

# Detection of cell assemblies with extracellular multi-electrode recordings

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# Outline

## Background

- Cell assemblies
- Spatiotemporal spike patterns in monkey motor cortex
- Cell-assembly structure and detectability

## Model

- Model of the measurement setup
- Minimal assembly model
- Pattern statistics

## Fitting procedure and results

## Summary

## Ressources

- Pattern statistics
- Assembly detectability

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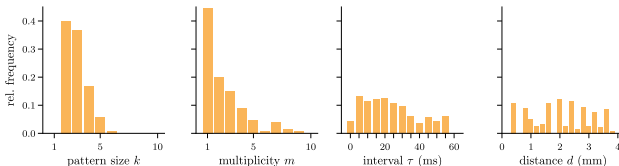
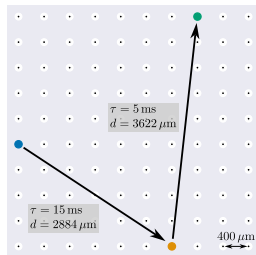
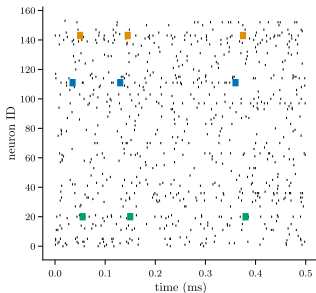
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  - neurons that reliably and recurrently generate spatio-temporal spike patterns with high temporal precision, such as neurons in a synfire chain (Abeles 1991) or in a braid network (polychronous patterns) (Bienenstock 1995; Izhikevich 2006)



# Spatiotemporal spike patterns in monkey motor cortex

- single-unit spiking activity from reach-to-grasp experiment (Riehle et al. 2013)
- extracellular recordings with  $10 \times 10$  Utah array,  $400\mu\text{m}$  spacing
- identification of spatio-temporal patterns with millisecond precision by SPADE analysis

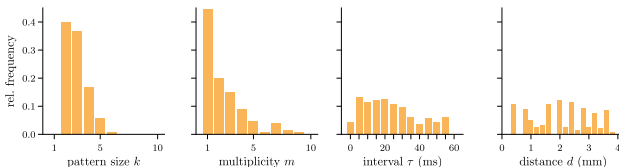
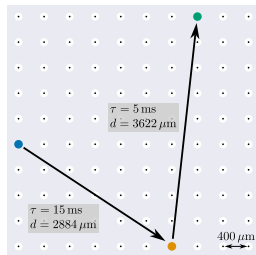
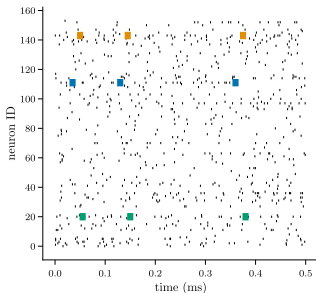
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Neuronal substrate generating such patterns? Spatiotemporal structure of these assemblies?

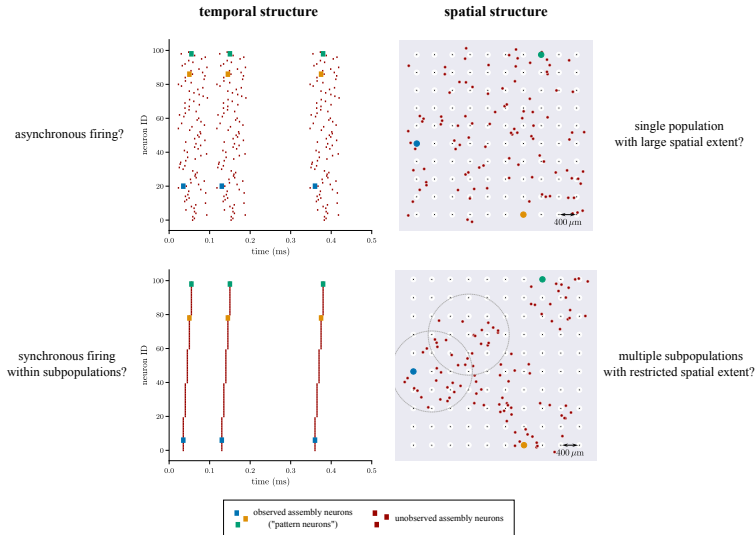
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## What does the rest of the iceberg look like?



# Questions

- Can we infer the cell-assembly structure (e.g., number of neurons, number of assemblies, spatial extent) from knowledge of
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  - the recording constraints, and
  - the statistics of observed patterns?
- given a certain recording configuration (e.g., type/number of/distance between electrodes):  
**How likely is it to observe cell assemblies with a specific structure?**  
(not discussed in this talk)

# Model

## Model of the measurement setup

- total number of electrodes  $K$
- total monitored volume  $V$  (volume containing potential cell assemblies), e.g., layer 2/3 below  $4 \times 4 \text{ mm}^2$  Utah array

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- example:  $K = 96$ ,  $V = 4 \times 4 \times 1.5 \text{ mm}^3$ ,  $U = 1.1$

$$q = \begin{cases} 0.0001 & \text{if } \rho = 35000 / \text{mm}^3 \\ 0.002 & \text{if } \rho = 2100 / \text{mm}^3 \end{cases}$$

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- no assumptions on network connectivity and dynamics
- assumptions:
  - probed volume  $V$  contains  $A$  cell assemblies
  - each cell assembly composed of  $M$  neurons
  - assembly neurons are uniformly and independently distributed across  $V$

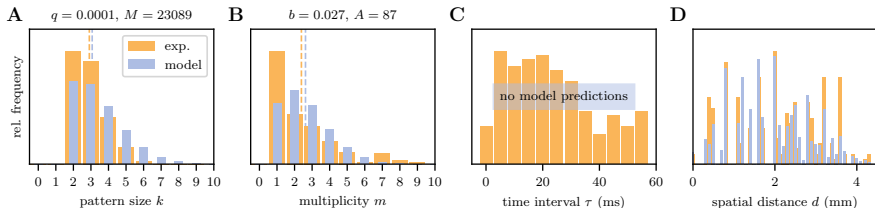


# Pattern statistics

- **pattern size  $k$** : probability of detecting  $k$  neurons in a given assembly

$$p(k; q, M) = \binom{M}{k} q^k (1 - q)^{M-k}$$

with neuron-detection probability  $q = KU/\rho V$  and assembly size  $M$



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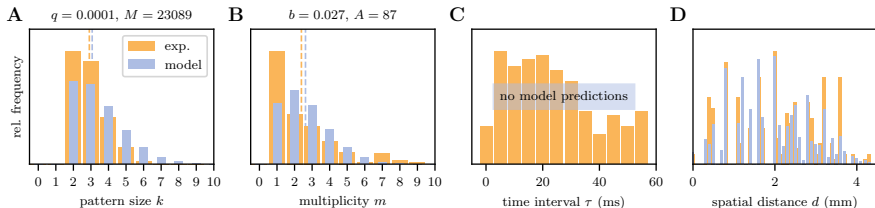
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- **membership multiplicity  $m$** : probability of some neuron participating in  $m$  different assemblies

$$u(m; b, A) = \binom{A}{m} b^m (1 - b)^{A-m}$$

with assembly-participation probability  $b = M/\rho V$  and total number of assemblies  $A$



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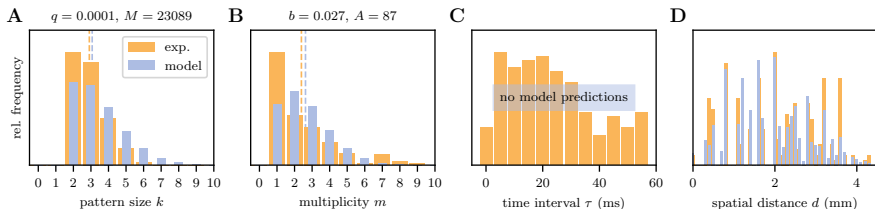
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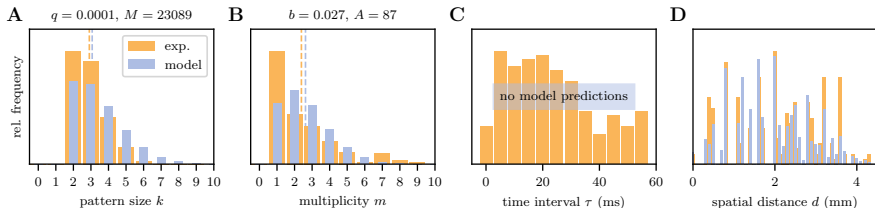
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- **pattern spike interval  $\tau$** : probability of observing time interval  $\tau$  between consecutive pattern spikes
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- **pattern neuron distance  $d$** : probability of Euclidean distance  $d$  between two pattern neurons
  - = frequency of inter-electrode distance  $d$  (independent + uniform neuron positions within observed volume)



## Fitting procedure and results

- fix  $q = KU/\rho V$  with  $K = 96$ ,  $U = 1.1$ ,  $V = 4 \times 4 \times 1.5 \text{ mm}^3$ ,  $\rho = 2100, \dots, 35000 \text{ mm}^{-3}$
- adjust model parameters  $M$ ,  $b = M/\rho V$  and  $A$  by maximizing sum of normalized model likelihoods, i.e., by minimizing cost function

$$E = -S_k^{-1} \sum_{i=1}^{S_k} \log [p(k_i; q, M)] - S_m^{-1} \sum_{j=1}^{S_m} \log [u(m_j; b, A)]$$

with model distributions  $p(\cdot)$  and  $u(\cdot)$ , empirical pattern sizes and multiplicities  $k_i$  and  $m_j$ , and sample sizes  $S_k$  and  $S_m$

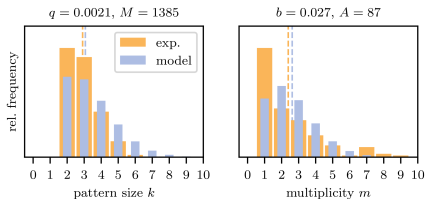
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$\rho = 2100 \text{ mm}^{-3}$ :



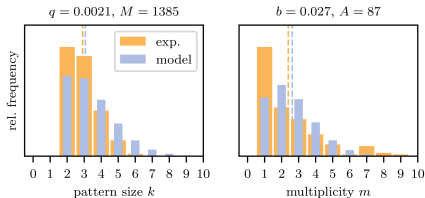
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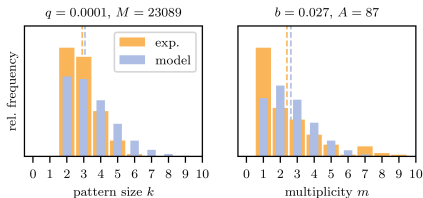
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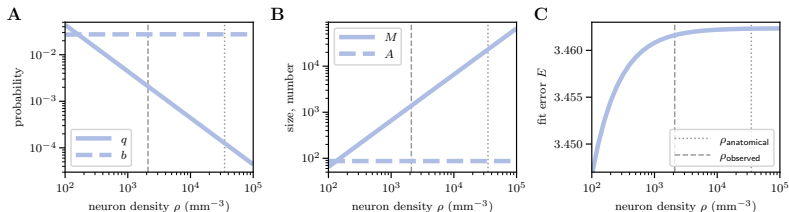
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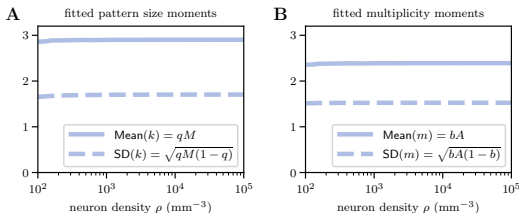
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- best-fit assembly sizes  $M$  proportional to  $\rho$ , with little effect on fit error (same for  $V$ )
- best-fit assembly participation probability  $b = 0.027$  and number of assemblies  $A = 87$  independent of  $\rho$

best-fit parameters and fit error:



best-fit moments:

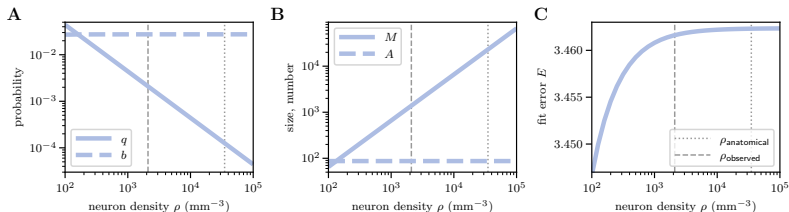




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best-fit parameters and fit error:



explanation: Poisson theorem

$$p(k; q, M) = \binom{M}{k} q^k (1 - q)^{M-k} \xrightarrow{q \rightarrow 0, Mq = \text{const.}} \frac{\lambda^k}{k!} e^{-\lambda} \quad \text{with} \quad \lambda = Mq$$

$$q = \frac{KU}{\rho V} \quad \leadsto \quad \lambda = Mq = \frac{MKU}{\rho V} \quad \leadsto \quad M = \frac{\rho V \lambda}{KU} \quad \leadsto \quad b = \frac{M}{\rho V} = \frac{\lambda}{KU}$$

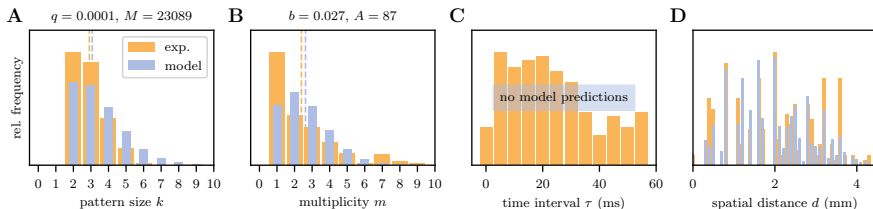
# Summary

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  - many ( $\sim 100$ ) and
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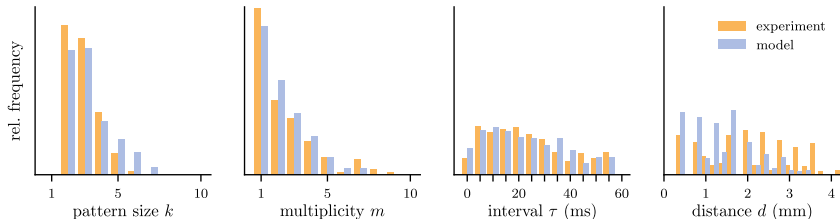
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- minimal assembly model and more complex synfire-chain model make similar predictions

## minimal assembly model:



## synfire-chain model:



# Outlook

- include minimal model of spike timing (asynchronous firing of assembly neurons) to predict pattern spike interval distributions
- quantitative comparison between minimal assembly model and synfire-chain model (use same metrics for fit performance)

# Resources

- **scientific tools:**

python, numpy, scipy, matplotlib

- **workflow tools:**

snakemake

- **project locations:**

[https://github.com/INM-6/simulate\\_patterns\\_from\\_synfire\\_chains](https://github.com/INM-6/simulate_patterns_from_synfire_chains)

[https://github.com/INM-6/synfire\\_manuscript](https://github.com/INM-6/synfire_manuscript)

- **data sources:**

pattern characteristics (pattern sizes, multiplicities, pattern spike intervals, pattern neuron distances)

[https://github.com/INM-6/simulate\\_patterns\\_from\\_synfire\\_chains/blob/master/minimal\\_assembly\\_model/py/experimental\\_results.npy](https://github.com/INM-6/simulate_patterns_from_synfire_chains/blob/master/minimal_assembly_model/py/experimental_results.npy)

obtained from reach-to-grasp data (Riehle et al. 2013)

data set: <https://doi.gin.g-node.org/10.12751/g-node.f83565>

metadata: [https://github.com/INM-6/DataGrasp\\_Metadata](https://github.com/INM-6/DataGrasp_Metadata)

- **computing:**

laptop

*Thanks*

# References I

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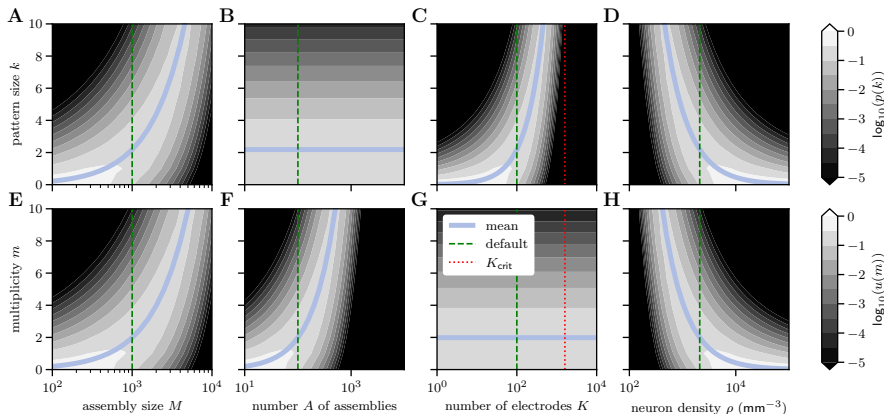
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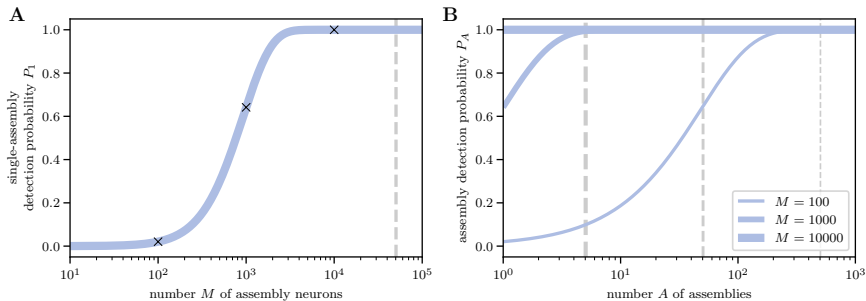
## Appendix

# Pattern statistics



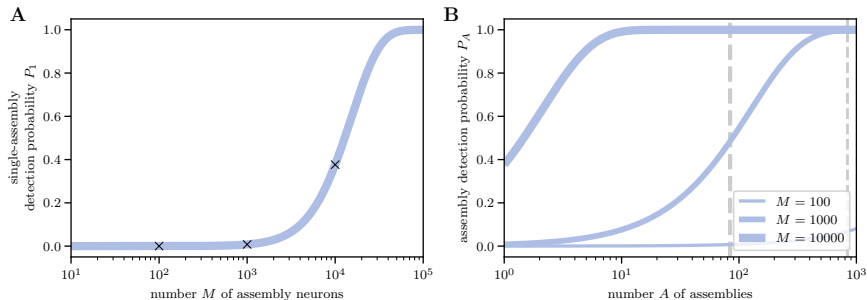
**Pattern statistics predicted by the simple assembly model.** Dependence of distributions  $p(k)$  and  $u(m)$  (contours) of pattern sizes  $k$  (A-D) and multiplicities  $m$  (E-H) on the assembly size  $M$  (A,E), the number  $A$  of assemblies (B,F), the number  $K$  of electrodes (C,G), and the density  $\rho$  of eligible neurons (D,H). Blue curves represent the mean of the respective distribution. Dashed green vertical lines depict default parameters (see below). Dotted red vertical lines in C and G show the maximum number  $K_{\text{crit}} = (L/2R)^2 = 1600$  of electrodes consistent with the assumption of non-overlapping sensitivity ranges for a Utah array with side length  $L = 4$  mm and electrode sensitivity radius  $R = 0.05$  mm. Default parameters:  $V = 24.0 \text{ mm}^3$ ,  $\rho = 2100 \text{ mm}^{-3}$ ,  $K = 100$ ,  $U = 1.1$ ,  $M = 1000$ ,  $A = 100$ .

# Assembly detectability



**Assembly detectability. A:** Dependence of the probability  $P_1$  of detecting a specific assembly (two or more neurons in this assembly) on the assembly size  $M$ . The dashed vertical gray line marks the point where the number  $M = \rho V$  of assembly neurons equals the total number of eligible neurons within the observed volume  $V$ . The crosses mark the assembly sizes  $M$  used in panel B. **B:** Dependence of the probability  $P_A$  of detecting one or more assemblies on the number  $A$  of assemblies for different assembly sizes  $M$  (see legend). The dashed vertical gray lines indicate where  $MA = \rho V$ . Latest at this point, assemblies start to overlap. Default parameters:  $V = 24.0 \text{ mm}^3$ ,  $\rho = 2100 \text{ mm}^{-3}$ ,  $K = 100$ ,  $U = 1.1$ ,  $M = 1000$ ,  $A = 100$ .

# Assembly detectability



**Assembly detectability. A:** Dependence of the probability  $P_1$  of detecting a specific assembly (two or more neurons in this assembly) on the assembly size  $M$ . The dashed vertical gray line marks the point where the number  $M = \rho V$  of assembly neurons equals the total number of eligible neurons within the observed volume  $V$ . The crosses mark the assembly sizes  $M$  used in panel B. **B:** Dependence of the probability  $P_A$  of detecting one or more assemblies on the number  $A$  of assemblies for different assembly sizes  $M$  (see legend). The dashed vertical gray lines indicate where  $MA = \rho V$ . Latest at this point, assemblies start to overlap. Default parameters:  $V = 24.0 \text{ mm}^3$ ,  $\rho = 35000 \text{ mm}^{-3}$ ,  $K = 100$ ,  $U = 1.1$ ,  $M = 1000$ ,  $A = 100$ .