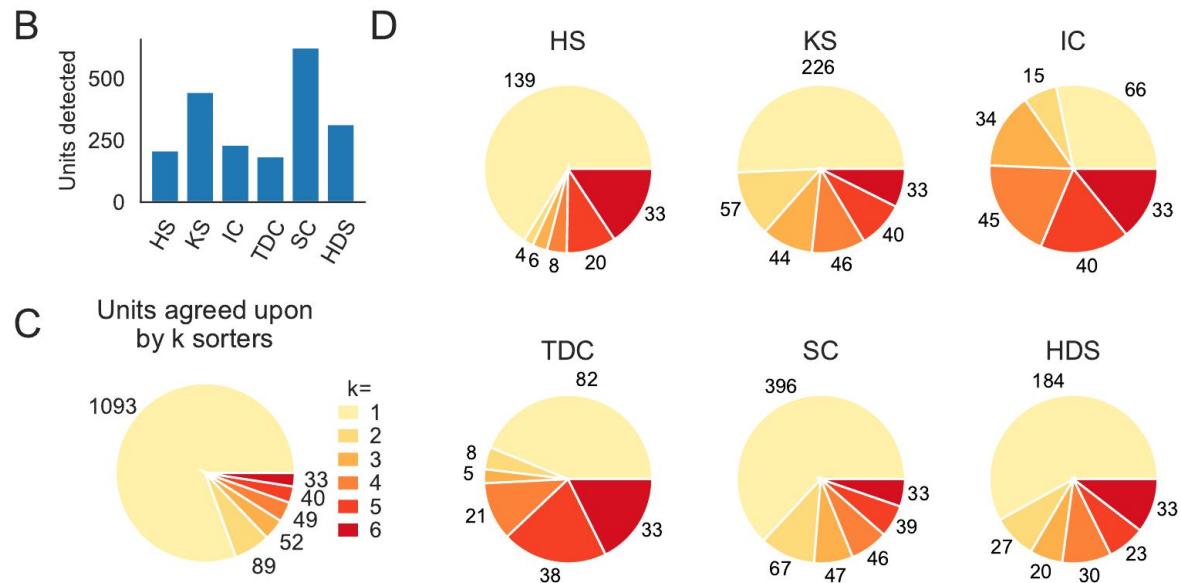
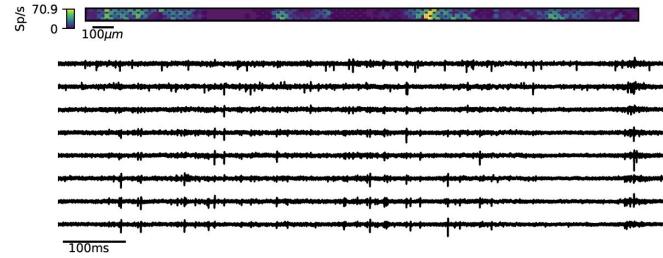
Multiple sorter comparison:

- Performs comparisons for all spike sorting pairs
- Computes agreement between all units
- Matches units and computes agreement with a graph-based analysis

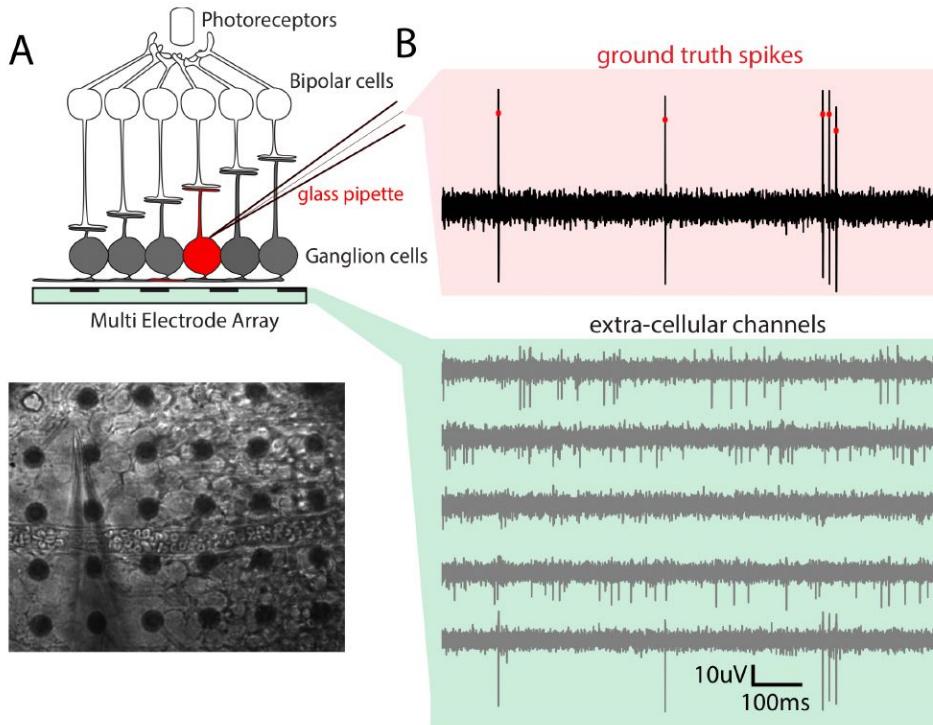


# Comparison reveals very low agreement between six spike sorters

Allen Brain Observatory Neuropixels dataset 15 minutes, 246 active channels



# Ground-truth *in vitro* with paired recordings: one cell at a time



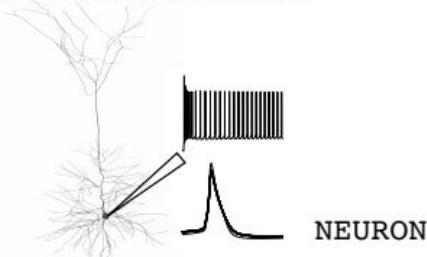
[Yger et al. 2018]

# Ground-truth *in silico* simulations: all cells are available

**MEAreC  
simulator**

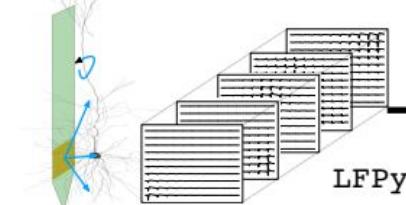
## A Templates Generation

Intracellular simulation



Extracellular simulation

random location  
random rotation



template library

## B Recordings Generation

template library

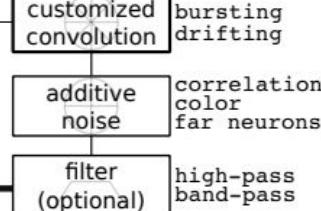
templates  
locations  
rotations  
cell types  
info

template selection  
location amplitude overlap  
template pre-process  
jitter resample pad

recordings

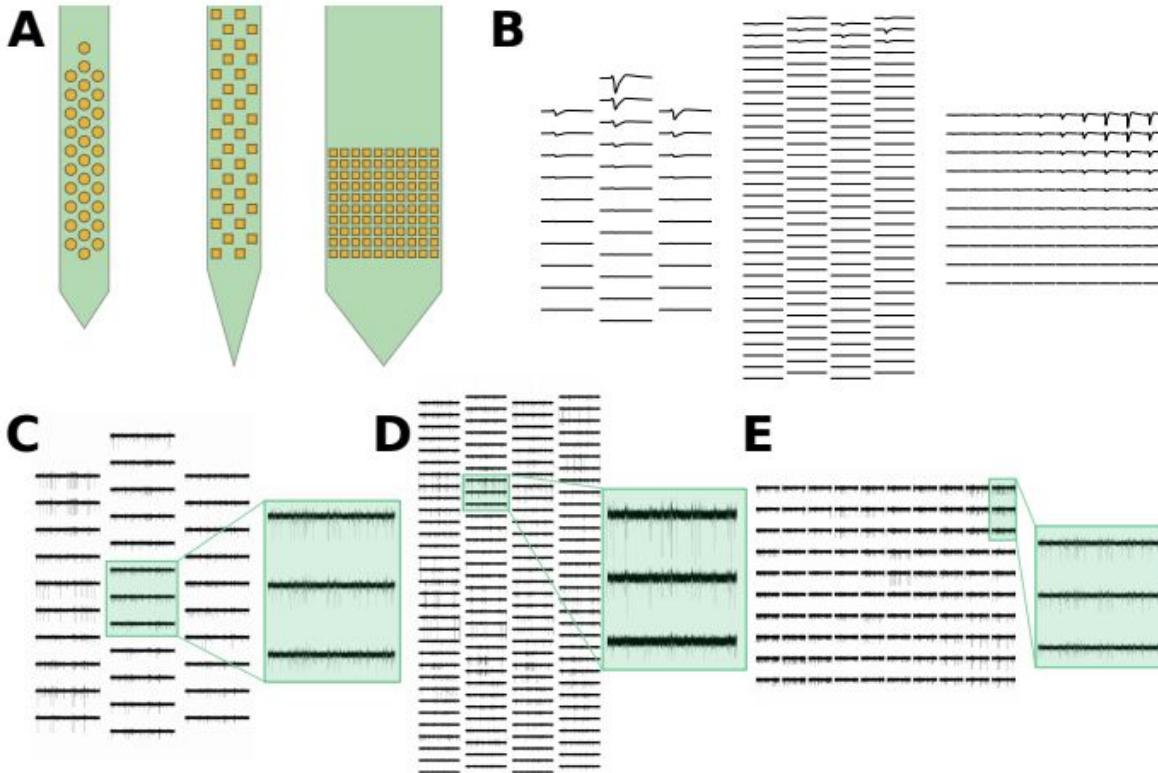
recordings  
templates  
electrodes  
spike trains  
info

Spike trains Generation

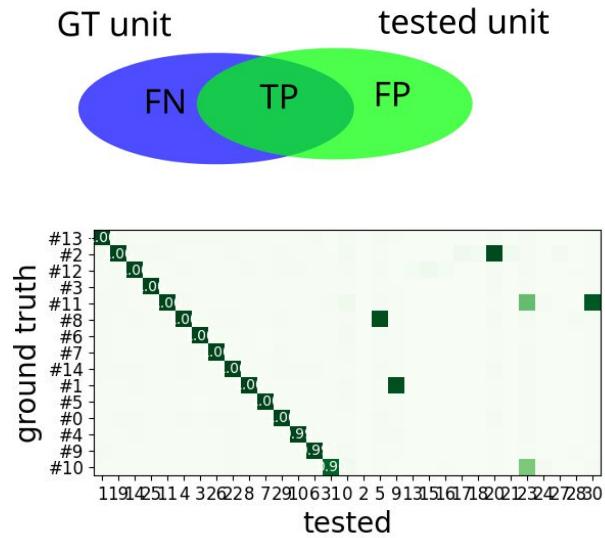
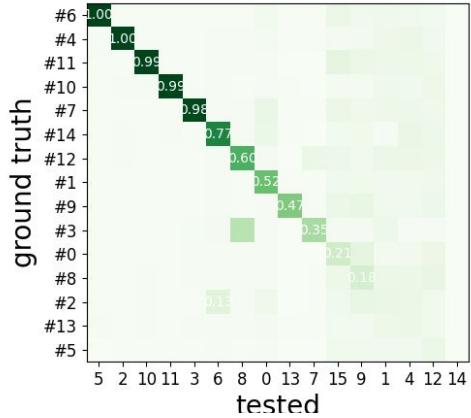


# Ground-truth *in silico* simulations: all cells are available

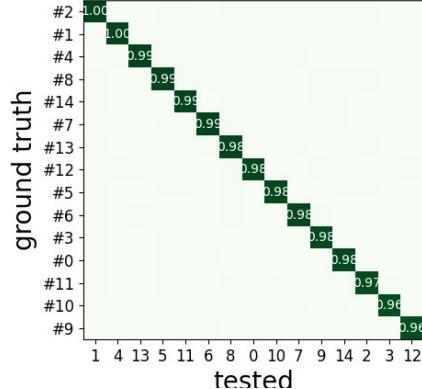
**MEAreC  
simulator**



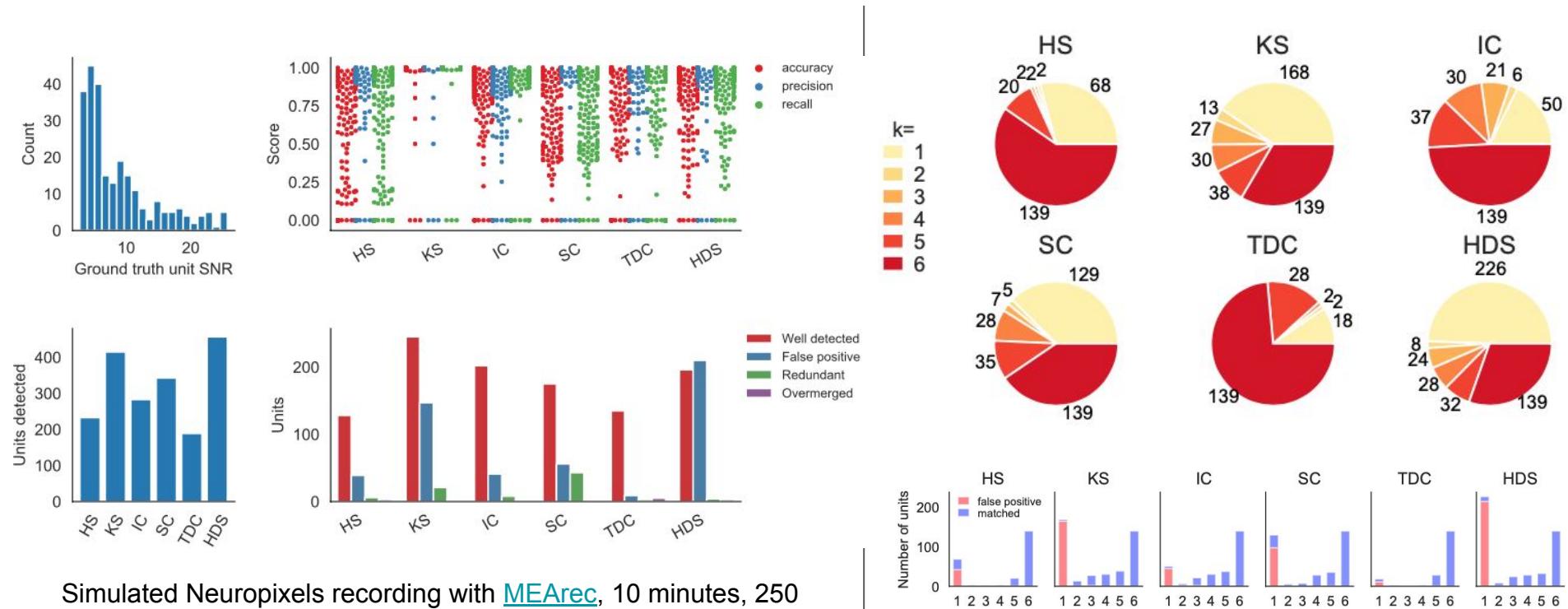
# Ground truth data help to explore strength and weakness of different sorter



**Agreement matrix**

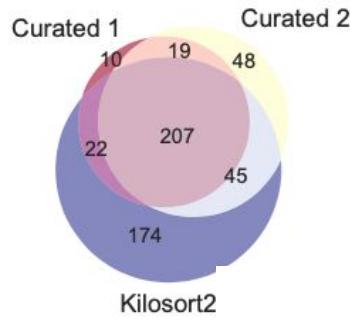


# Ground truth simulated data shows same trend Ensemble sorting identifies true positive units

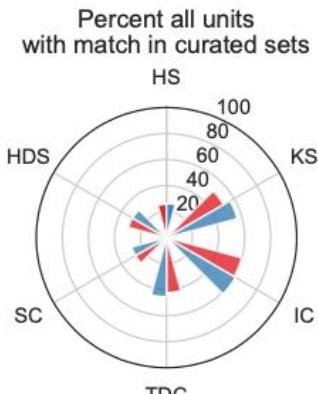


# Comparison with hand curated data support ensemble sorting strategy

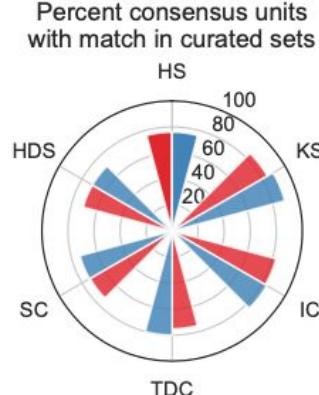
A



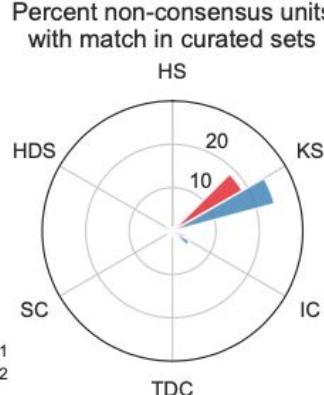
B



C



D



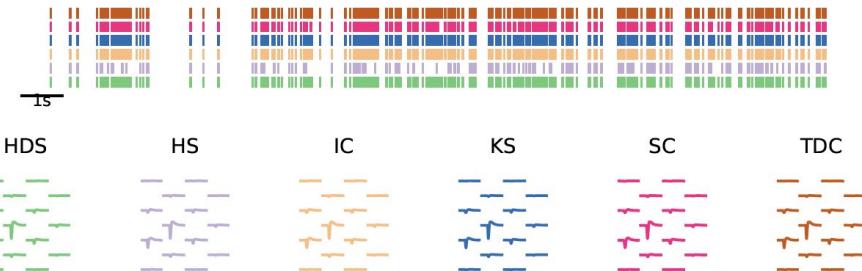
- *Consensus units* show very high agreement with hand-curated units
- Ensemble spike sorting could be an automatic alternative to manual curation

# Other features of SpikeInterface

## Quality metrics

Metric	Description
Signal-to-noise ratio	The signal-to-noise ratio computed on unit templates.
Firing rate	The average firing rate over a time period.
Presence ratio	The fraction of a time period in which spikes are present.
Amplitude Cutoff	An estimate of the miss rate based on an amplitude histogram.
Maximum drift	The maximum change in spike position (computed as the center of mass of the energy of the first principal component score) throughout a recording.
Cumulative drift	The cumulative change in spike position throughout a recording.
ISI violations	The rate of inter-spike-interval (ISI) refractory period violations.
Isolation Distance	Radius of the smallest ellipsoid that contains <i>all</i> the spikes from a cluster and an equal number of spikes from other clusters (centered on the specified cluster).
L-ratio	Assuming that the distribution of spike distances from a cluster center is multivariate normal, L-ratio is the average value of the tail distribution for non-member spikes of that cluster.
D-Prime	The classification accuracy between two units based on linear discriminant analysis (LDA)
Nearest-neighbors	A non-parametric estimate of unit contamination using nearest-neighbor classification.
Silhouette score	The ratio between cohesiveness of a cluster (distance between member spikes) and its separation from other clusters (distance to non-member spikes).

## Visualization Widgets

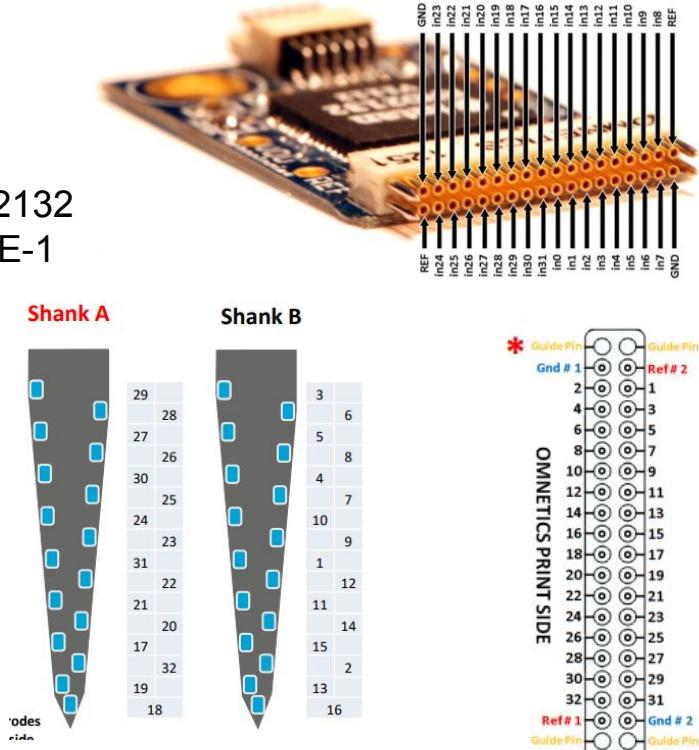


## Recording manipulation

- Select channels/time intervals
- Concatenate recordings

# Other features of SpikeInterface: probe geometry and channel mapping with *ProbeInterface*

Intan RHD2132  
ASSY-116-E-1



# SpikeForest is a twin project aimed to benchmark existing spike sorters against ground truth

SpikeForest

Project totals: 1.3 TB of recordings, 34,773 ground truth units; 411 compute hours Analysis updated: Mar 23, 2020, 10:04 AM

Heatmap Recordings Algorithms Metrics Archive About



<https://spikeforest.flatironinstitute.org/>

[Magland et al. 2020]



- **Achilleas Koutsou**, @G-Node
- **Alan Liddell**, Vidrio Technologies
- **Alessio Buccino**, ETH
- **Alexander Morley**, MRC BNDU (University of Oxford)
- **Ben Dichter**, CatalystNeuro
- **Cody Baker**
- **Cole Hurwitz**, University of Edinburgh
- **Fernando J. Chaire**, University of Buenos Aires
- **Garcia Samuel**, CNRS, Centre de recherche en neuroscience de Lyon
- **James Jun**, Facebook, Agios-CTRL
- **Jasper Wouters**
- **Jeremy Magland**
- **Jose Guzman**, Austrian Academy of Sciences - OEAW
- **Josh Siegle**, Allen Institute for Brain Science
- **Luiz Tauffer**, @kth
- **Manish Mohapatra**
- **Martino Sorbaro**, Neuroinformatics, UZH & SynSense.ai
- **Matthias H. Hennig**, University of Edinburgh
- **Mikkel Elle Lepperød**
- **NMI Biomedical Micro and Nano Engineering**
- **Pierre Yger**, Institut de la Vision
- **Roger Hurwitz**
- **Roland Diggelmann**, ETH Zurich
- **Shawn Guo**, Computer Laboratory, University of Cambridge
- **TRRuikes**
- **Yaroslav Halchenko**, Dartmouth College, @Debian, @DataLad, @PyMVPA
- **Michael Scudder**



# Thank you!!!



## Have fun spike sorting :)

- Achilleas Koutsou, @G-Node
- Alan Liddell, Vidrio Technologies
- Alessio Buccino, ETH
- Alexander Morley, MRC BNDU (University of Oxford)
- Ben Dichter, CatalystNeuro
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