Detection of cell assemblies with extracellular multi-electrode recordings

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JÜLICH Forschungszentrum

Outline

Cell assemblies

- term “cell assembly” coined by Hebb (1949): “…network of neurons that is being activated repeatedly during a certain mental process, and in this way, the excitatory synaptic connections among its members are being strengthened…” (Abeles 2011)

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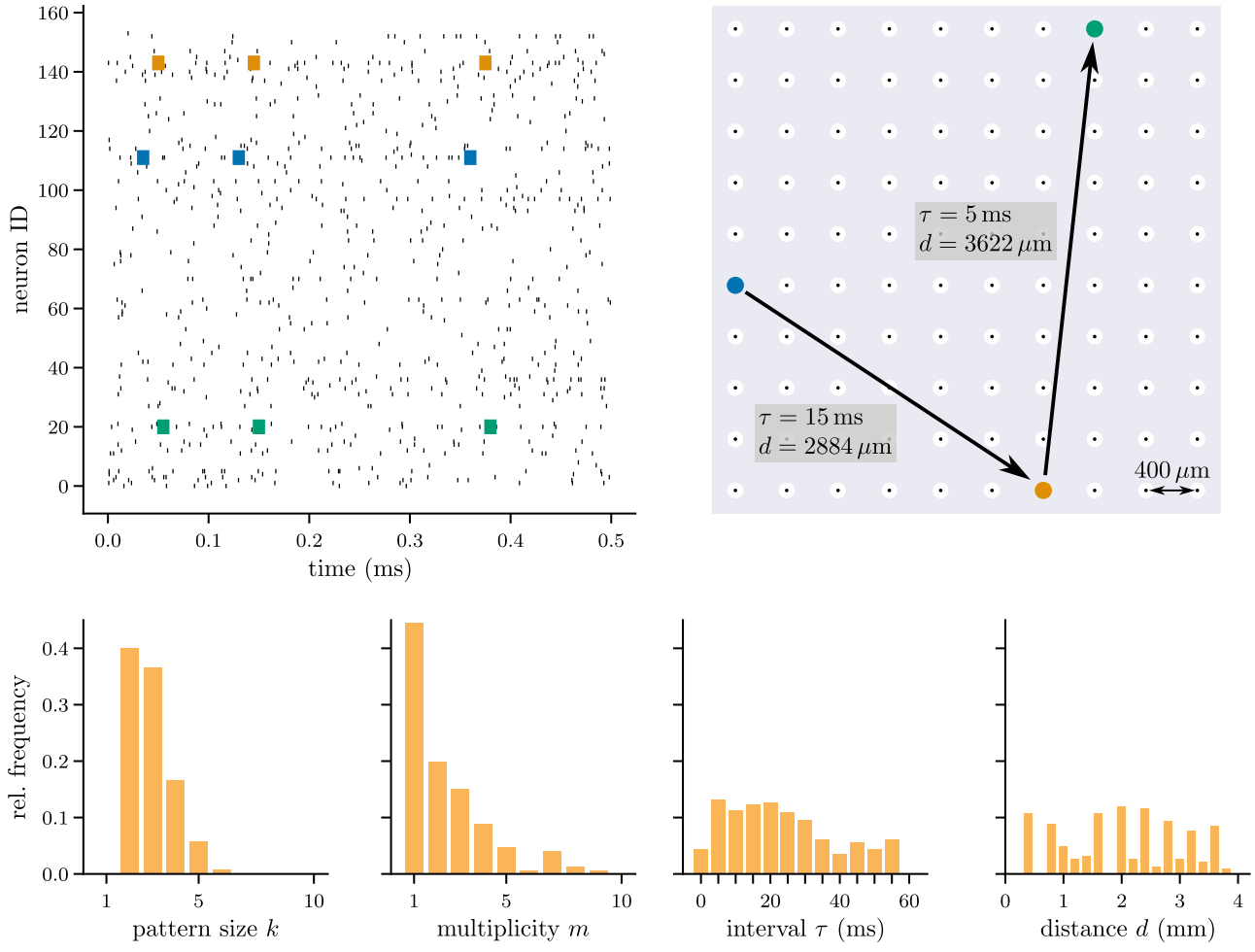
  - neurons that reliably and recurrently generate spatio-temporal spike patterns with high temporal precision, such as neurons in a synfire chain (Abeles 1991) or in a braid network (polychronous patterns) (Bienenstock 1995; Izhikevich 2006)

Spatiotemporal spike patterns in monkey motor cortex

- single-unit spiking activity from reach-to-grasp experiment (Riehle et al. 2013)
- extracellular recordings with 10×10 Utah array, 400μm spacing
- identification of spatio-temporal patterns with millisecond precision by SPADE analysis

(Torre et al. 2013; Stella et al. 2019)



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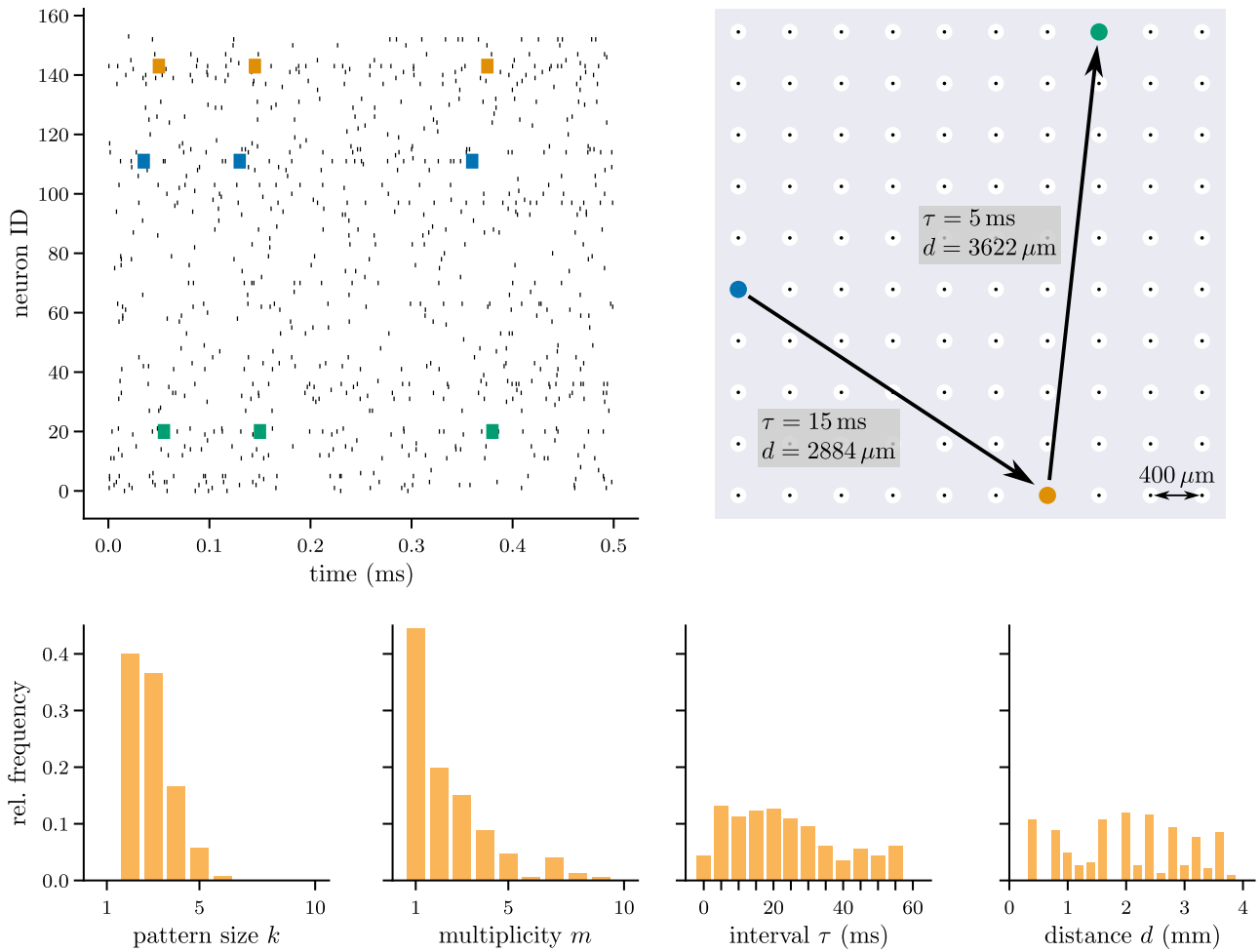

Neuronal substrate generating such patterns? Spatiotemporal structure of these assemblies?

Spatiotemporal cell-assembly structure

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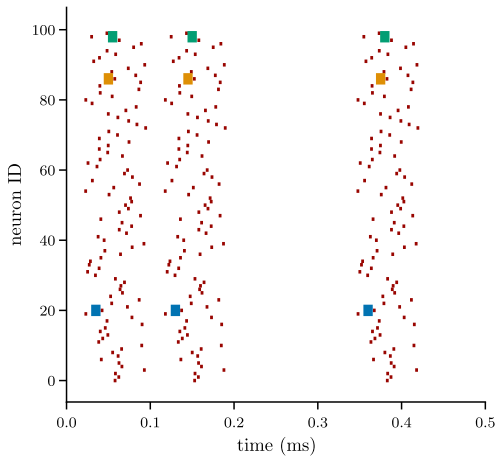
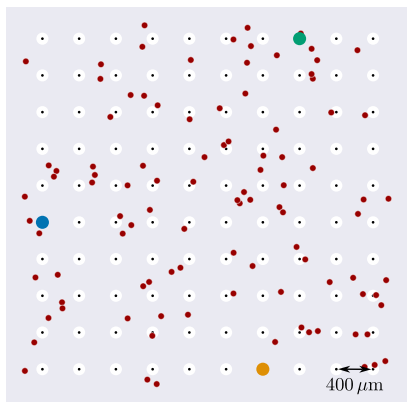
What does the rest of the iceberg look like?

temporal structure **spatial structure**

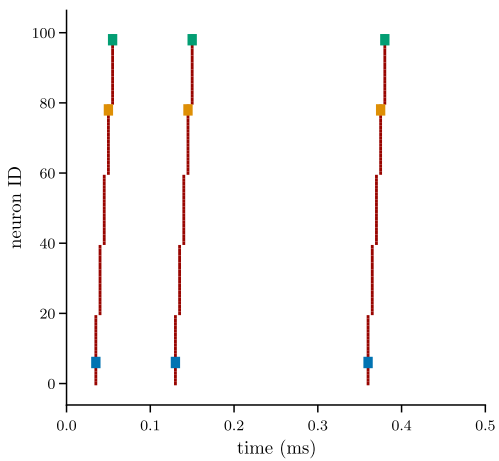
asynchronous firing?

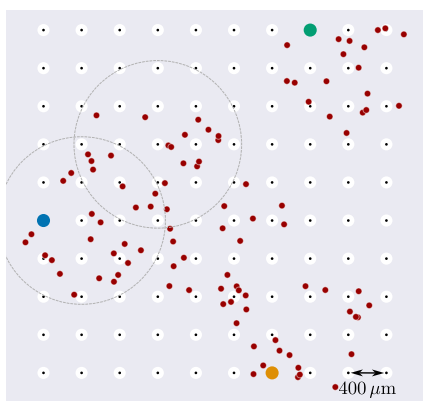




single population
with large spatial extent?

synchronous firing
within subpopulations?





multiple subpopulations
with restricted spatial extent?

Questions

- Can we infer the cell-assembly structure (e.g., number of neurons, number of assemblies, spatial extent) from knowledge of
  - the recording constraints, and
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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)

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

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

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Minimal assembly model

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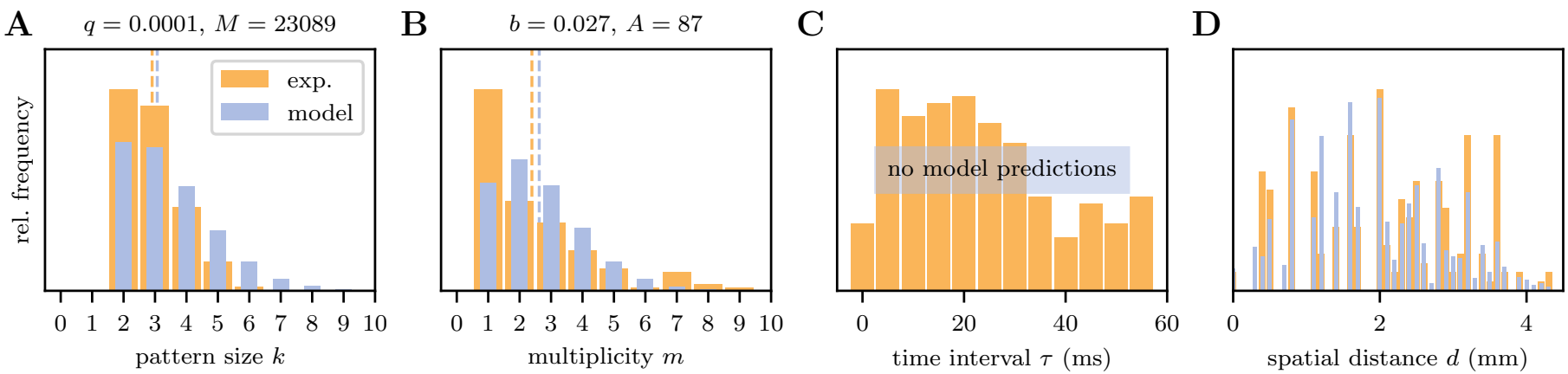
- no assumptions on network connectivity and dynamics
- assumptions:
  - probed volume V contains A cell assemblies
  - each cell assembly composed of M neurons
  - assembly neurons are uniformly and independently distributed across V

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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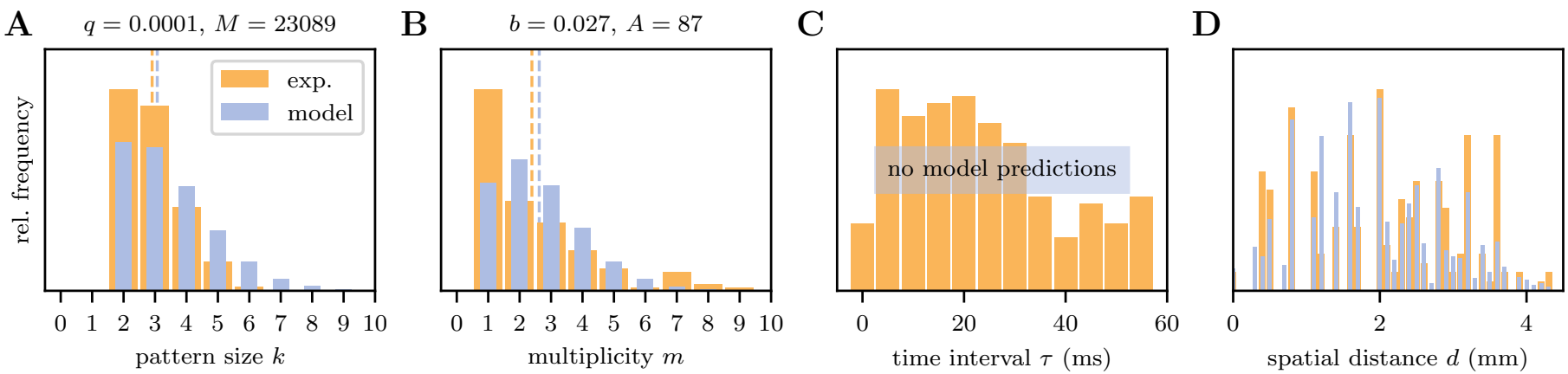

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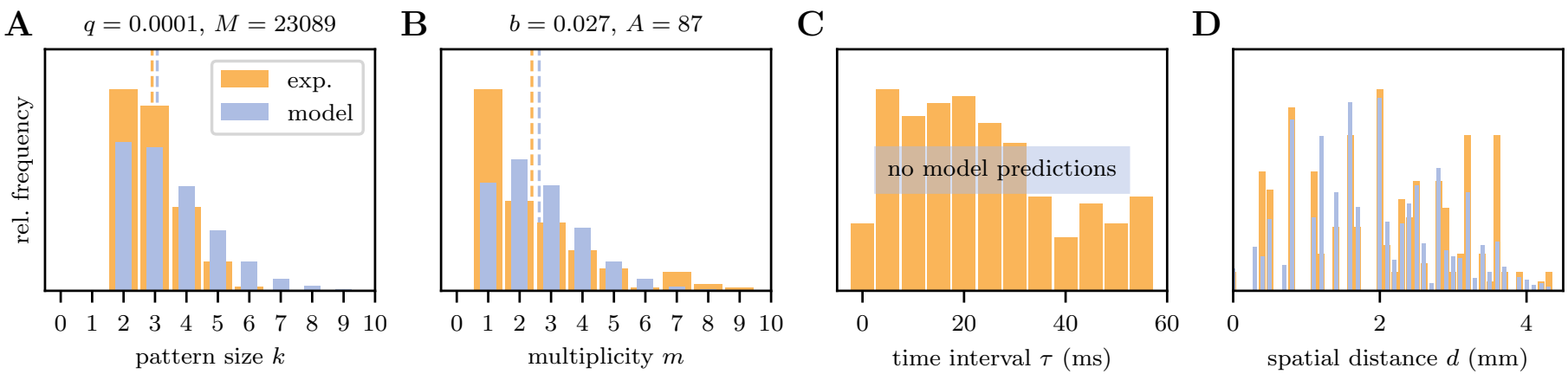
  - not predicted by the minimal model (ignorant of temporal structure of assembly activity)



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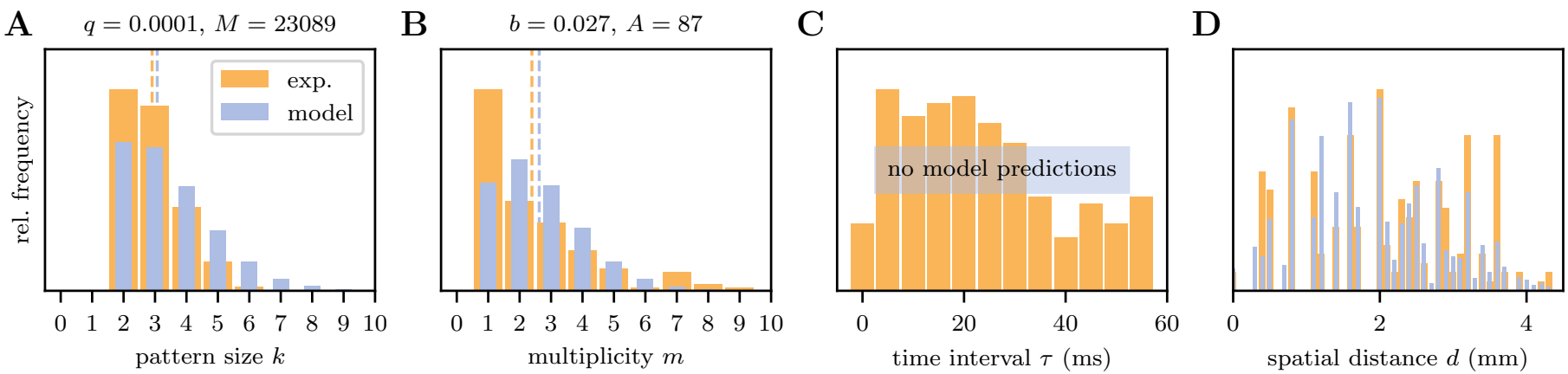
- **pattern neuron distance d**: probability of Euclidean distance d between two pattern neurons
  - = frequency of inter-electrode distance d (independent + uniform neuron positions within observed volume)



Fitting procedure and results

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

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

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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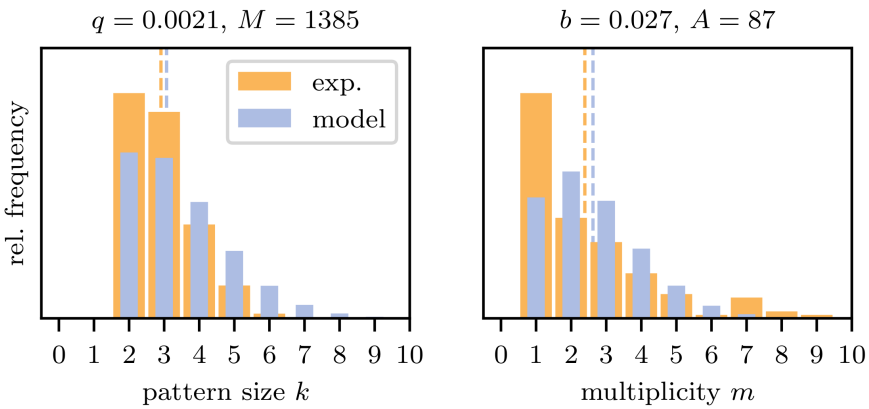

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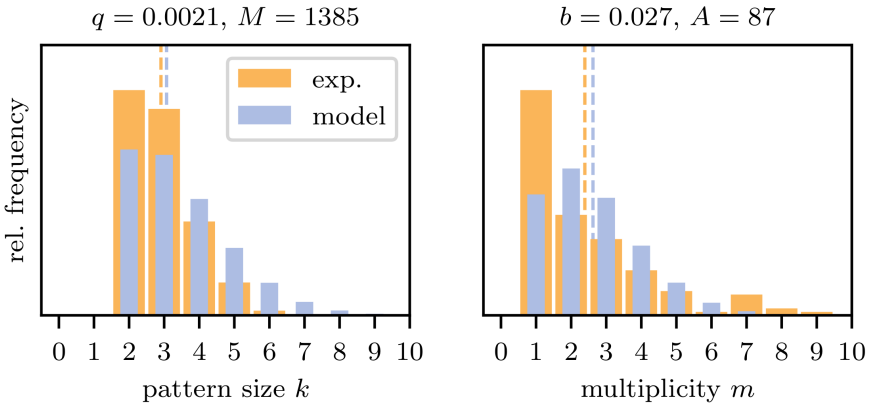

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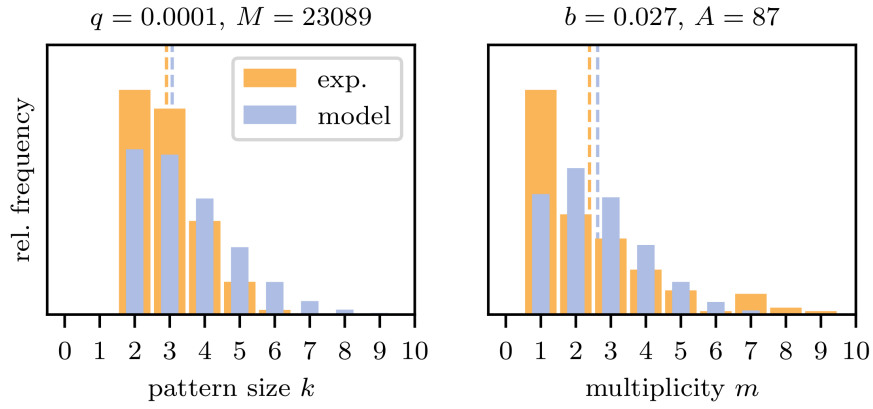
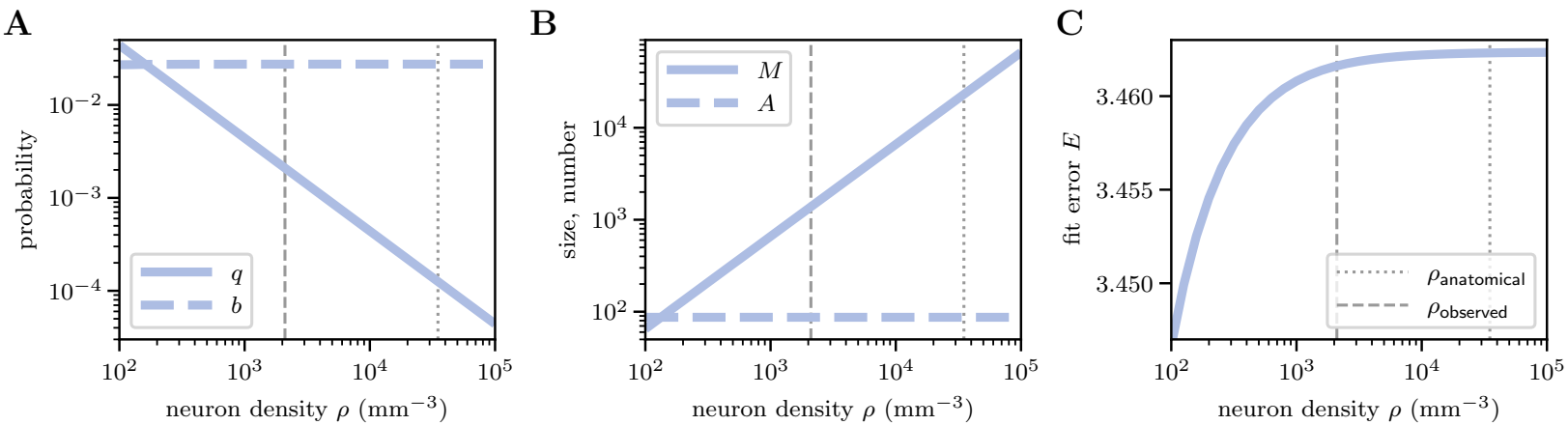


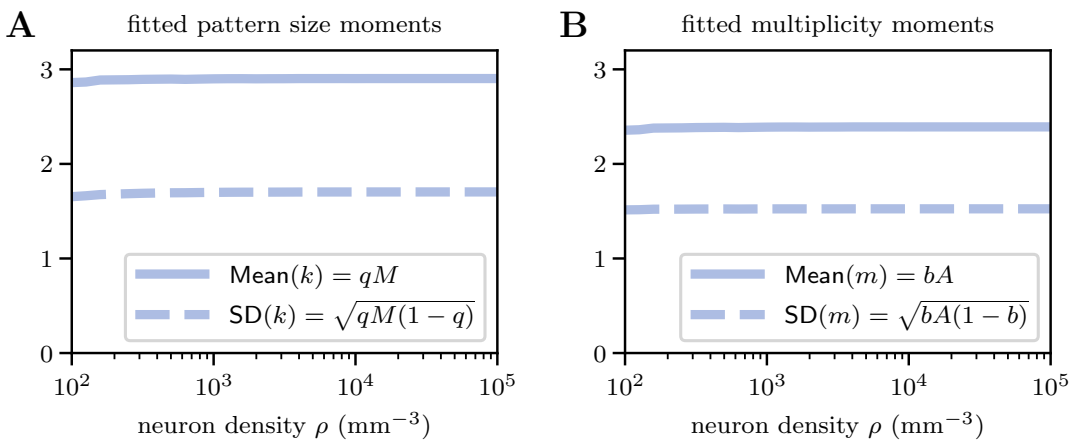
Fitting procedure and results

- best-fit assembly sizes M proportional to ρ, 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 ρ

best-fit parameters and fit error:



best-fit moments:



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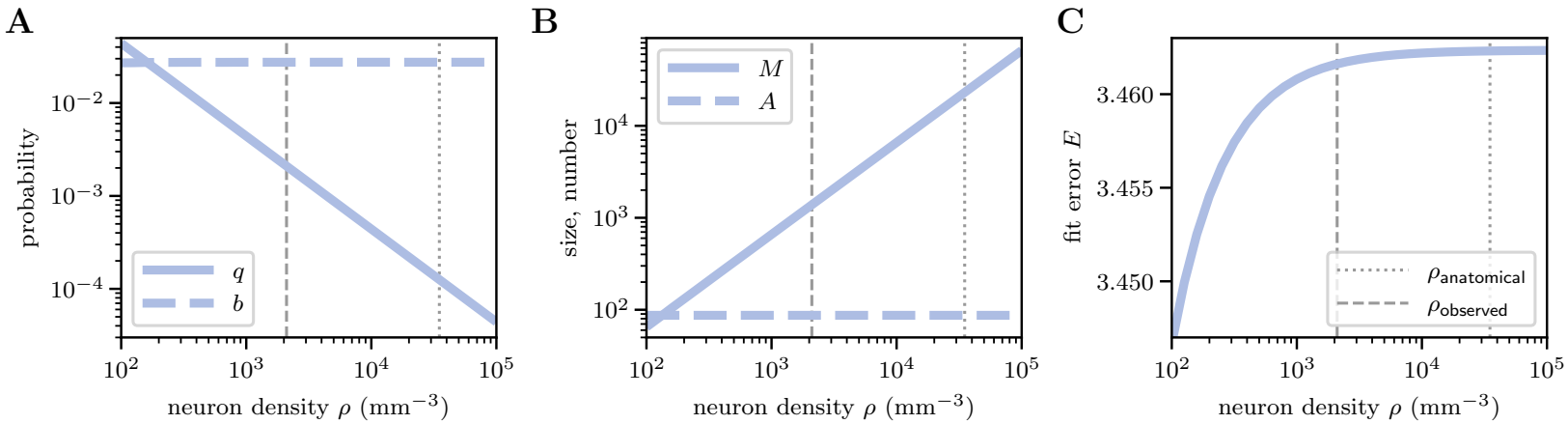

explanation: Poisson theorem

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

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

Summary

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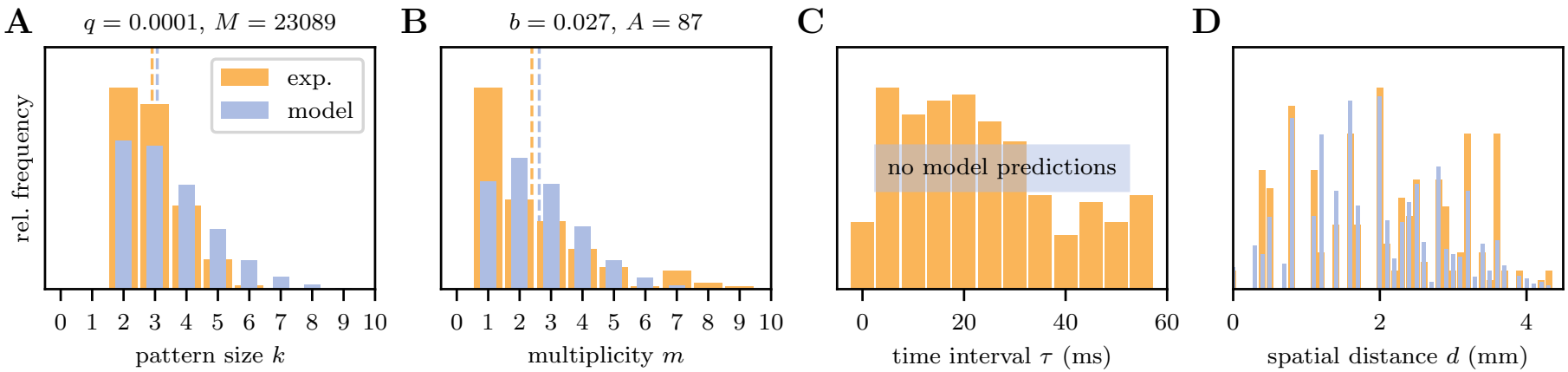
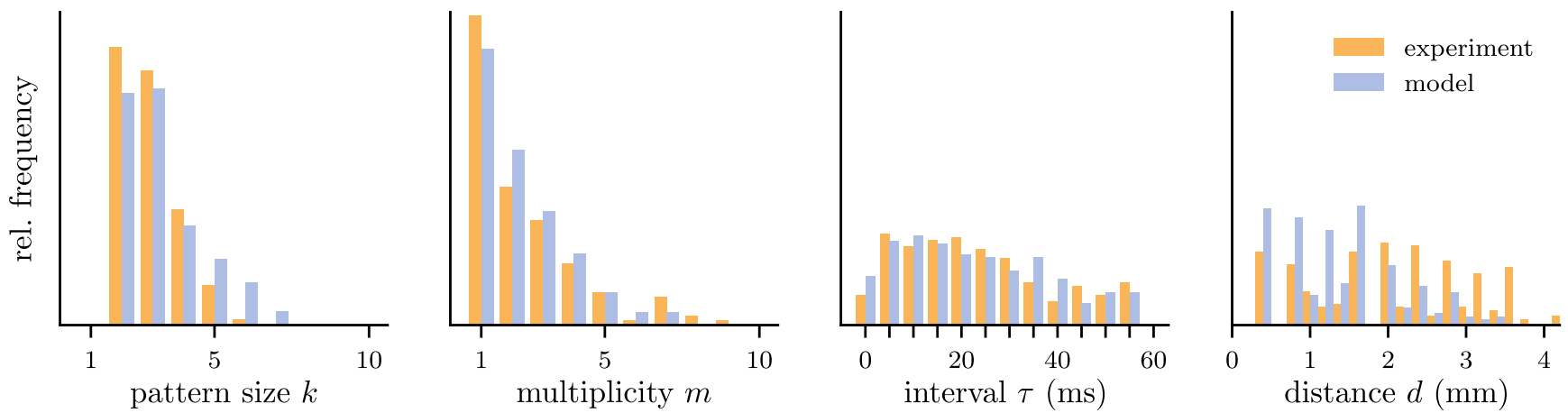
- minimal assembly model and more complex synfire-chain model make similar predictions

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)

Ressources

- **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/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`

  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`
- **computing:**
  laptop

Thanks

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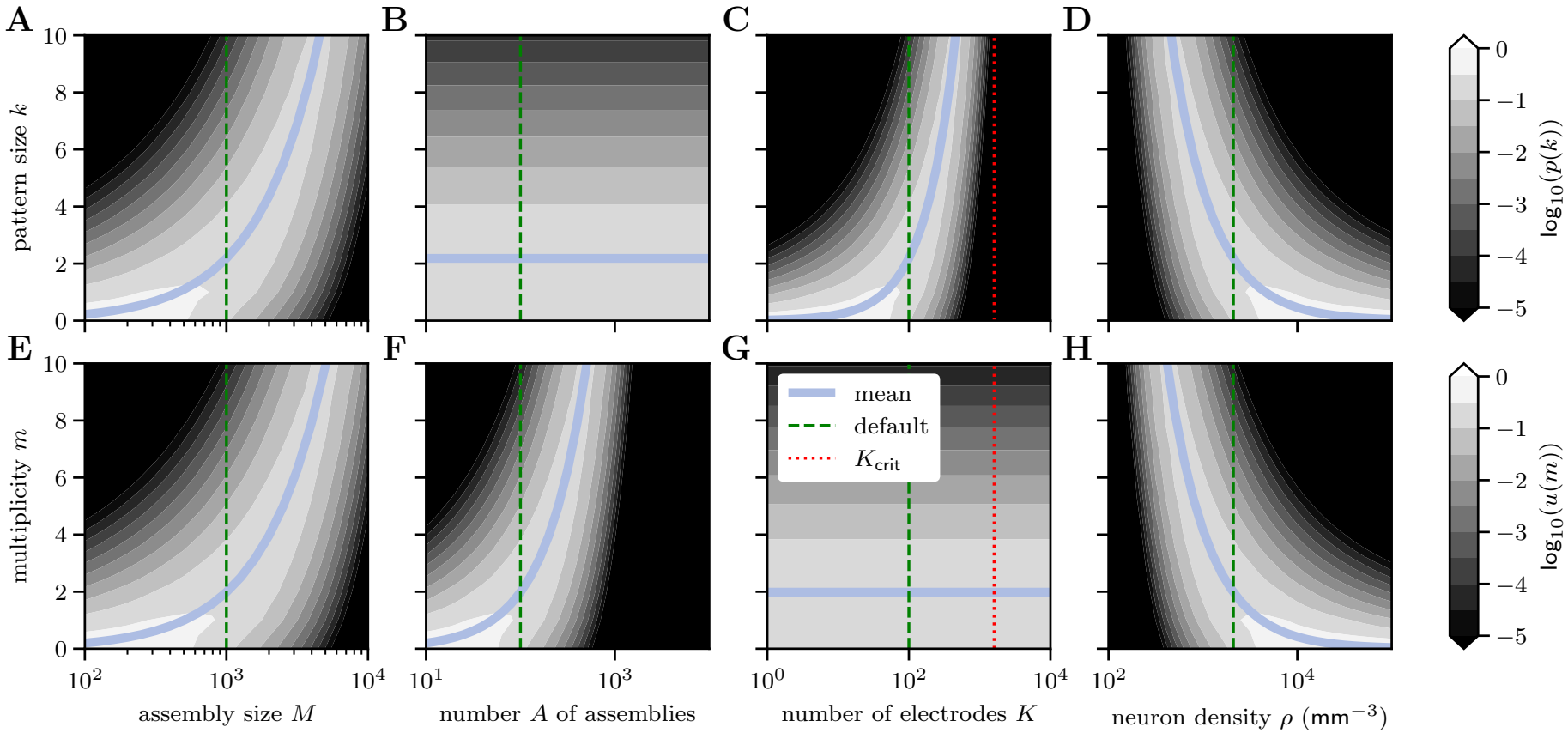
Appendix

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 ρ 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 sensivitiy ranges for a Utah array with side length $L = 4$ mm and electrode sensitivity radius $R = 0.05$ mm. Default parameters: $V = 24.0\,\text{mm}^3$, $\rho = 2100\,\text{mm}^{-3}$, $K = 100$, $U = 1.1$, $M = 1000$, $A = 100$.

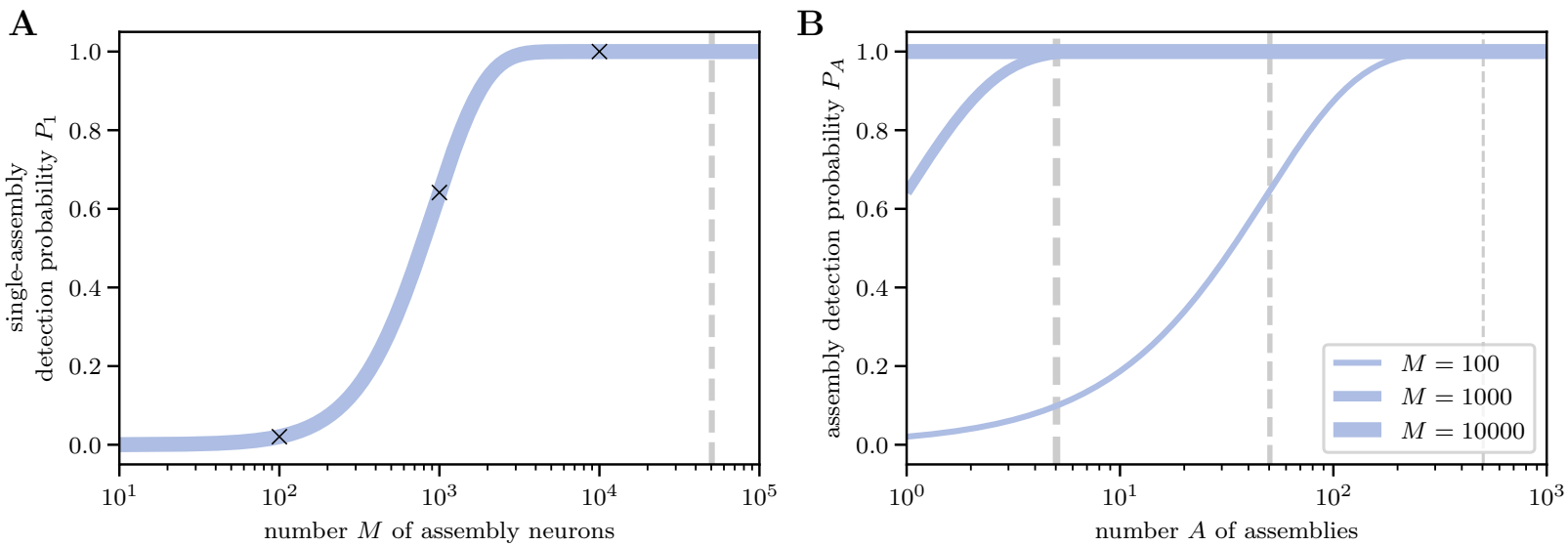
Assembly detectability

- definition: an assembly is **detected** if at least two of its neurons are detected
- single-assembly detection probability:

$$P_1(q, M) = 1 - p(k = 0) - p(k = 1) = 1 - (1 - q)^M - Mq(1 - q)^{M-1}.$$

- probability of observing at least one assembly within an ensemble of A assemblies:

$$P_A = 1 - (1 - P_1)^A.$$



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

- definition: an assembly is **detected** if at least two of its neurons are detected
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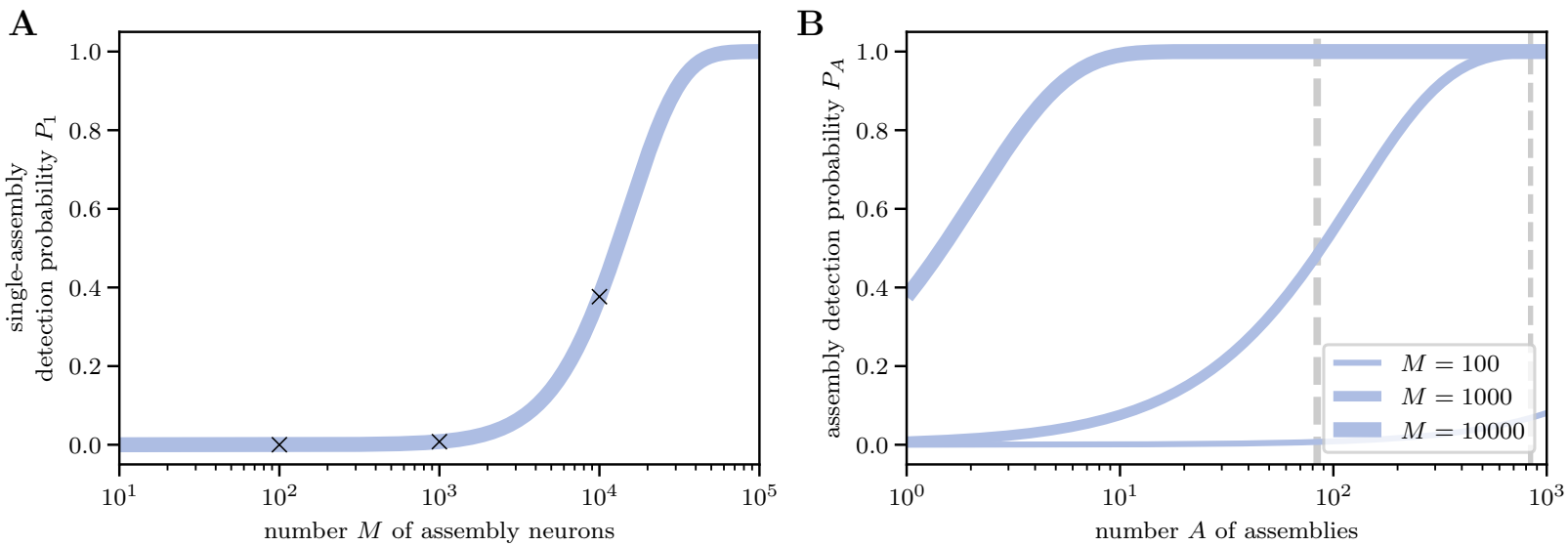
$$P_A = 1 - (1 - P_1)^A.$$



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: $V = 24.0\,\text{mm}^3$, $\rho = 35000\,\text{mm}^{-3}$, $K = 100$, $U = 1.1$, $M = 1000$, $A = 100$.