Multiplexing neurons and multiple overlapping cell assemblies active during motor behavior

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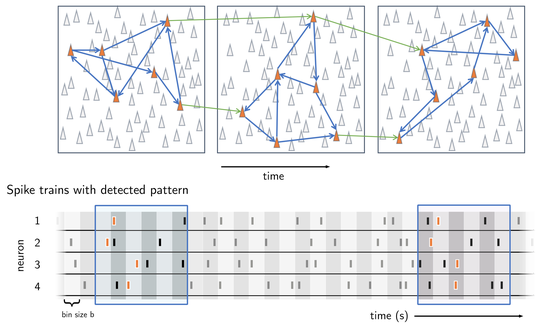
Background

The Hebbian hypothesis [1, 2, 3] assumes that **assemblies** of co-active neurons act as information processing units. We hypothesize that assembly activity is expressed by precise **spatio-temporal patterns** (STPs) of spikes repeating identically over time, and with precise (5ms) temporal delays between the spikes.



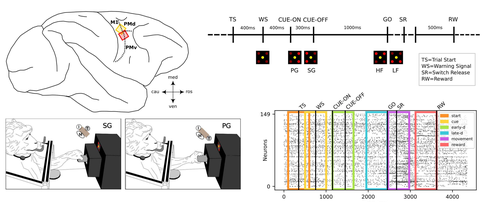
Hebbian assemblies and spatio-temporal patterns. Top. Schematic representation of cell assemblies. Each triangle represents a neuron and each arrow a synapse. In each subfigure, one cell assembly is active (orange triangles). The synapses (blue arrows) propagate the spikes with different synaptic delays. As time progresses, other synapses (green arrows) activate other assemblies on the same space of neurons. Figure adapted from [5]. Bottom. Sketch of parallel spike trains with detected pattern, in orange. Figure adapted from [11].

Materials and methods

Spike train analysis method

We developed the **SPADE method** [4, 7, 11] to detect significant STPs in massively parallel spike trains. SPADE involves three steps:

1. it identifies repeating STPs using Frequent Itemset Mining [11];
2. it evaluates the detected patterns for significance through surrogate generation;
3. it removes the false positive patterns that are a by-product of true patterns and the background



Representation of the experiment. Top right, electrode site for the two monkeys. Bottom right, experimental protocol. Left, trial protocol (top) and data segmentation (bottom).

Experimental data [8, 10]

- Pre-/motor cortex of two **macaque monkeys**
- Activity recorded by a **10x10 Utah multielectrode array**
- Monkeys engaged in a **reach-to-grasp task**
- From 56 to 167 neurons recorded in parallel
- Hypersynchronous artefacts are removed

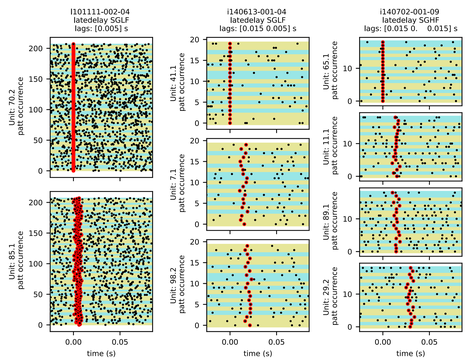
Task

- Reach an object and grasp it with side grip (SG) or precision grip (PG)
- Pull the object using high force (HF) or low force (LF) and hold it in a fixed position for 500ms
- Visual cues inform the animal about the grip and force

Spatio-temporal patterns in experimental data

Results of the analysis:

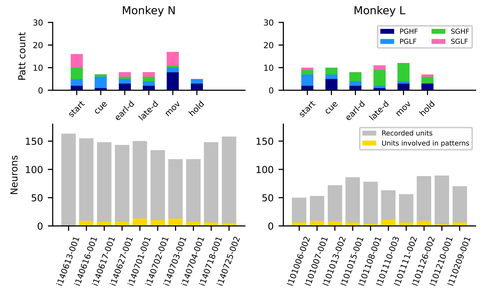
- Pattern statistics across sessions:
  - Significant patterns are **detected across all phases of the behavior** (trial types and trial epochs)
  - Significant patterns are of **different sizes** (2 to 6 neurons involved)
  - Significant patterns exhibit different **occurrence frequencies** (10 to 280) depending on the size
  - Larger patterns occur less frequently than smaller patterns
  - Patterns have different temporal lags between spikes, but do not show a particular oscillatory tendency
- Pattern characteristics within sessions:
  - Patterns are **spatially distributed across the whole electrode array** for both monkeys, differently distributed for the two grip types (PG/SG)
  - The pattern spatial distribution is uniform across the whole array (not shown)
  - Fraction of neurons involved in patterns similar between monkeys, despite having a different amount of recorded neurons per monkey and session
  - Patterns are **different in composition depending on the behavioral context**
  - Patterns are **temporally precise (+/- 5ms)**
  - Frequency of pattern repetition does not change within session



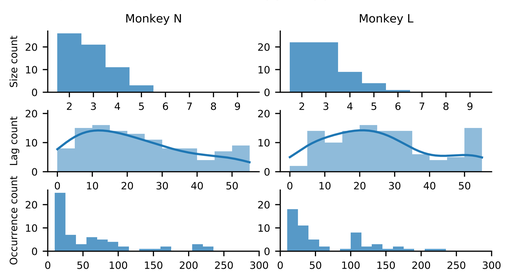
Patterns aligned on the first spike. Pattern occurrences are aligned to the first spike of the pattern. Spikes belonging to the pattern are marked in red. Different colored bands represent the pattern occurrence within one trial. Trials are ordered along the y-axis. The left panel represents a pattern of two neurons detected in session i101111-002-04 (monkey L) in the epoch late-delay, with trial type SGLF. The central panel depicts one pattern of three spikes, detected in session i140613-001-04 (monkey N) in the epoch late-delay, trial type SGLF. The right panel represents a pattern of four spikes detected in session i140702-001-09 (monkey N) in the epoch late-delay, trial type SGHF.

Spatio-temporal pattern analysis:

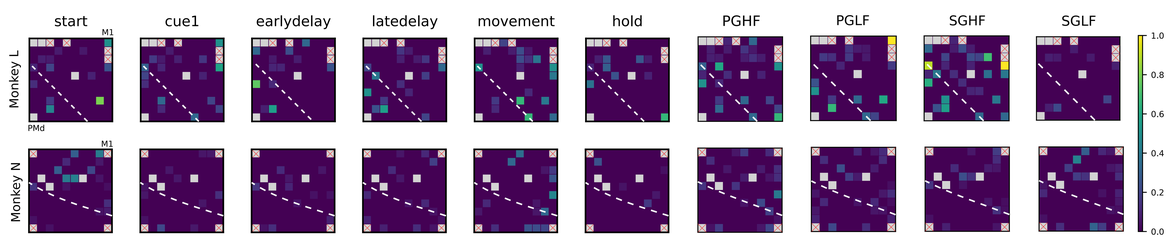
- 20 analyzed sessions (10 per monkey)
- $\sim$ 30 trials per trial type per session
- Trials segmented into 6 task-related epochs (500ms long)
- 24 behavioral contexts (6 epochs $\times$ 4 trial types)
- Temporal resolution of the analysis = 5 ms
- Maximal STP duration = 60 ms



Patterns detected in experimental data across behavioral contexts. Top. Histogram of pattern count in all behavioral epochs. Bottom. Percentage involvement of units participating in patterns over the total number of units analyzed per session. Bar height represents the percentage, number on top of bar represents the total number of units per session, after spike sorting, data cleaning and preprocessing. Sessions named with code i14[...] and i10[...] indicate monkeys N and L, respectively.



Pattern statistics. Distribution of pattern size (top), pattern lag (middle), and pattern occurrences (bottom).



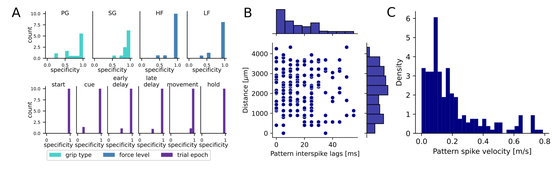
Count of number of patterns for each electrode of the Utah Array, for each monkey (rows), trial type, and trial epoch (columns). For each session, we count the number of times neurons are detected on each electrode participated in an STP, and then sum over all sessions, separately per monkey and trial type. The count is normalized by the number of SUAs detected in each electrode, over all sessions. The lighter the color, the more patterns have members detected on the electrode. Red crosses indicate the four unconnected electrodes; gray squares indicate the electrodes in which no SUA was detected. Dotted lines indicate the estimated anatomical separation between PMd/PMv and M1.

Conclusions

- Analysis of 20 sessions of experimental data from macaque pre-/motor cortex with the SPADE method
- Numerous significant STPs occur in relation to behavior
- STPs occur in all phases of the behavior, and, within a single session, are specific to a behavioral condition $\rightarrow$ different assemblies are activated in each behavioral context
- A few individual neurons appear as hubs, as they are involved in several patterns
- Pattern neurons are not located within a small region, but distributed across the entire cortical surface covered by the Utah array

Specificity of STPs to behavior and STP velocity

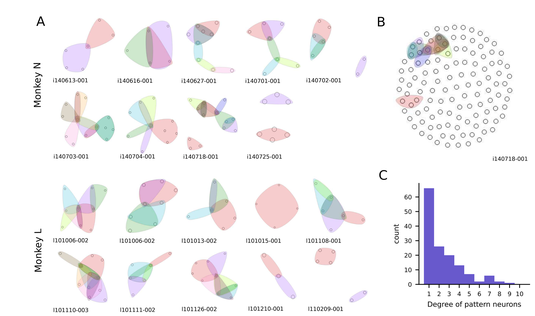
- Patterns are **highly specific** to the behavioral context, for every context
- There is no relation between temporal lag between pattern spikes and distance between units on the Utah array
- Pattern spike velocity in agreement with biological observations



Pattern specificity and velocity. Panel A. Histograms of STP specificity to behavioral context. The colors represent the pattern specificity at each instance of the three behavioral contexts: grip type (PG vs SG; light blue), force level (HF vs LF; blue), epoch (violet) across all data sets and monkeys. The specificity index does not take into account pattern lags. Panel B. Scatter plot of temporal lags between subsequent neurons in a STP against their distance. Distributions are projected on the x and y axes. Panel C. STP spike velocity calculated as a ratio between the aforementioned values.

Overlap of STPs in neuronal membership

- STPs can be represented as a hypergraph, where nodes represent neurons and sets represent membership to a STP
- In many sessions, there are **neurons which are involved in several patterns across different behavioral contexts (hubs)**
- However, most of the neurons are involved in only one STP
- Different STPs almost never overlap completely in the neuronal membership



Pattern overlaps in neuronal membership. Panel A. Hypergraph representation of neurons involved in patterns within one experimental session. Each dot represents a unit. Each color groups together units involved in a single STP. Panel B. Hypergraph representation including all neurons not involved in any STP within the session. Panel C. Degree distribution of STP members calculated across all sessions. The degree of a unit is calculated as the number of STPs it participates in. Hypergraph visualization originally designed by [15].

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