

# Toward Bayesian permutation inference for identifying neurons in *C. elegans*.

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## Summary

### Overarching goal

- State and infer Bayesian hierarchical models for the activity in C.elegans combining information (calcium traces) from several worms.
- This is possible as C.elegans nervous system is stereotypical, neurons and connectome don't change across individuals.

### Challenge

- If neural identity is known for each trace, one can apply standard bayesian methodology
- In practice, laborious human supervision is needed to match recorded traces to canonical neural identities (i.e. names)

### Our contribution

- We developed three methods for learning latent matchings. These can be used in variational inference (VI) to jointly estimate a dynamical system and the matching between traces and true neural identities.
- Potentially it may serve to automatize the matching procedure.
- From a statistical machine learning perspective, the relevance is that outperforms a simple MCMC sampler for permutations.

### Future work

- We used real connectome a position information. In the future we plan to use real traces.
- Two new levels of complexity: partially observed brain recordings, more sophisticated dynamical systems.

## Model

Simple linear autoregressive model for neural dynamics,

$$\tilde{Y}_t^{(j)} = (W \odot A) \tilde{Y}_{t-1}^{(j)} + \epsilon_t^{(j)}, \quad (1)$$

where  $W \in \mathbb{R}^{N \times N}$  is the weight matrix (gaussian prior);  $A \in \{0, 1\}^{N \times N}$  is the connectome;  $\epsilon_t^{(j)} \sim \mathcal{N}(0, \sigma^2 I)$ ; and  $\tilde{Y}_t^{(j)} \in \mathbb{R}^N$  is the measured neural activity at time  $t$  in worm  $j$ . The catch is that  $\tilde{Y}_t^{(j)}$  is assumed to be in canonical order; i.e. in the same order as the rows and columns of  $W$  and  $A$ . We actually observe,

$$Y_t^{(j)} = P^{(j)} \tilde{Y}_t^{(j)}. \quad (2)$$

We aim to perform posterior inference of  $p(\{W, P^{(j)}\} | A, \{Y^{(j)}\})$ .

The permutations are constrained by side information: we use neural position along the worm's body to constrain the possible neural identities for a given recorded neuron. We only allow an observed neuron to be mapped to a known identity if the observed location is within  $\eta$  of the expected location.

## Experimental setup

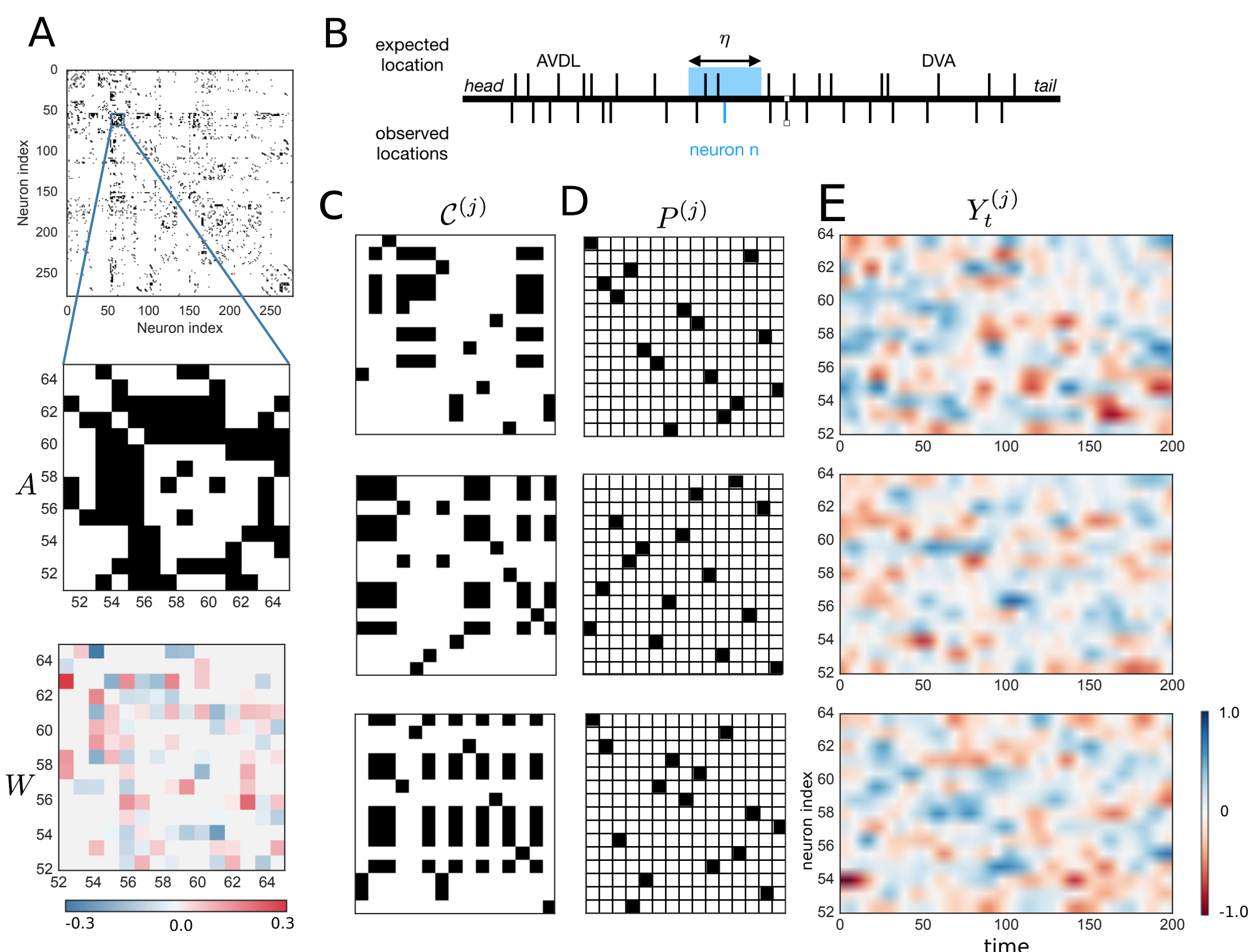


Figure:

**Hierarchical Bayesian framework.** **A** Adjacency matrix (connectome)  $A$  from [11]. We wish to infer the corresponding weight matrix  $W$ . **B** We know the typical locations of the neurons [12, 8]. We constrain possible assignments to neuron identities within  $\eta$  of the observed location. **C** These constraints are represented as a matrix  $\mathcal{C}^{(j)}$  for worm  $j$  specifying possible assignments of observed neurons to identities. **D** To infer the weights, we must first infer the permutation  $P^{(j)}$  that matching observed neurons to the set of known identities. **E** The observed data is a matrix  $Y^{(j)}$  with non-canonical order.

## Three reparameterizations for permutations

We extend to permutations the *Concrete* or *Gumbel softmax* relaxations [2, 9] in three different ways. In all relaxations we are concerned with  $\mathcal{B}_N$ , the Birkhoff polytope or set of doubly-stochastic matrices.

## Stick-Breaking and Rounding

On the stick-breaking we generalize the construction on the simplex [6] to  $\mathcal{B}_N$ . For the rounding construction, we start with a noise distribution and force it to be close to permutation matrices by rounding them towards the extreme-points of  $\mathcal{B}_N$ .

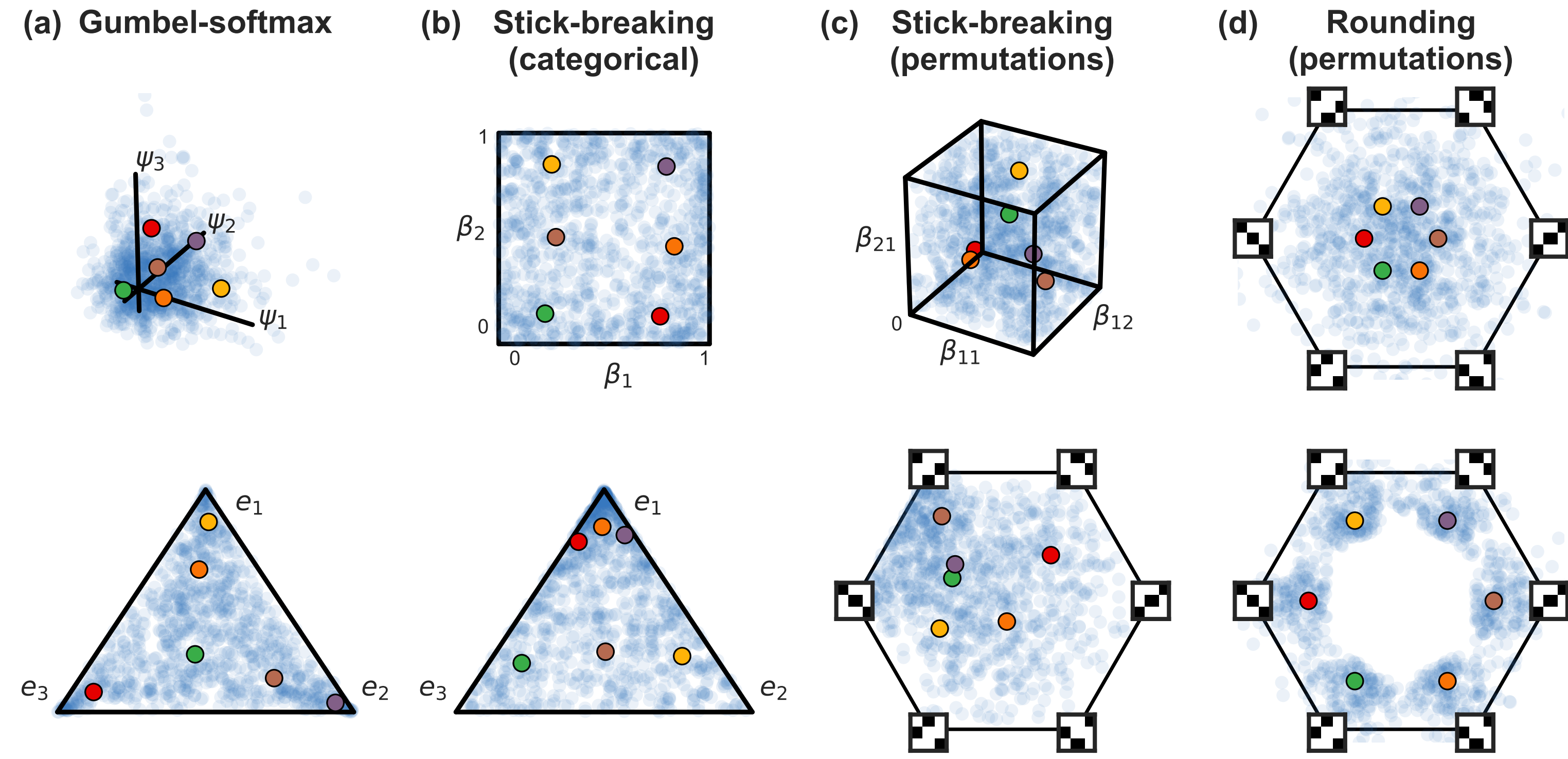


Figure: Rounding and Stick-breaking transformations of noise, and relation to constructions in the simplex

## Gumbel-Sinkhorn ( $\mathcal{G.S.}$ ) distribution

We use the *Sinkhorn operator*  $S(\cdot)$ , the successive row and column normalization of a matrix. This approximates the choice of a permutation  $M(X)$ ; i.e.  $M(X) = \lim_{\tau \rightarrow 0} S(X/\tau)$ . By adding Gumbel noise we conceive the Gumbel Matching distribution and its approximation, the *G.S. distribution*.

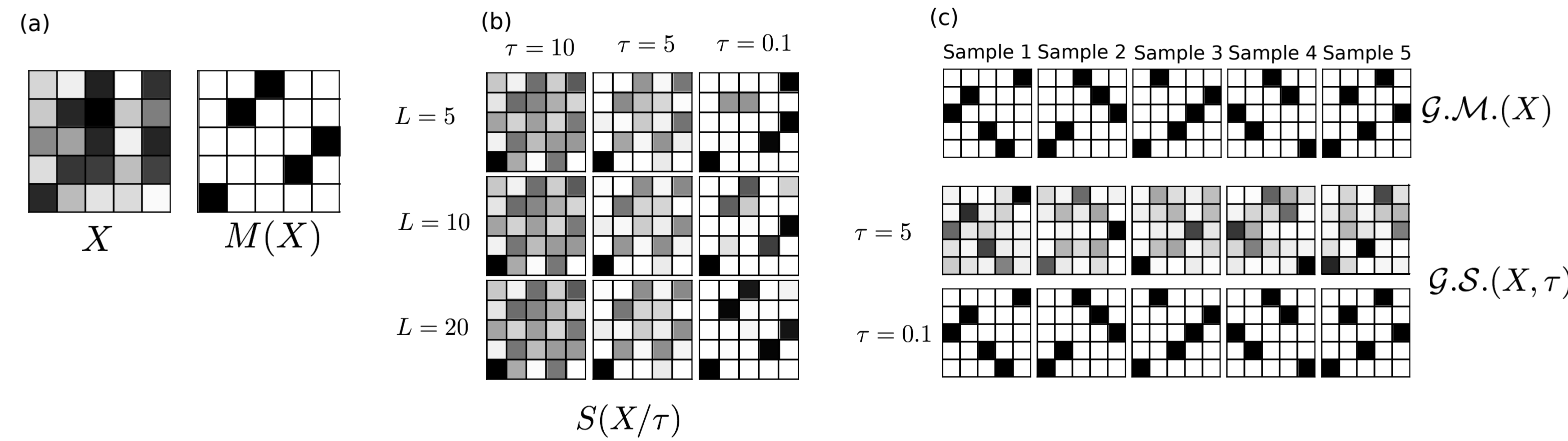


Figure: Matching and Sinkhorn operators, and the Gumbel-Matching and Gumbel-Sinkhorn distributions.

## Results

We compared against: (i) naïve variational inference, where we do not enforce the constraint that  $P^{(j)}$  be a permutation; (ii) MCMC, where we alternate between sampling from the conditionals of  $W$  (Gaussian) and  $P^{(j)}$ , from which one can sample by proposing local swaps, as described in [1], and (iii) MAP estimation.

Table: Accuracy in the C.elegans neural identification problem, for varying mean number of candidate neurons (10, 30, 45, 60) and number of worms.

	10		30		45		60	
	1 worm	4 worms	1 Worm	4 worms	1 worm	4 worms	1 worms	4 worms
NAIVE VI	.34	.32	.16	.16	.13	.12	.11	.12
MAP	.34	.32	.17	.17	.14	.13	.13	.12
MCMC	.34	.65	.18	.28	.14	.17	.13	.15
VI	<b>.79</b>	<b>.94</b>	<b>.4</b>	<b>.69</b>	<b>.25</b>	<b>.51</b>	<b>.21</b>	<b>.44</b>

Table: Accuracy in inferring true neural identity for different of proportion of known neurons and  $\eta$ .

	40.%		30.%		20.%		10.%	
	$\eta = 0.1$	$\eta = 0.2$	$\eta = 0.1$	$\eta = 0.2$	$\eta = 0.1$	$\eta = 0.2$	$\eta = 0.1$	$\eta = 0.2$
Naive VI	.43	.41	.33	.31	.23	.22	.12	.1
MAP	.42	.41	.33	.32	.23	.22	.12	.11
MCMC	.85	.80	.52	.46	.3	.26	.15	.12
VI	<b>.97</b>	<b>.96</b>	<b>.92</b>	<b>.84</b>	<b>.74</b>	<b>.58</b>	<b>.44</b>	<b>.23</b>

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