Machine Learning Methods for Neural Data Analysis

Lecture 8: Encoding models of retinal ganglion cells

Scott Linderman

STATS 220/320 (NBIO220, CS339N). Winter 2021.

Announcements

- Lab 3 Errata:
  - See course announcement r/e correcting test case for 1a.

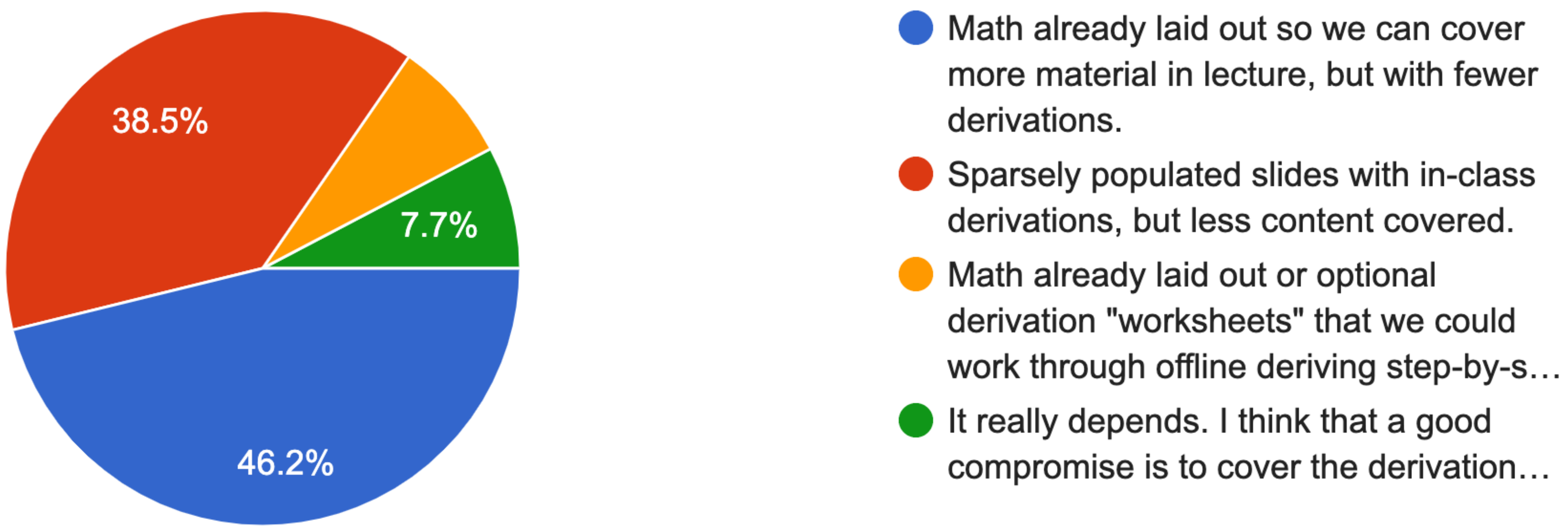
Poll results

- Lots of love for the labs (thank you!)
- Suggested improvements:
  - Longer Friday sessions
  - Official solutions
  - Bootcamps
  - More derivations in class
  - More math problems in the labs
  - More intuition / justification
  - Shorter labs. But also, more coding in the labs
  - Longer office hours

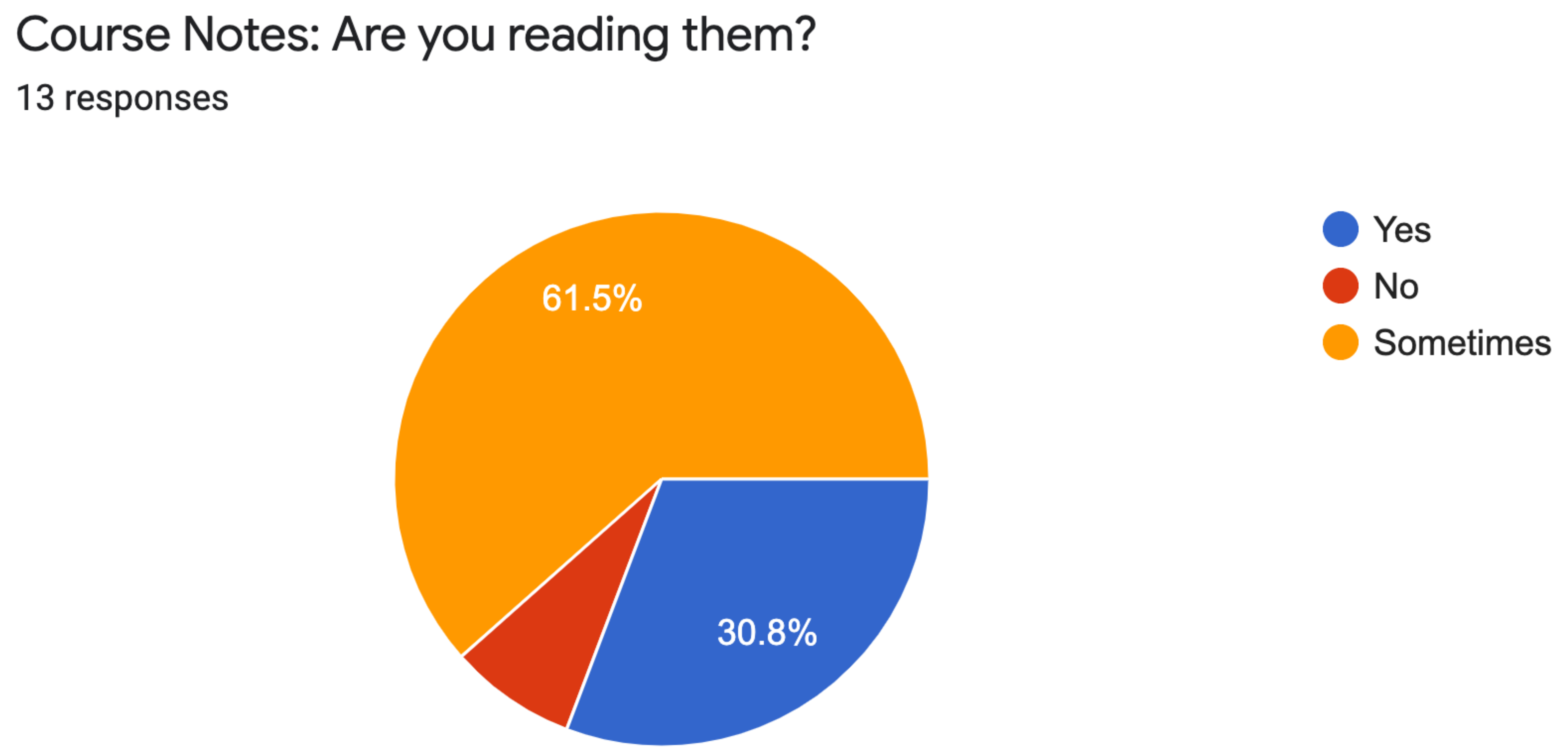
Poll results

Lectures: We've tried two styles, which do you prefer?

13 responses



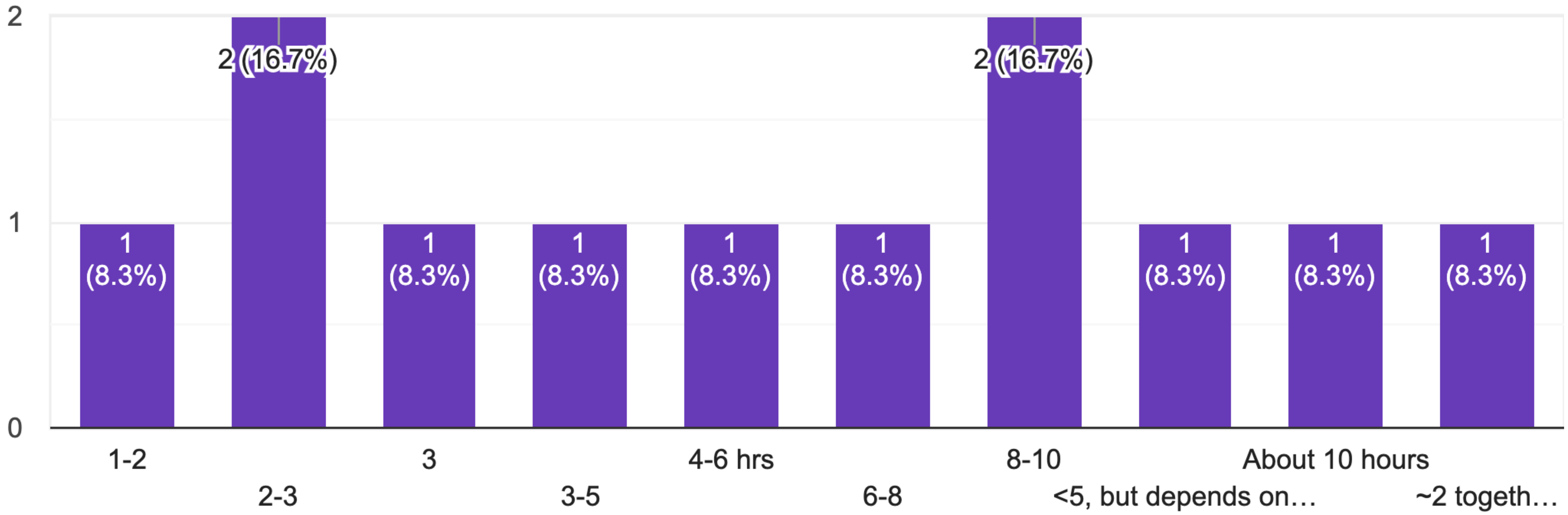
Poll results



Poll results

Labs: How many hours outside of class does it take to complete the lab?

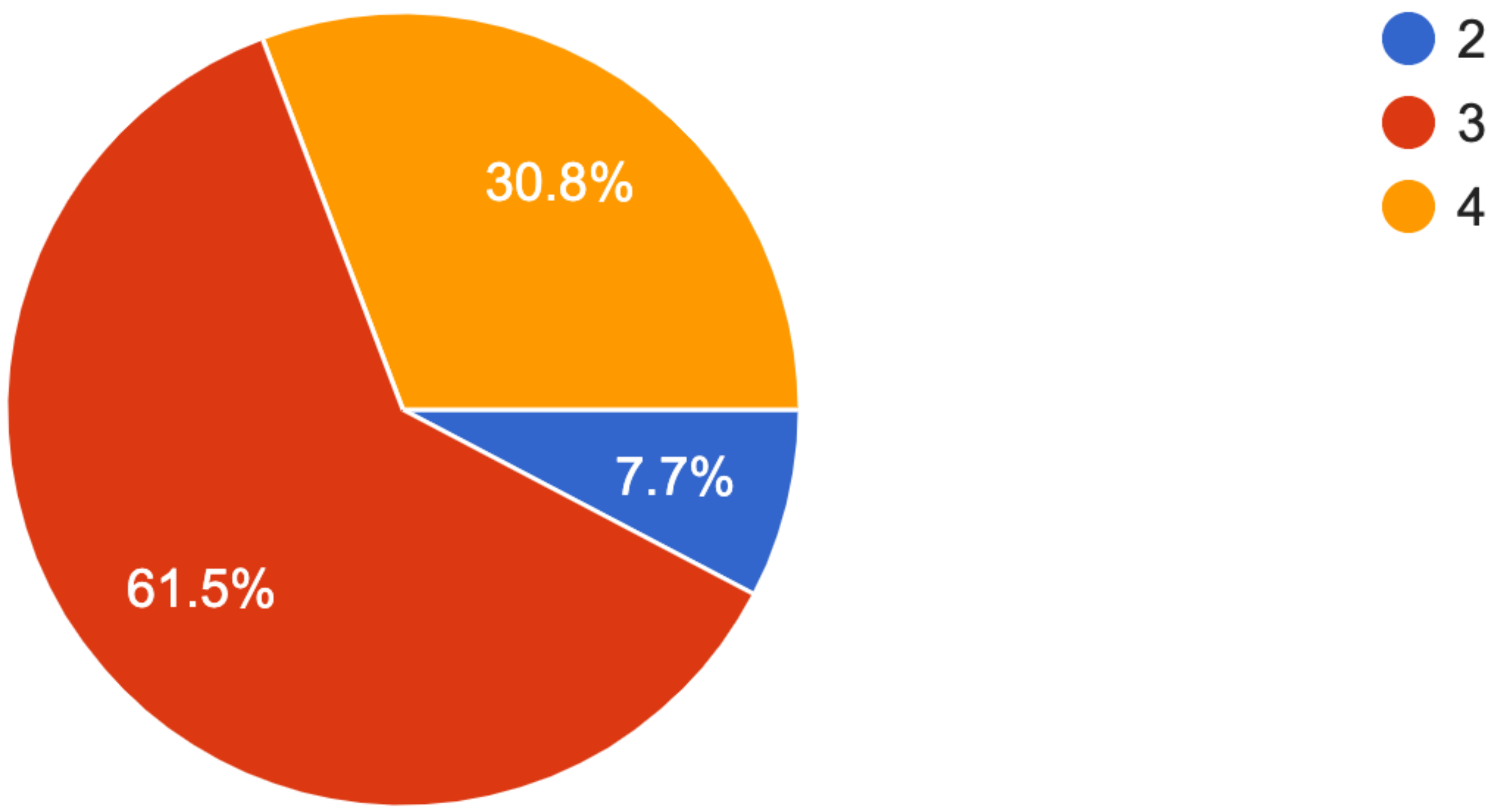
12 responses



Poll results

Labs: What size team would you prefer? We want each of you to get some time "at the helm."

13 responses



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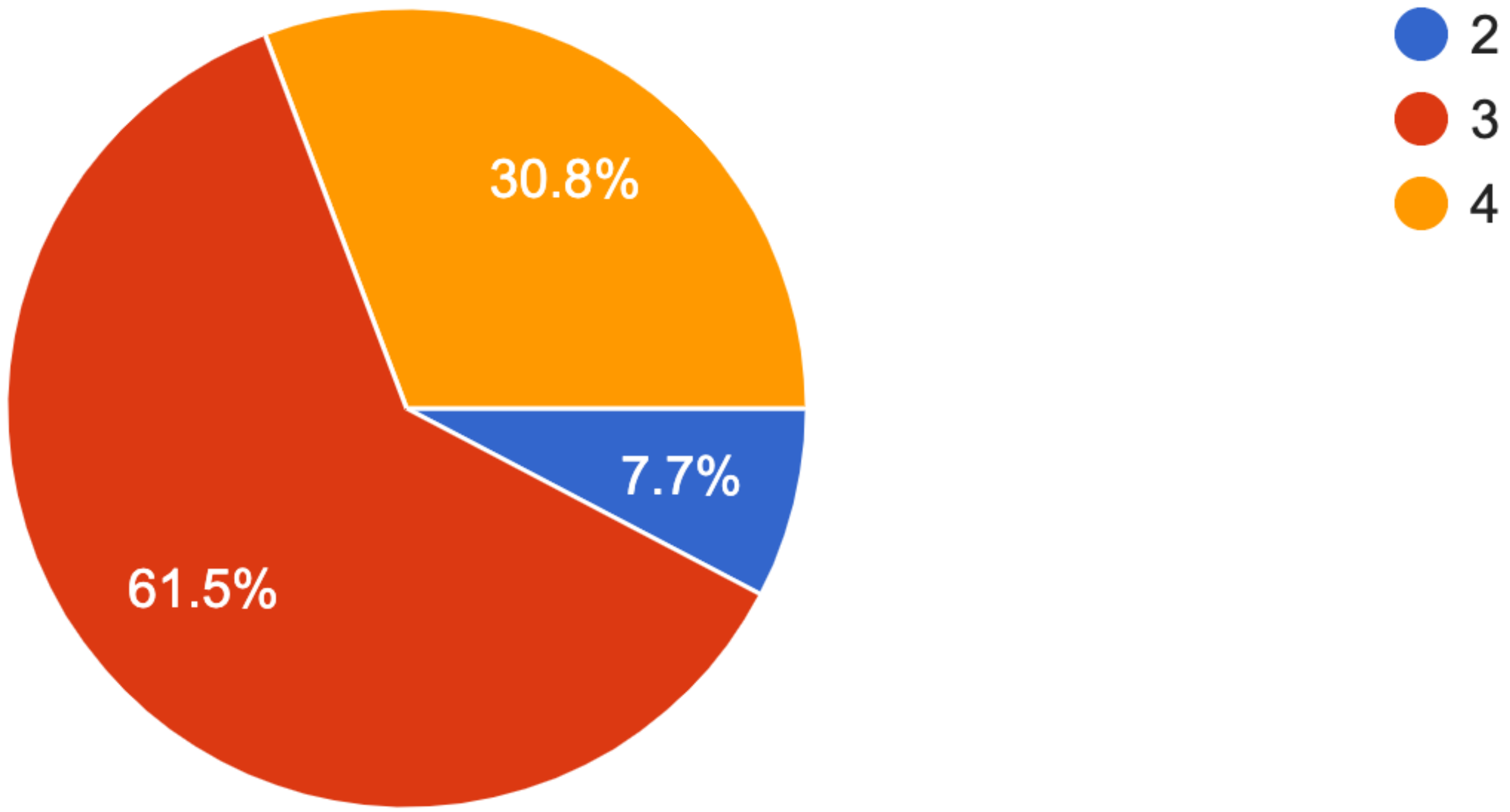
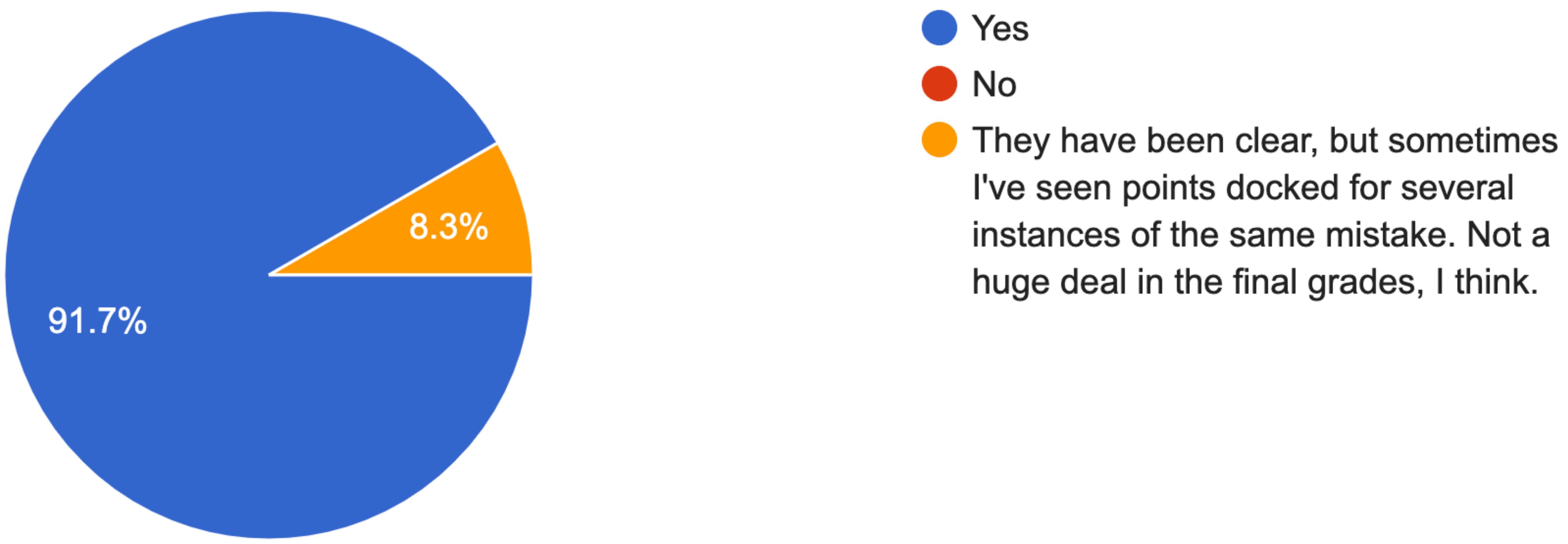


Poll results

Grading: Have the assessments and feedback been clear?

12 responses



Final project

- The final project is an opportunity to **apply what you've learned** to a **problem of interest** to you.
- For example, you could:
    - **Implement a method** from a recent research paper and recapitulate its results on synthetic data.
    - Apply methods developed in class to **study a dataset of interest** to you.
    - **Propose and implement an extension** to an existing method that would address some of its limitations.
    - Perform a **theoretical analysis** of a method to study its statistical properties.
    - Perform a **literature review** of neural data analysis methods for a certain problem.
- You'll submit a proposal partway through the course and a final report + code at the end.
- You can work individually or in a small team (expectations will be scaled appropriately).

Final project

- **Friday, February 19**: Initial proposal (~0.5-1pg).
  - Groups (1-3 people)
  - Topic / Type of project
  - Data (suggestions forthcoming)
- **Friday, March 5**: Final proposal (~1-2pg)
  - With some preliminary results (summary plots, etc.)
- **Friday, March 12**: Work on labs in class
- **Monday, March 15—Fri March 19**: In class presentations
- **Friday March 19**: Final report due (~5pg) + Colab notebook

Agenda

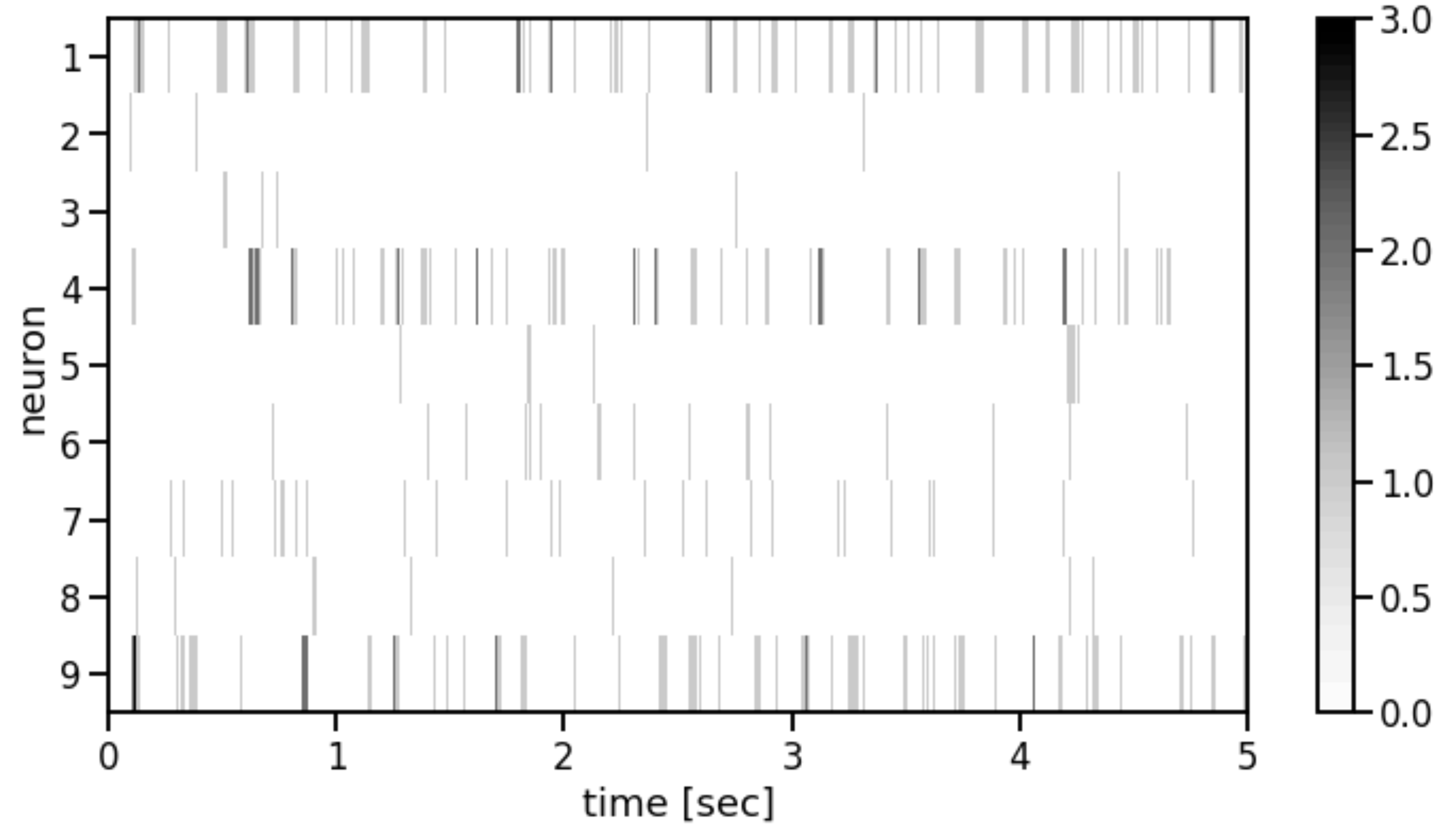
Unit II: Encoding and Decoding

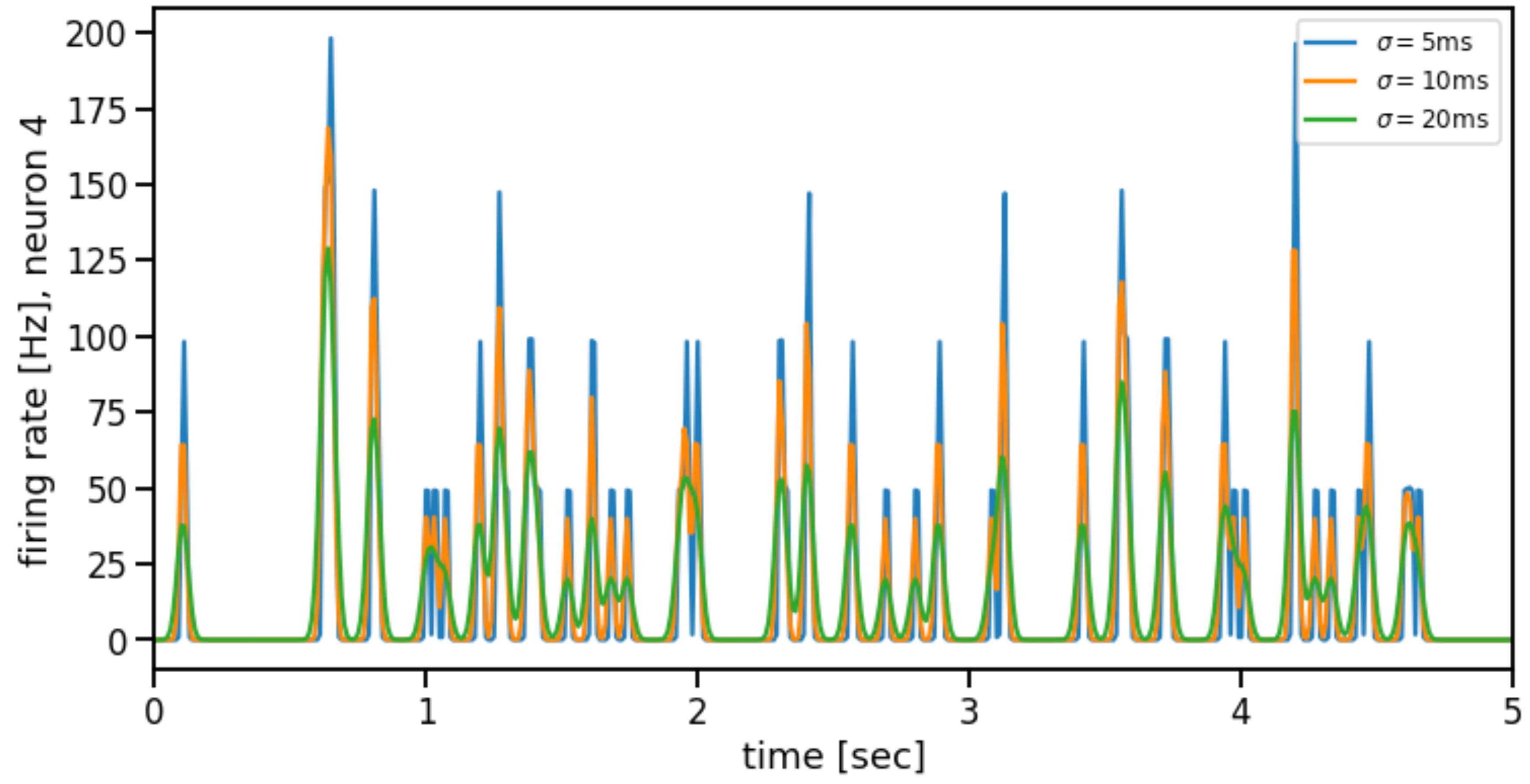
- You’ve got spikes. Now what?
- Retinal ganglion cells
- Encoding RGC responses with generalized linear models (GLMs)

You’ve got spikes. Now what?

Plot your data!

- **Spike train**: neuron x time array of spike counts in each time bin (e.g. 10ms).
- **Empirical firing rate**: smooth the spike train (e.g. with a Gaussian kernel).
- **Sanity checks:**
    - Are the spike trains plausible (e.g. 1-50 spikes/sec)?
    - Do the firing rates look similar in the beginning, middle, and end of the recording?



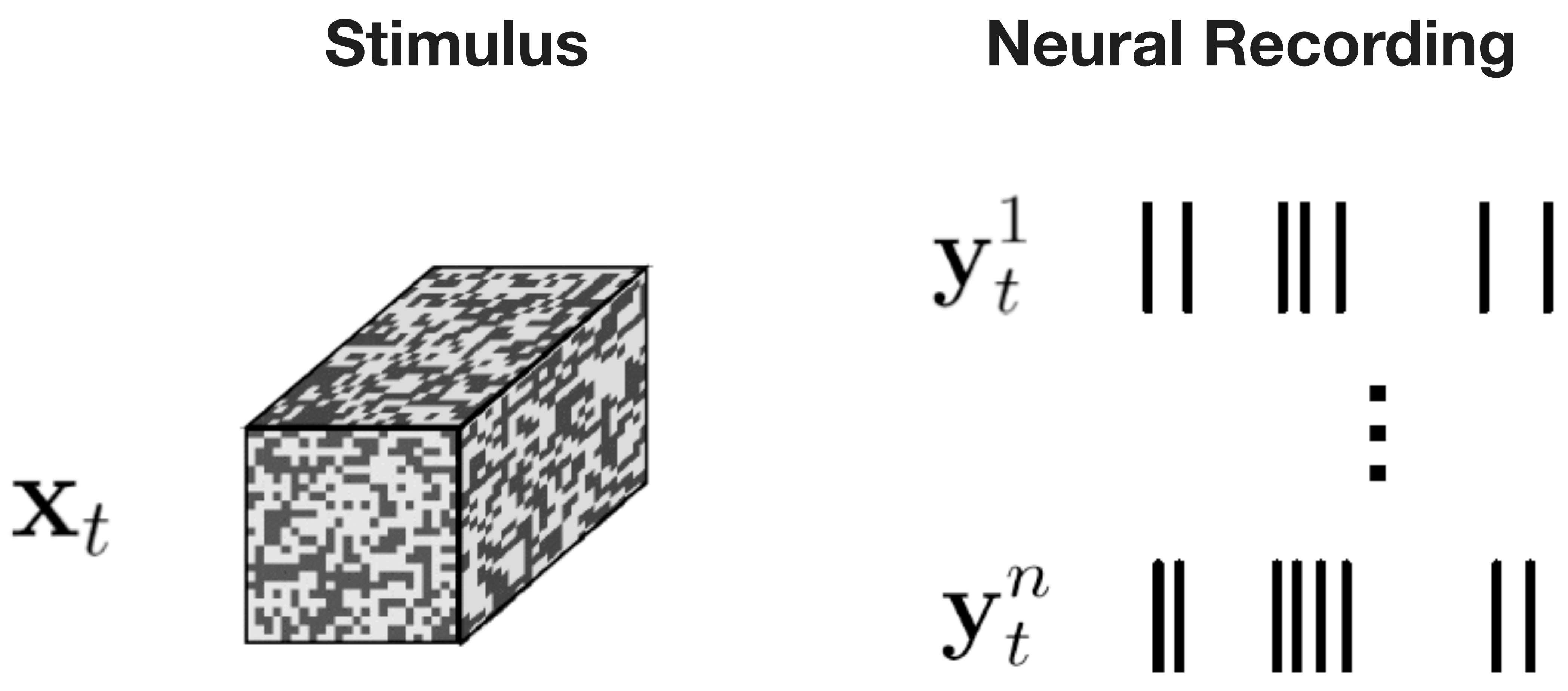


You’ve got spikes. Now what?

Spike triggered averages

- **Spike triggered average (STA):** What did the stimulus look like preceding (or surrounding) each spike?

- STA $\equiv$ conditional distribution of stimulus (x_{t-d}) given response ($y_t = 1$).



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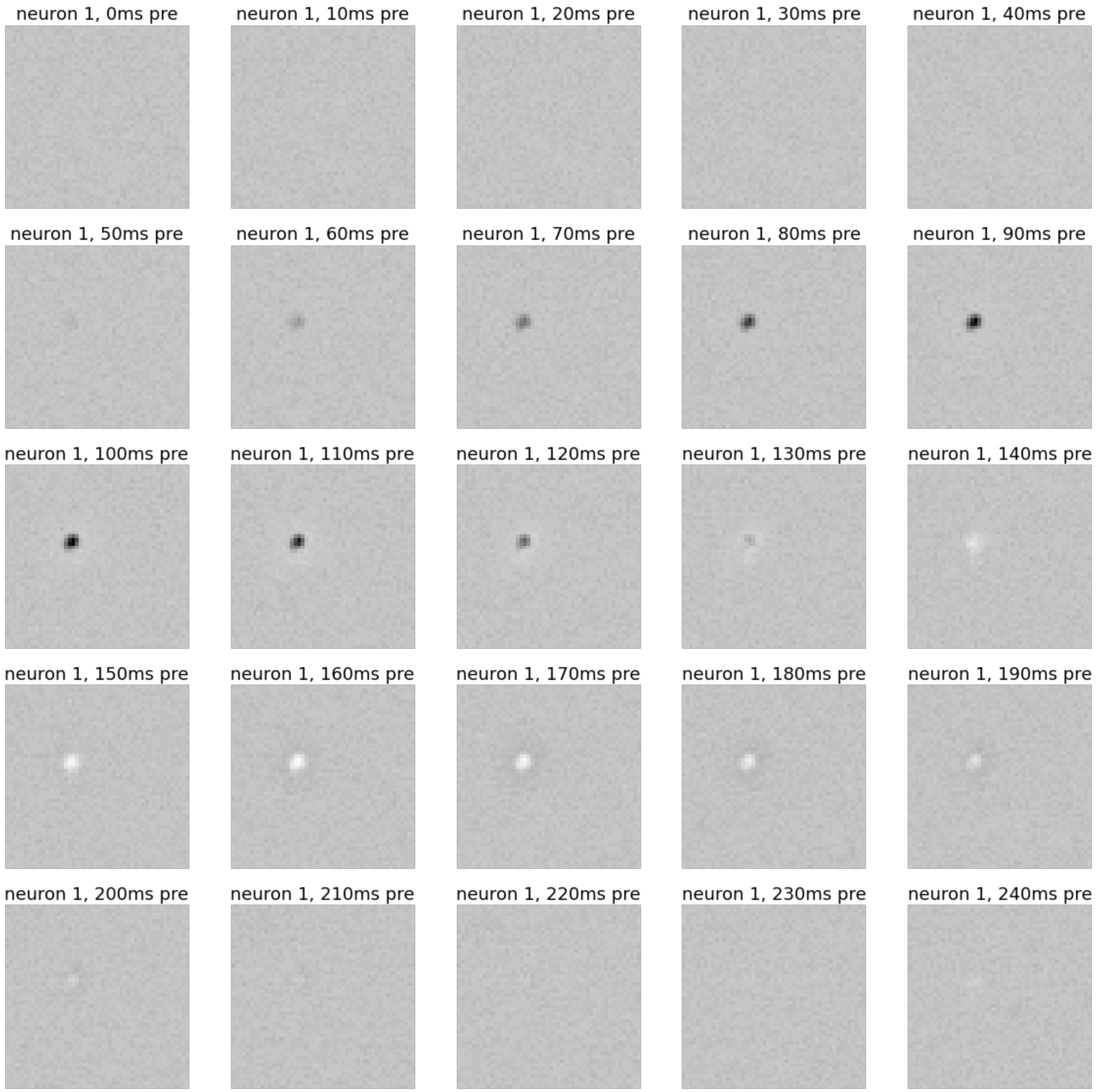
Spike triggered averages

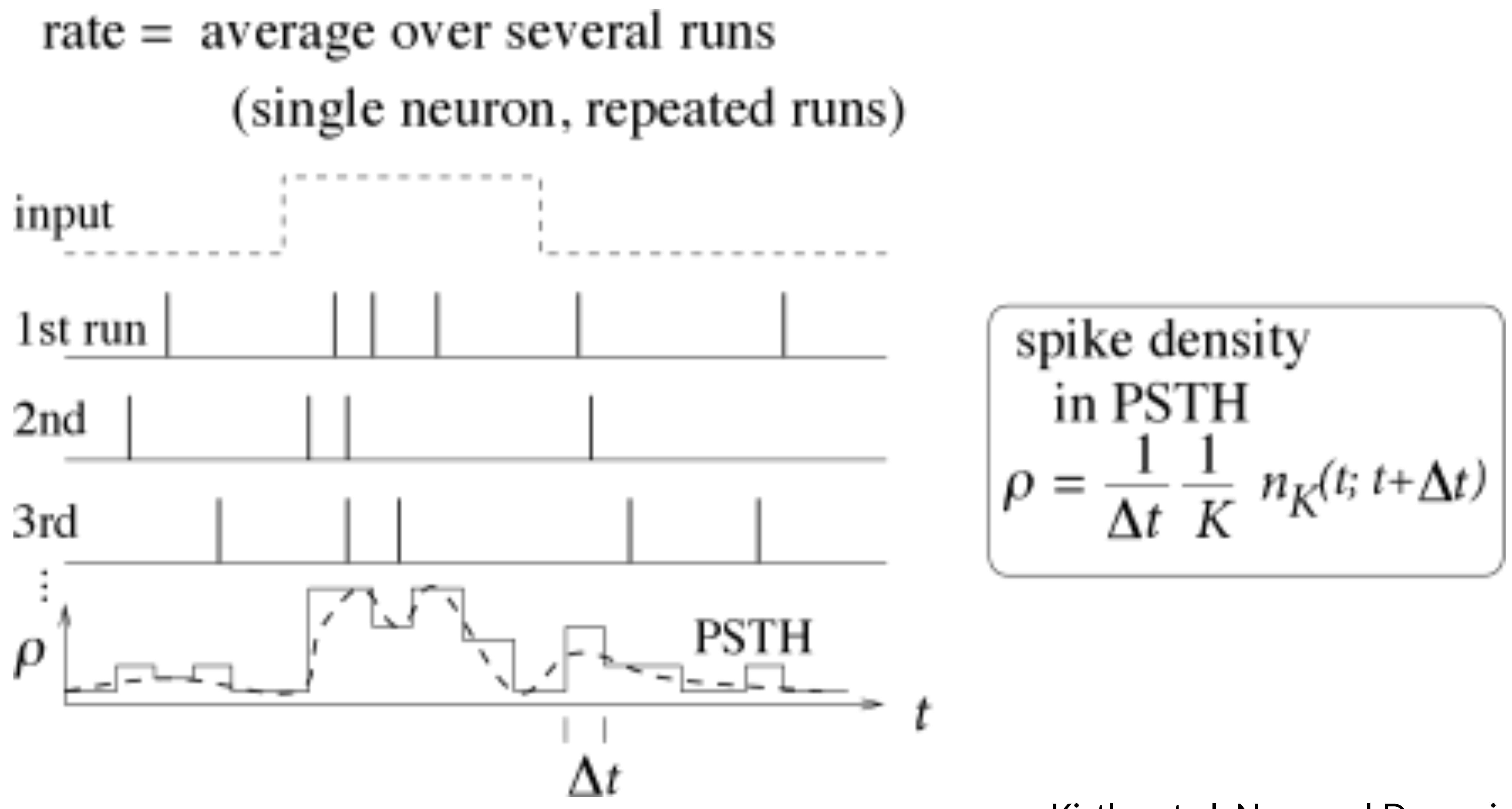
- **Spike triggered average (STA):** What did the stimulus look like preceding (or surrounding) each spike?
- STA $\equiv$ conditional distribution of stimulus (x_{t-d}) given response ($y_t = 1$).
- **Receptive field**: portion of stimulus to which neuron responds.



You’ve got spikes. Now what?

Peri-stimulus time histogram (PSTH)

- **Peri-stimulus time histogram (PSTH):** What did the response look like following (or surrounding) each stimulus presentation?
- PSTH $\equiv$ conditional distribution of spike train (y_{t+d}) given stimulus ($x_t = k$).



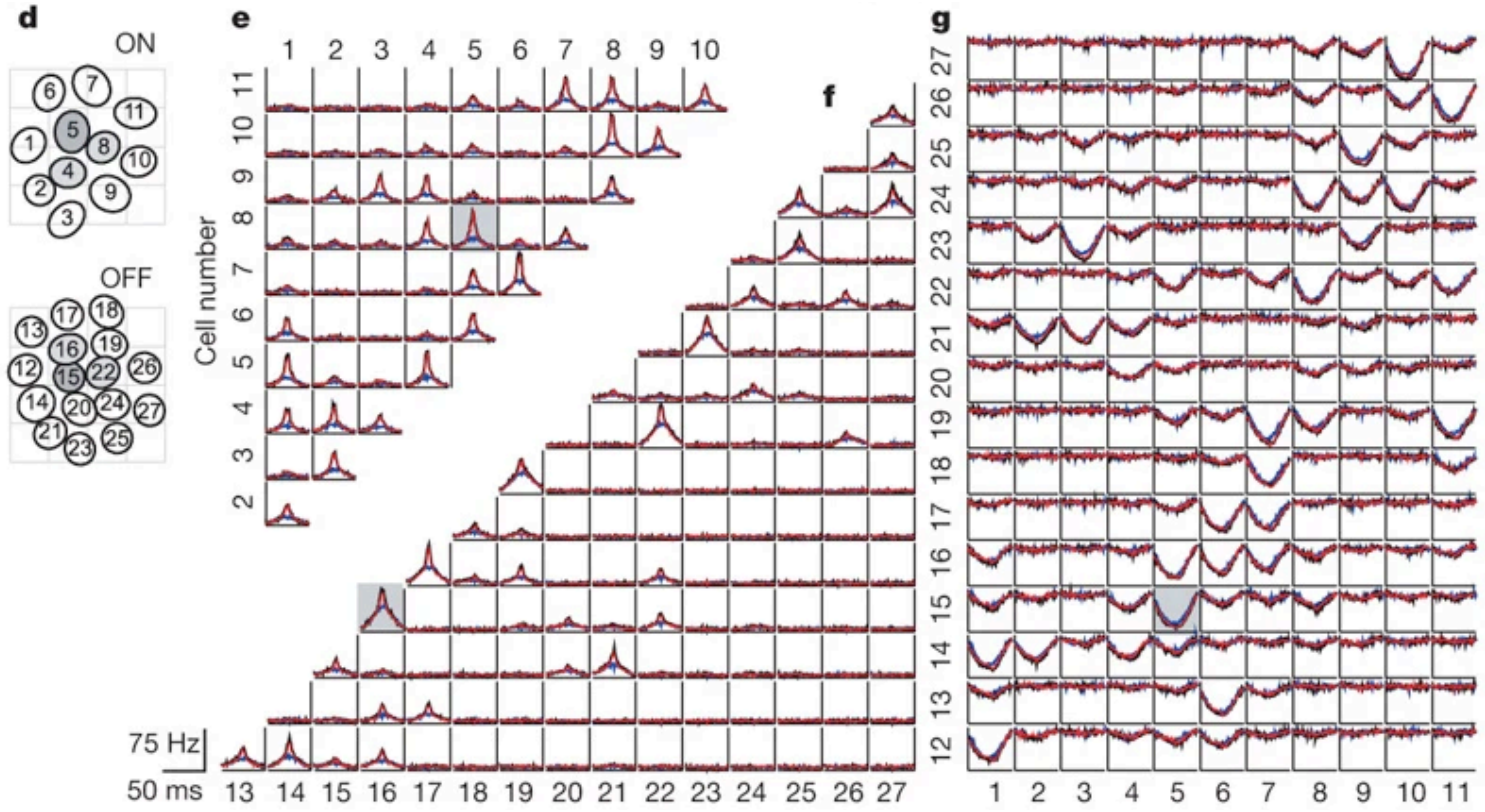
Kistler et al. Neuronal Dynamics

You’ve got spikes. Now what?

Cross-correlation function

- **Cross-correlation function (CCF):** what is the correlation between neuron n and neuron m as a function of delay of d?

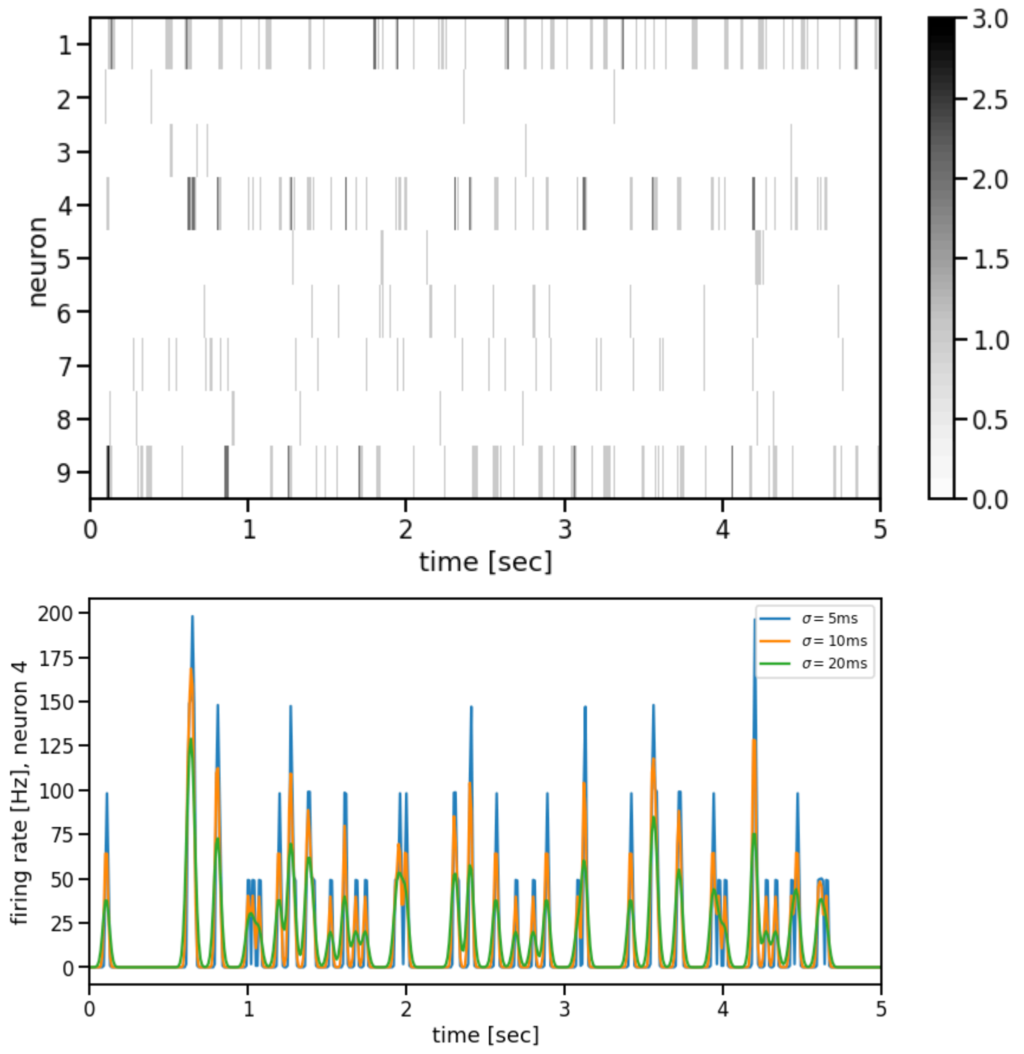
$$\mathbb{E}\left[\frac{(y_{m,t}-\mu_m)}{\sigma_m}\frac{(y_{n,t+d}-\mu_n)}{\sigma_n}\right]$$

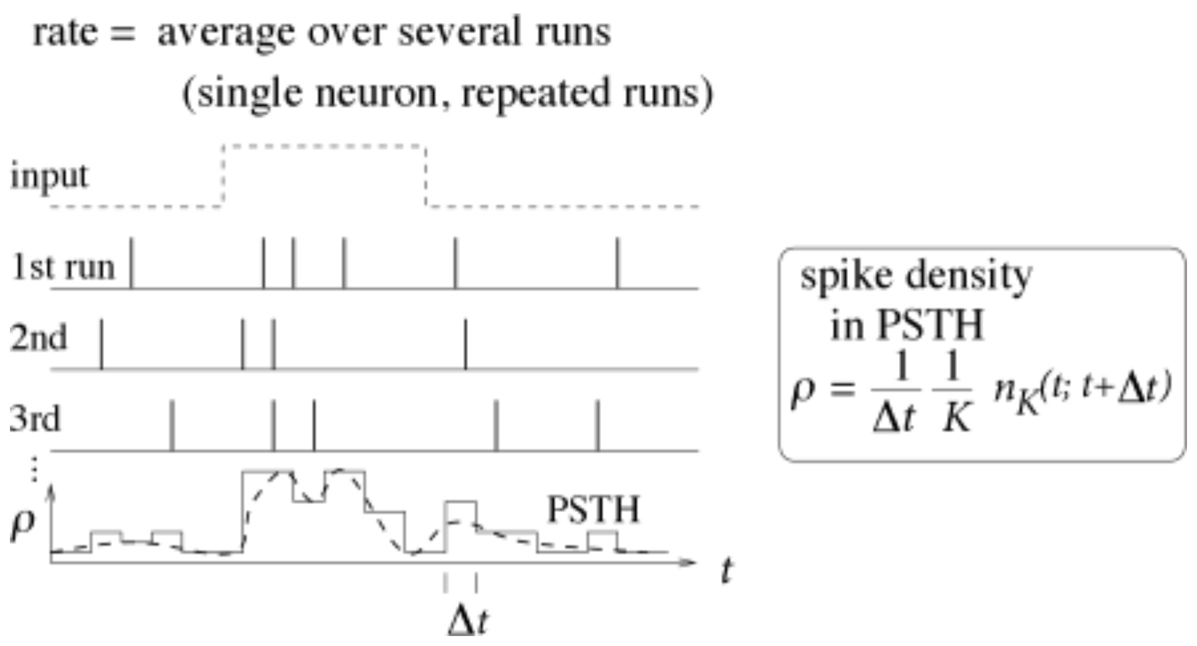


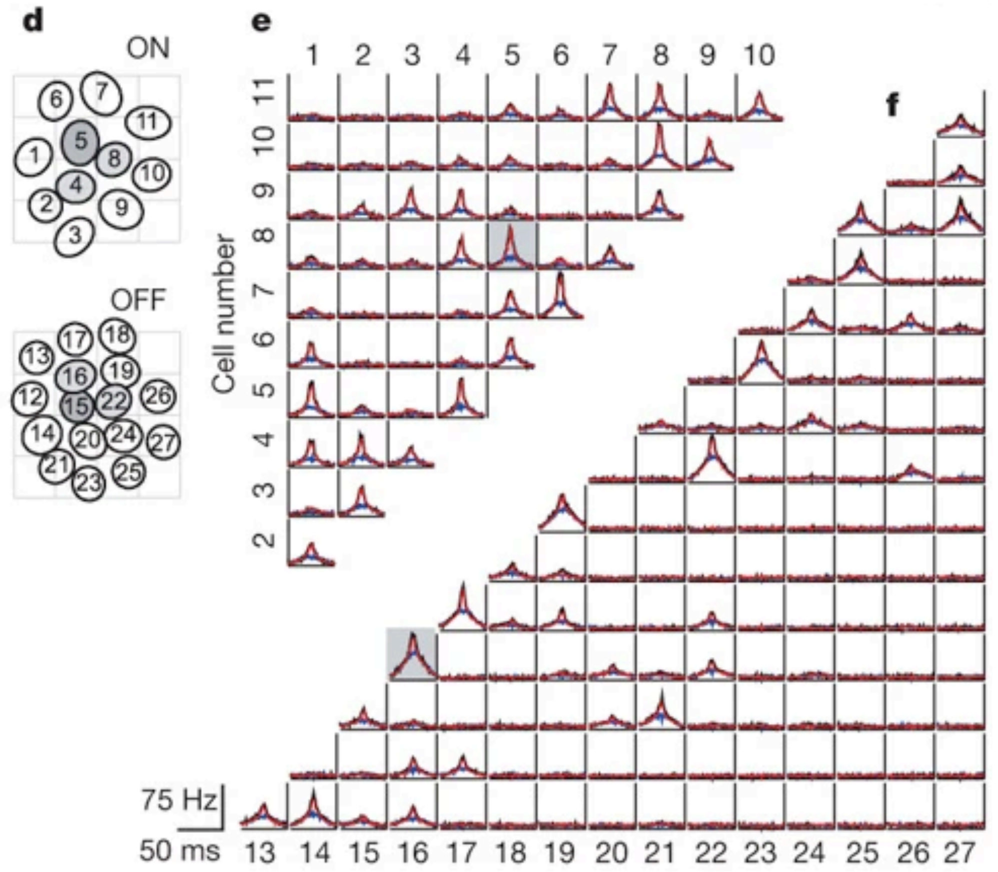
Pillow et al (*Nature*, 2008)

You’ve got spikes. Now what?

- A good model should **recapitulate these statistics** of the data.





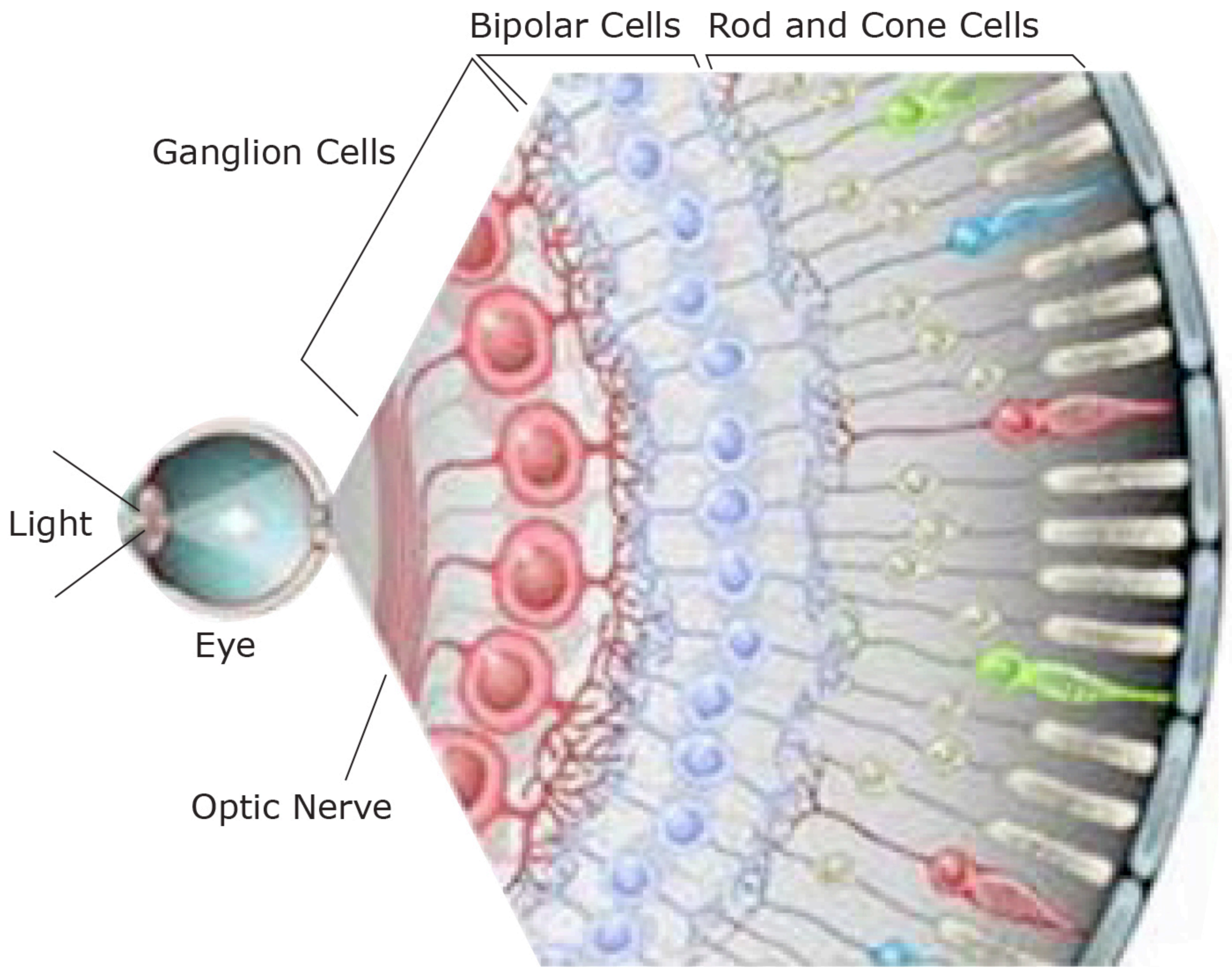


Retinal circuits

Retinal circuits

Basic architecture

- Incoming light stimulates **photoreceptors (rods and cones)** at the back of the eye.
- Rods and cones trigger an intermediate layer of **bipolar cells** and **amacrine cells.**
- Activity in these intermediate cells is pooled by **retinal ganglion cells (RGCs).**
- RGCs send action potentials down the **optic nerve** to the rest of the brain.
- The optic nerve innervates the **lateral geniculate nucleus (LGN)** of the thalamus and **primary visual cortex (V1)**



http://visionmagazineonline.co.za/2018/04/01/why-retinal-ganglion-cells-are-important-in-glaucoma/

Retinal circuits

Types of RGCs

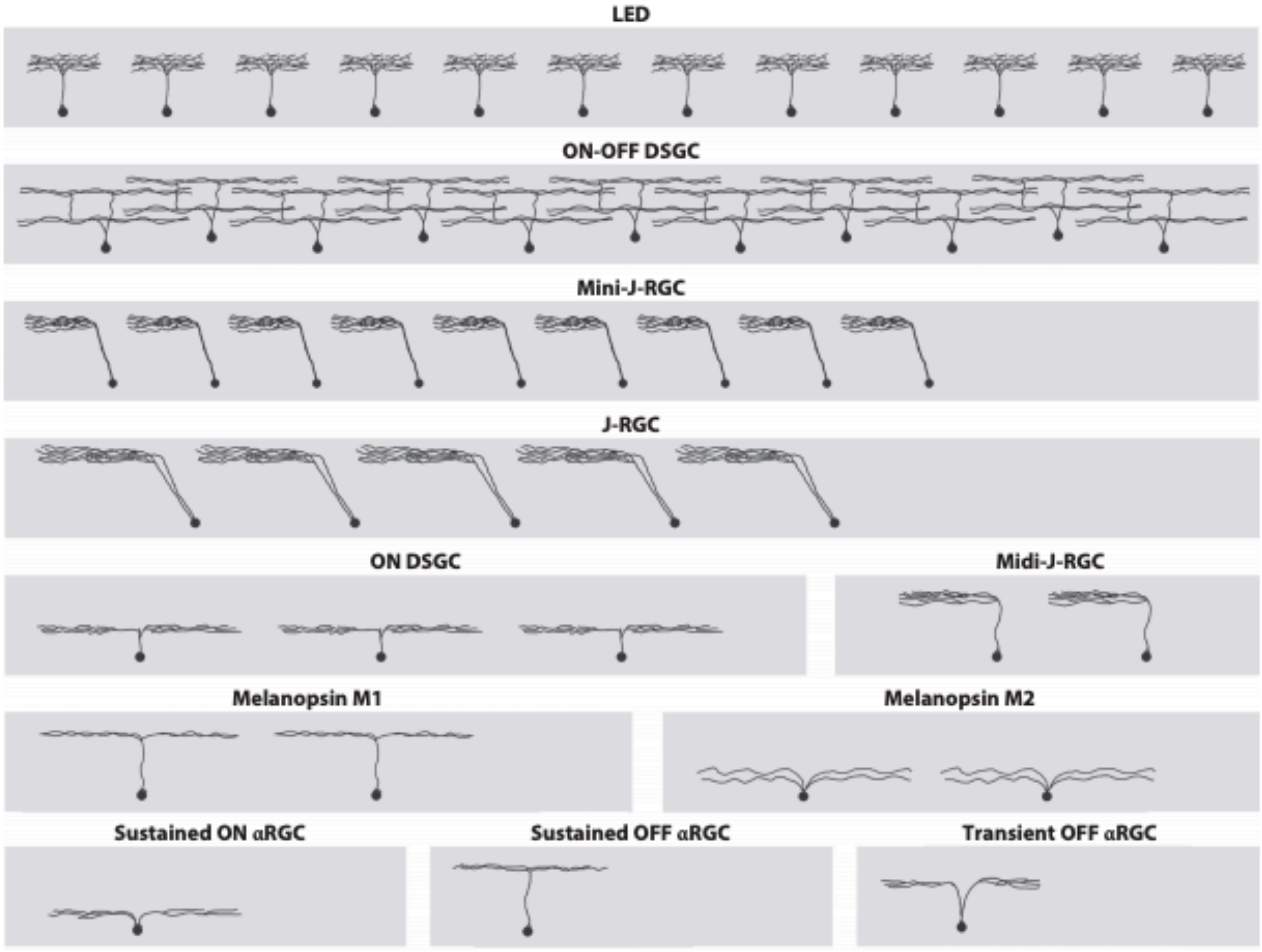
- RGCs have been subdivided into dozens of types based on their morphology and their response properties.

- To first approximation, two main types: **ON and OFF cells**.

    - **ON cells** fire action potentials in response to **increased light intensity** at the center of their receptive field.

    - **OFF cells** fire action potentials in response to **decreased light intensity** at the center of their receptive field.

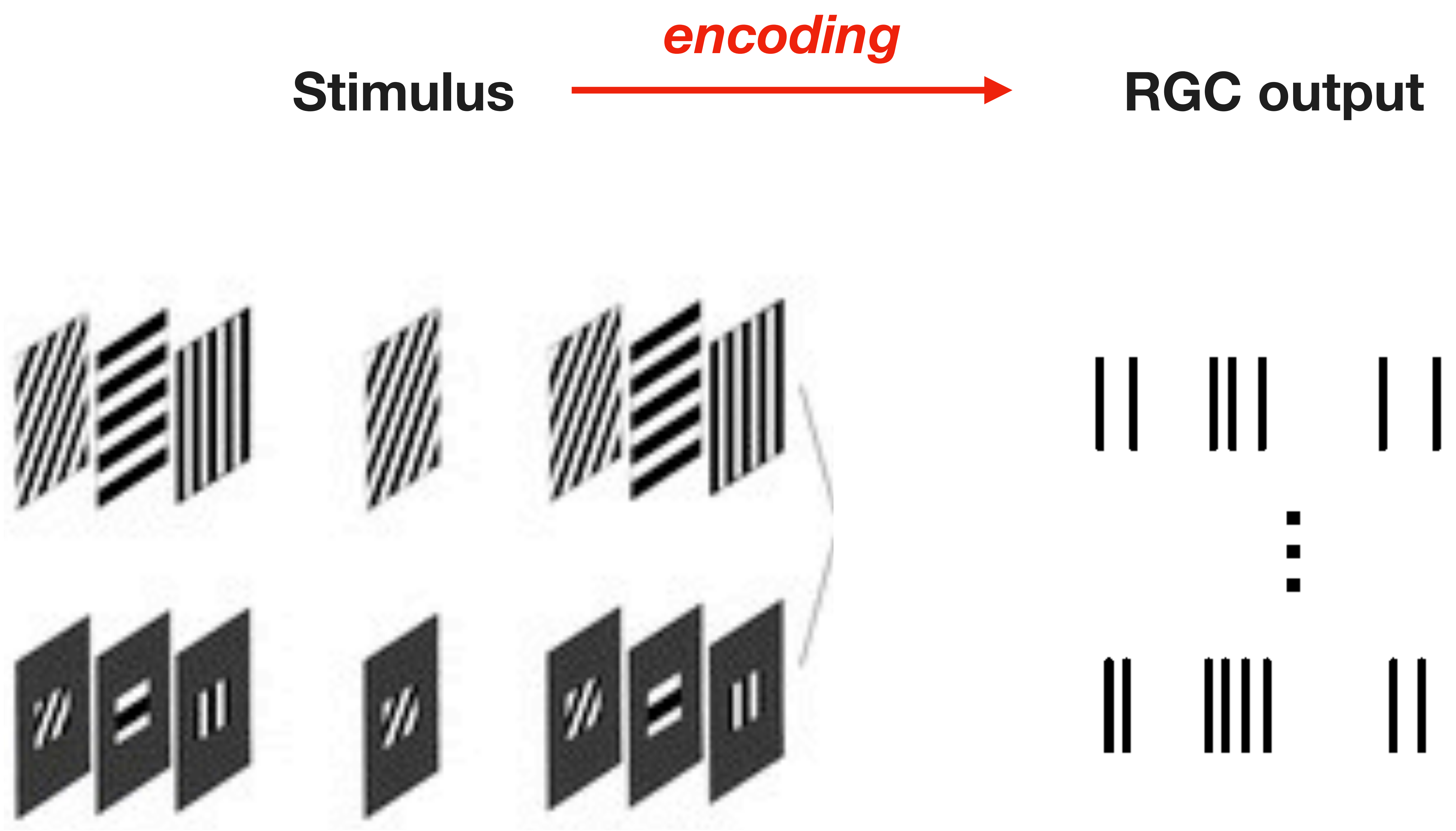
- Lots of **heterogeneity**; e.g. direction selective cells, transient and sustained responses, local edge detectors…



Sanes and Masland (*Ann. Rev. Neuro.*, 2014)

Retinal circuits

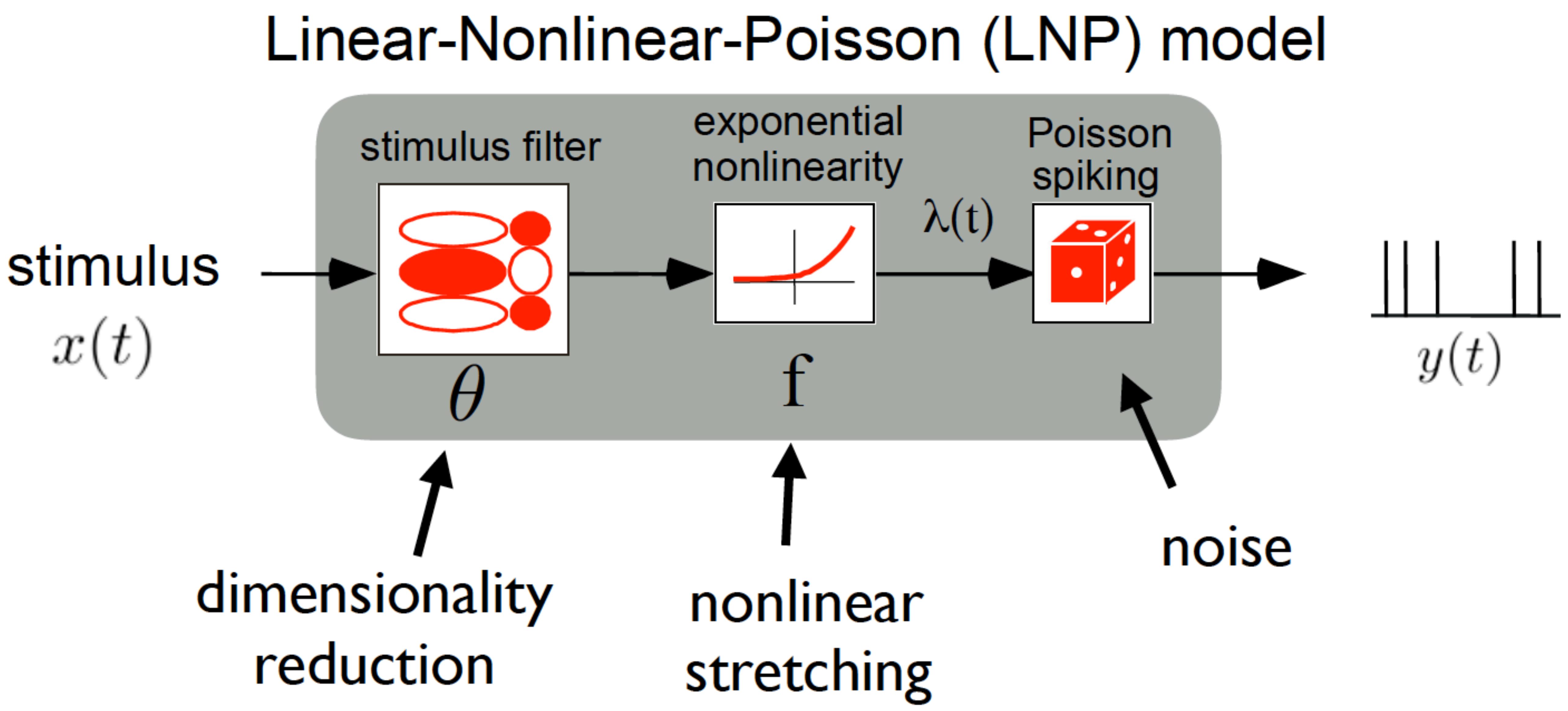
- **Key question**: *How are visual stimuli encoded in the output of these retinal circuits?*



Generalized linear models of RGC responses

Encoding models of RGC responses

Basic linear-nonlinear-Poisson (LNP) model



spike rate $\lambda = f(\vec{k} \cdot \vec{x})$

spike count $y \sim \mathrm{Poiss}(\lambda)$

In statistics, we call this a generalized linear model (GLM).

Slides from Jonathan Pillow

Encoding models of RGC responses

First things first: Linear models

- Let $Y \in \mathbb{N}$ denote an integer-valued random variable; e.g. a spike count.
- Let $X \in \mathbb{R}^p$ be a p-dimensional feature vector.
- **Linear regression** estimates the conditional expectation $\mu(X) \triangleq \mathbb{E}[Y \mid X]$ via a linear function $\hat{\mu} \triangleq \beta^\top X$, where $\beta \in \mathbb{R}^p$ is a vector of regression weights.
- **Question: What are some shortcomings of this linear regression model?**

Encoding models of RGC responses

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- **Question: What are some shortcomings of this linear regression model?**
  - **Negative means**
  - **Symmetric and homoskedastic noise (same variance for each input)**

Encoding models of RGC responses

Generalized linear models

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Encoding models of RGC responses

Generalized linear models

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- Let $\hat{\eta}(X) \triangleq \beta^\top X$ be a **linear predictor** defined by parameter β, which we will estimate.
- Map the predictor through a monotonic, continuous, non-linear **mean function** $g(\cdot) : \mathbb{R} \to \mathscr{M}$, where $\mathscr{M}$ is the space of conditional expectations of Y.
    - E.g. If $Y \in \mathbb{N}$ is a non-negative integer its expectations lie in $\mathscr{M} = \mathbb{R}_+$, so we might take $g(a) = e^a$.

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- Finally, plug the conditional expectation into a **conditional distribution** of Y given X.
    - E.g. $Y \mid X \sim \mathrm{Po}(g(\eta(X))$

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- Finally, plug the conditional expectation into a **conditional distribution** of Y given X.
    - E.g. $Y \mid X \sim \mathrm{Po}(g(\eta(X))$
- Generally, we assume the conditional distribution is a member of the **exponential family**.

Encoding models of RGC responses

Generalized linear models

- Let $X \in \mathbb{R}^{T \times P_H \times P_W}$ denote a stimulus movie and $Y \in \mathbb{N}^{N \times T}$ denote the resulting spike train.

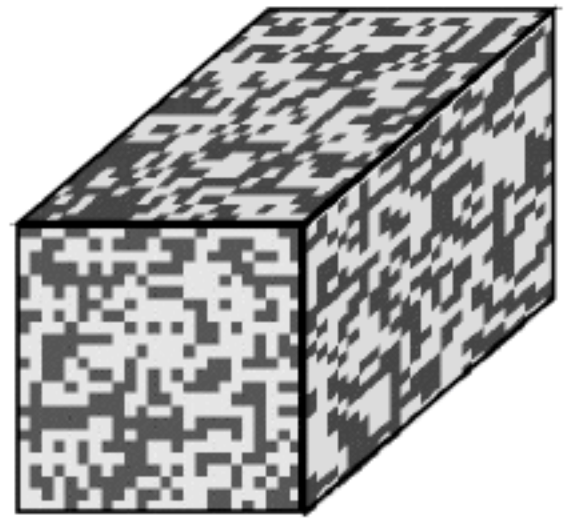
- Define a **Poisson GLM** to predict (encode) neural responses given the past D frames of stimulus.

Encoding models

Generalized linear models

Stimulus **Filter Weights** **Firing Rates** **Neural Recording**

$\mathbf{x}_t$



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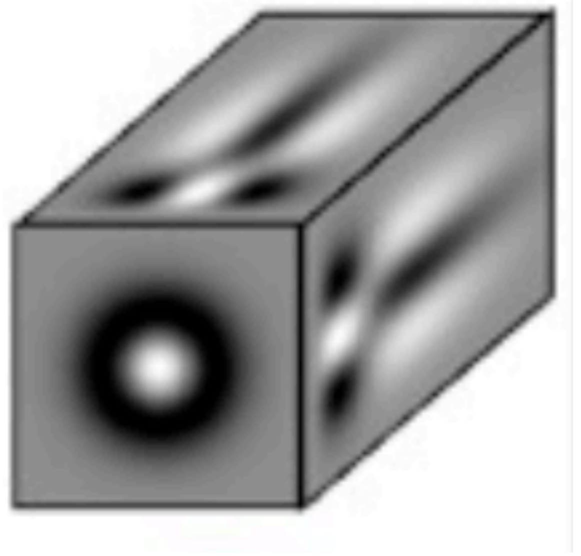
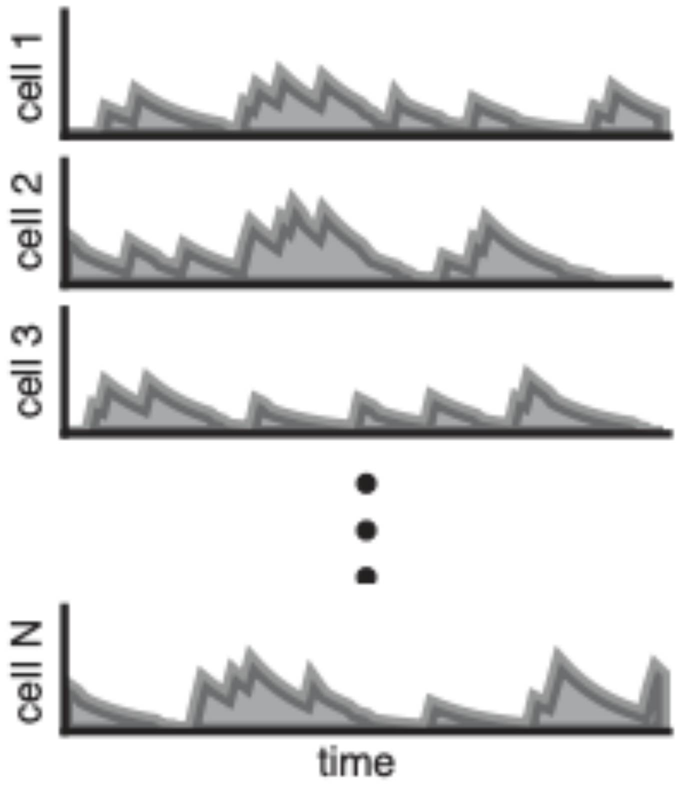


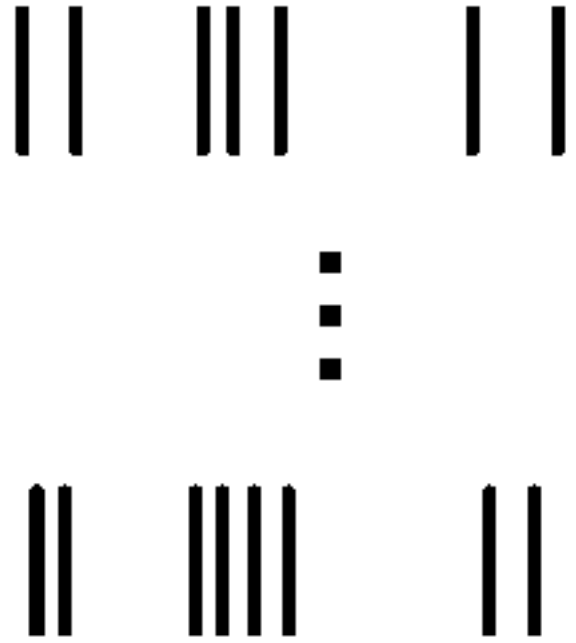
W_n

$\xrightarrow{f(\cdot)}$



$\longrightarrow$

$\mathbf{y}_t^1$



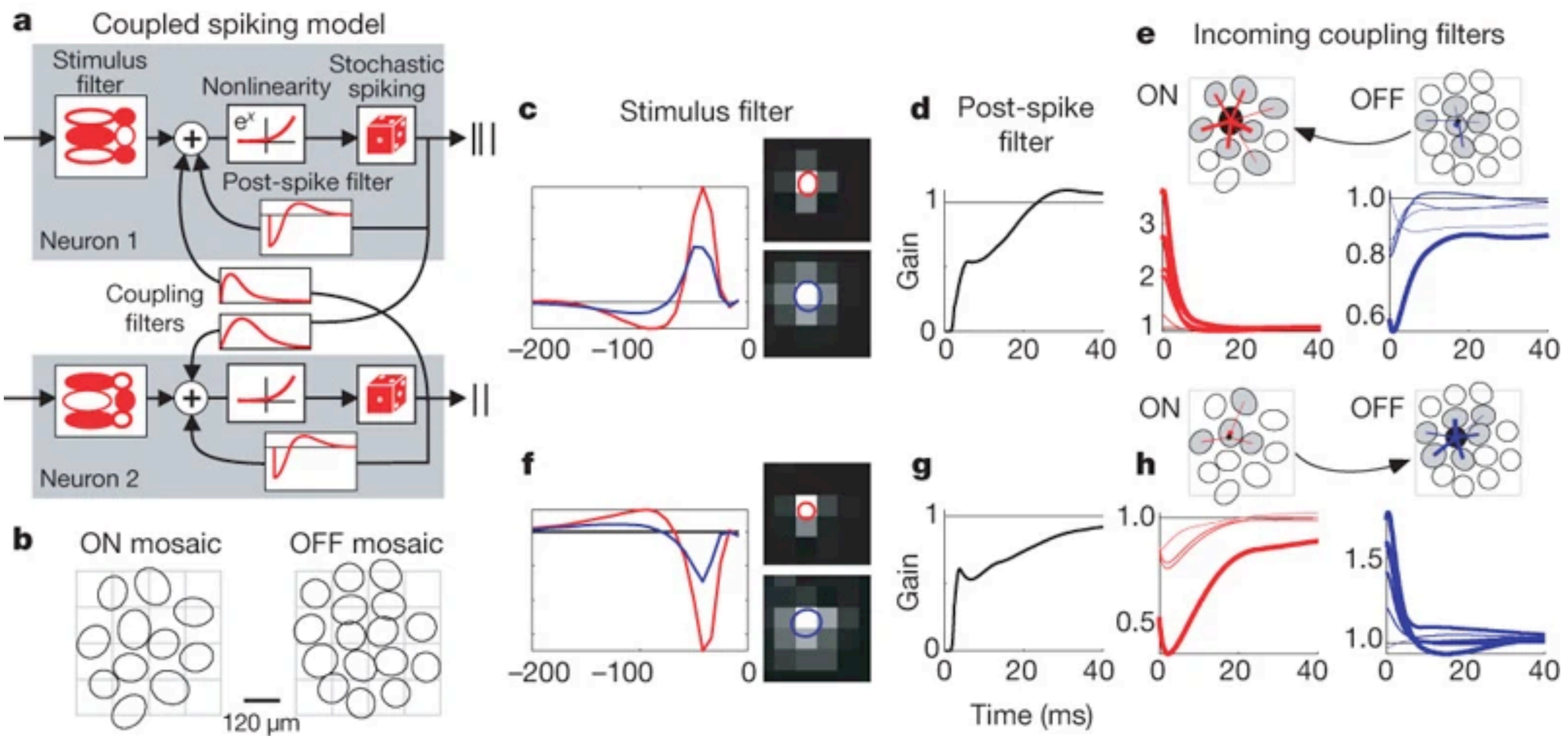
$\mathbf{y}_t^n$

$$\lambda_{nt} = g([X \star W_n]_t)$$

Slides from Jonathan Pillow

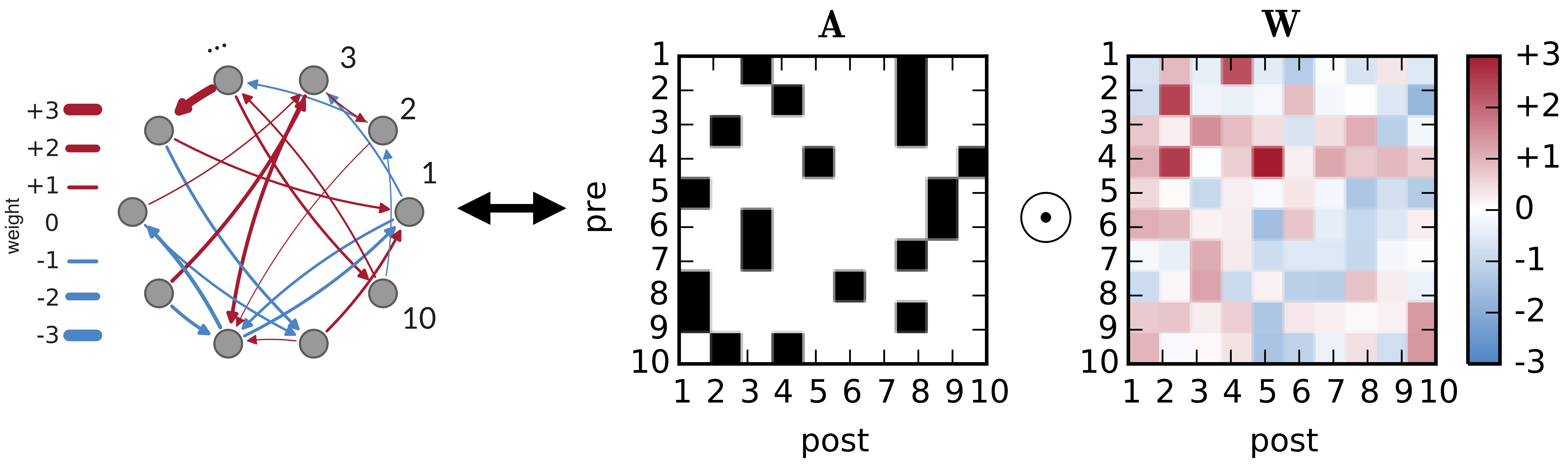
Encoding models of RGC responses

Adding coupling between neurons



Encoding models of RGC responses

Separately modeling the coupling sparsity and weights

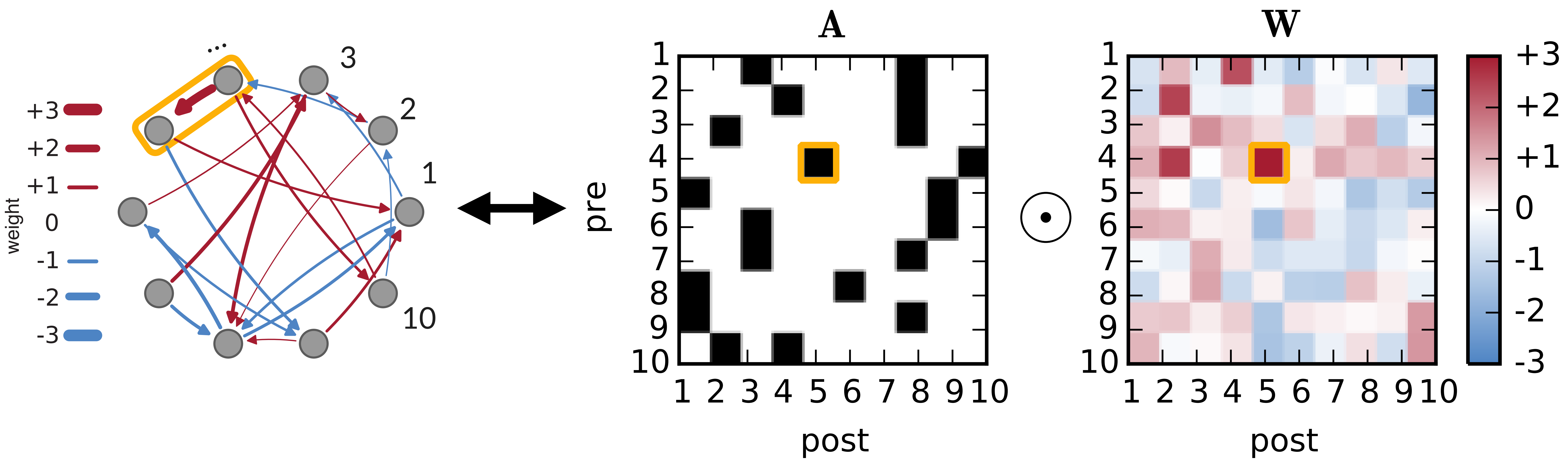


Binary Adjacency Matrix

Real-Valued Weight Matrix

Encoding models of RGC responses

Separately modeling the coupling sparsity and weights

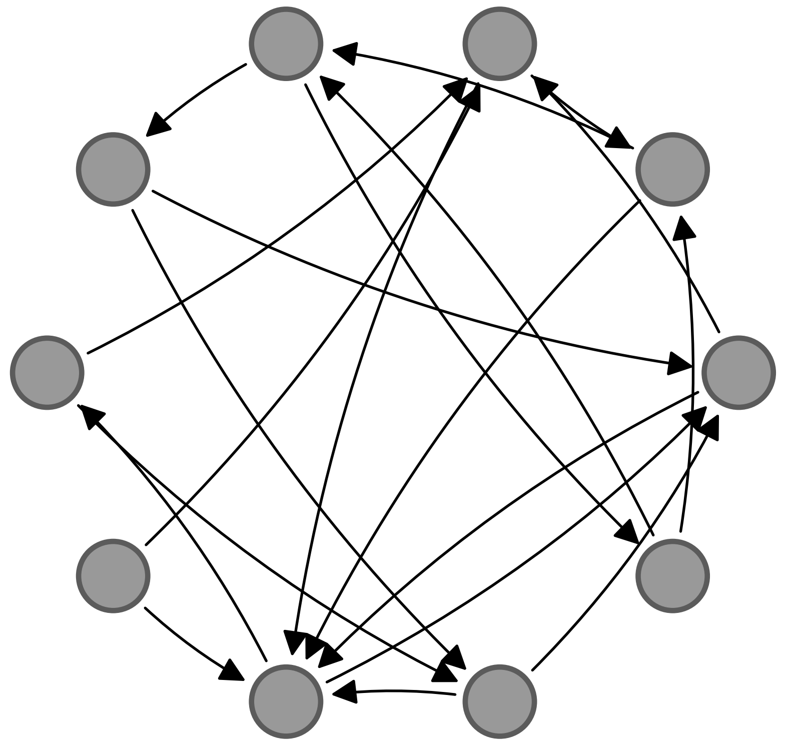
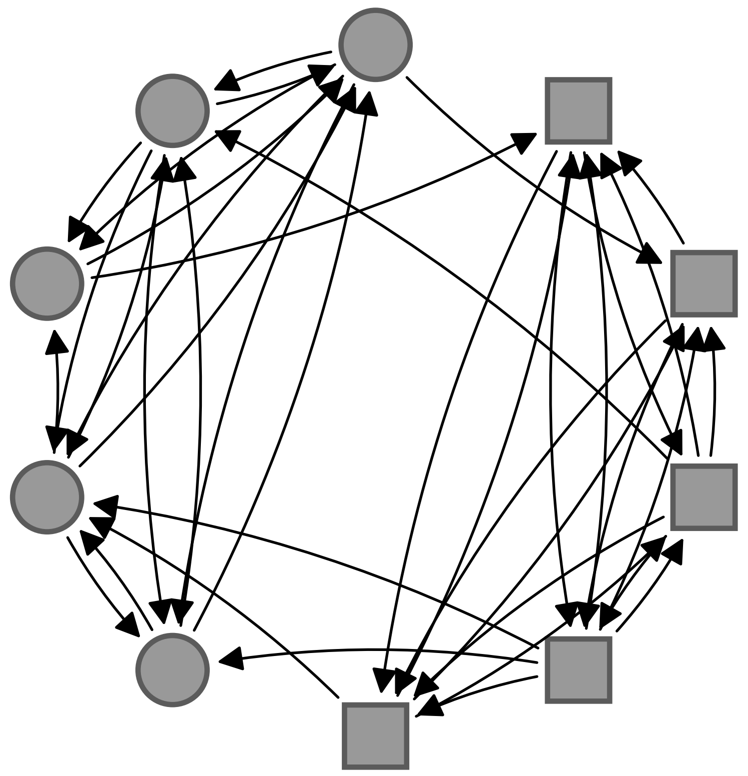
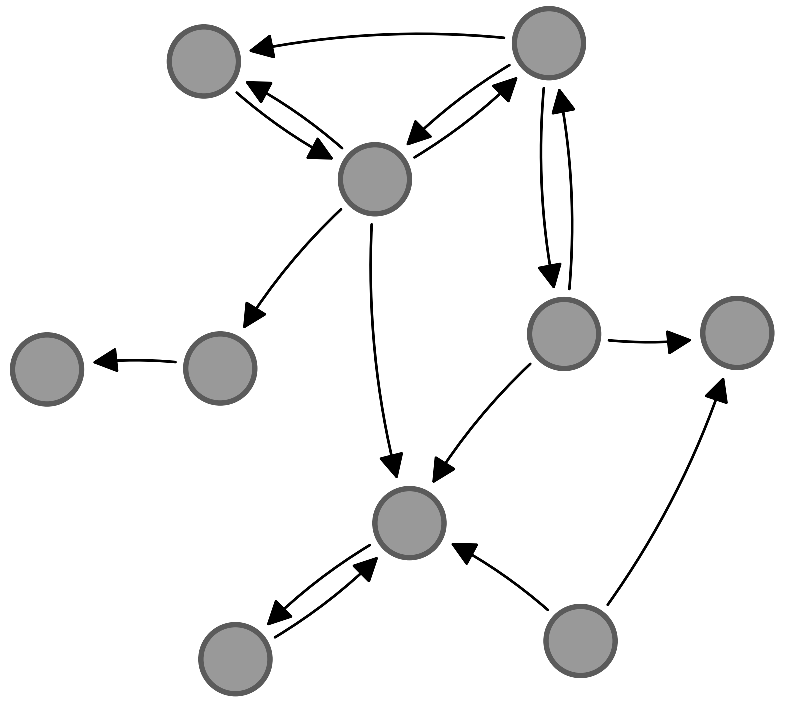


Binary Adjacency Matrix

Real-Valued Weight Matrix

Encoding models of RGC responses

Latent variable models for networks

	Independent Edge Model	Stochastic Block Model (SBM)	Latent Distance Model
Types or Features $\boldsymbol{Z}$	None	Type { ■, ● }	Location $\mathbb{R}^D$
Adjacency Models $\boldsymbol{A}$			

Hoff (*NeurIPS*, 2007)

Encoding models of RGC responses

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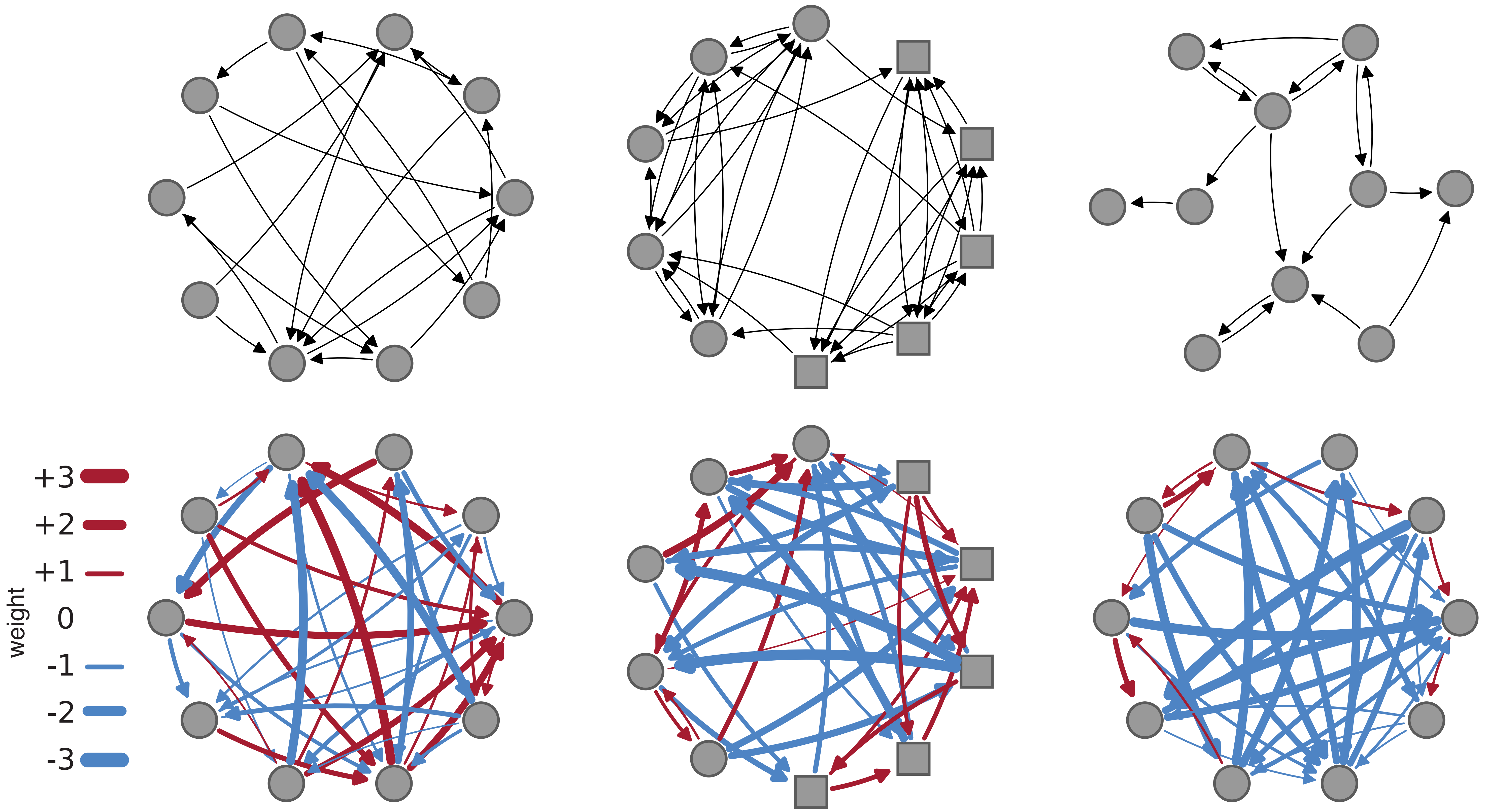
Adjacency Models A

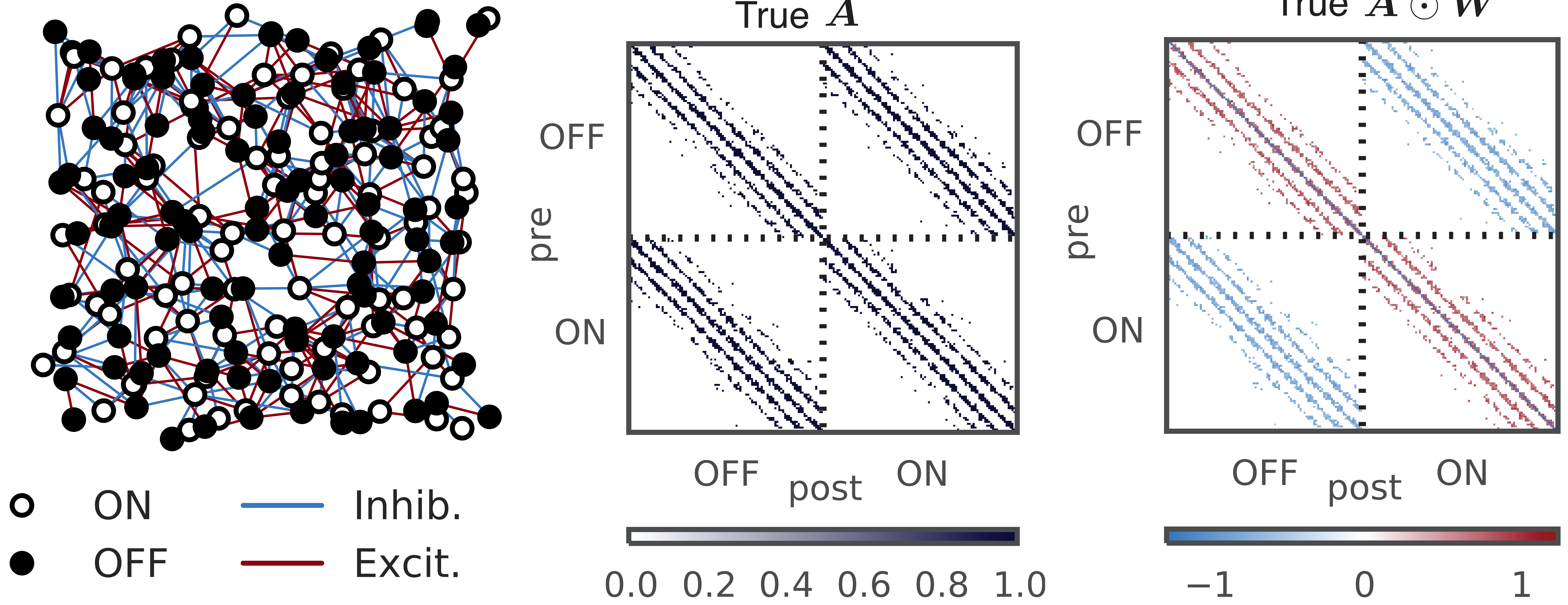
Weight Models W



Hoff (*NeurIPS*, 2007)

Example: a synthetic retina

Latent variables: types & locations. **Adjacency:** distance-dependent. **Weights:** type-dependent.



Linderman, Adams, Pillow (*NeurIPS*, 2016)

Application to real primate retina data

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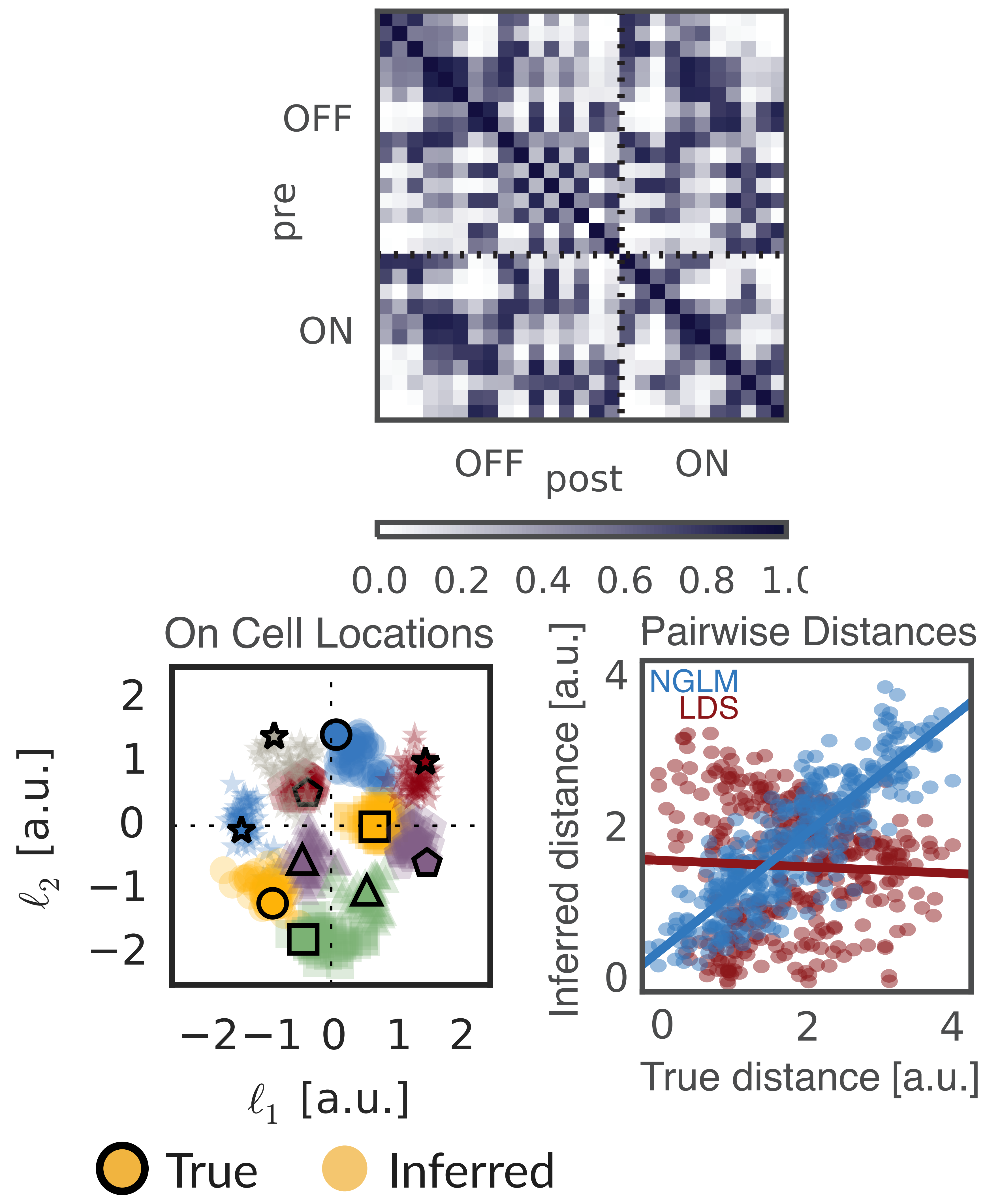
Inferring locations



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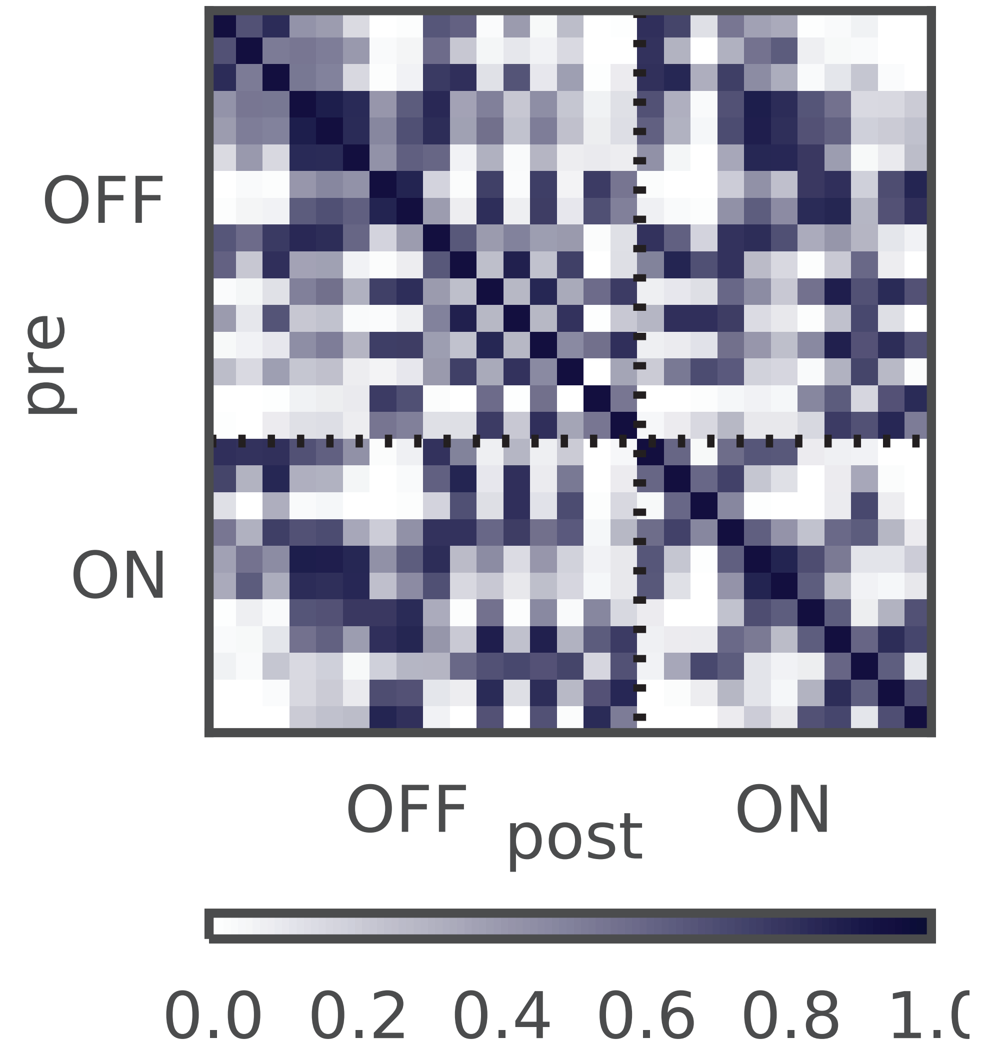
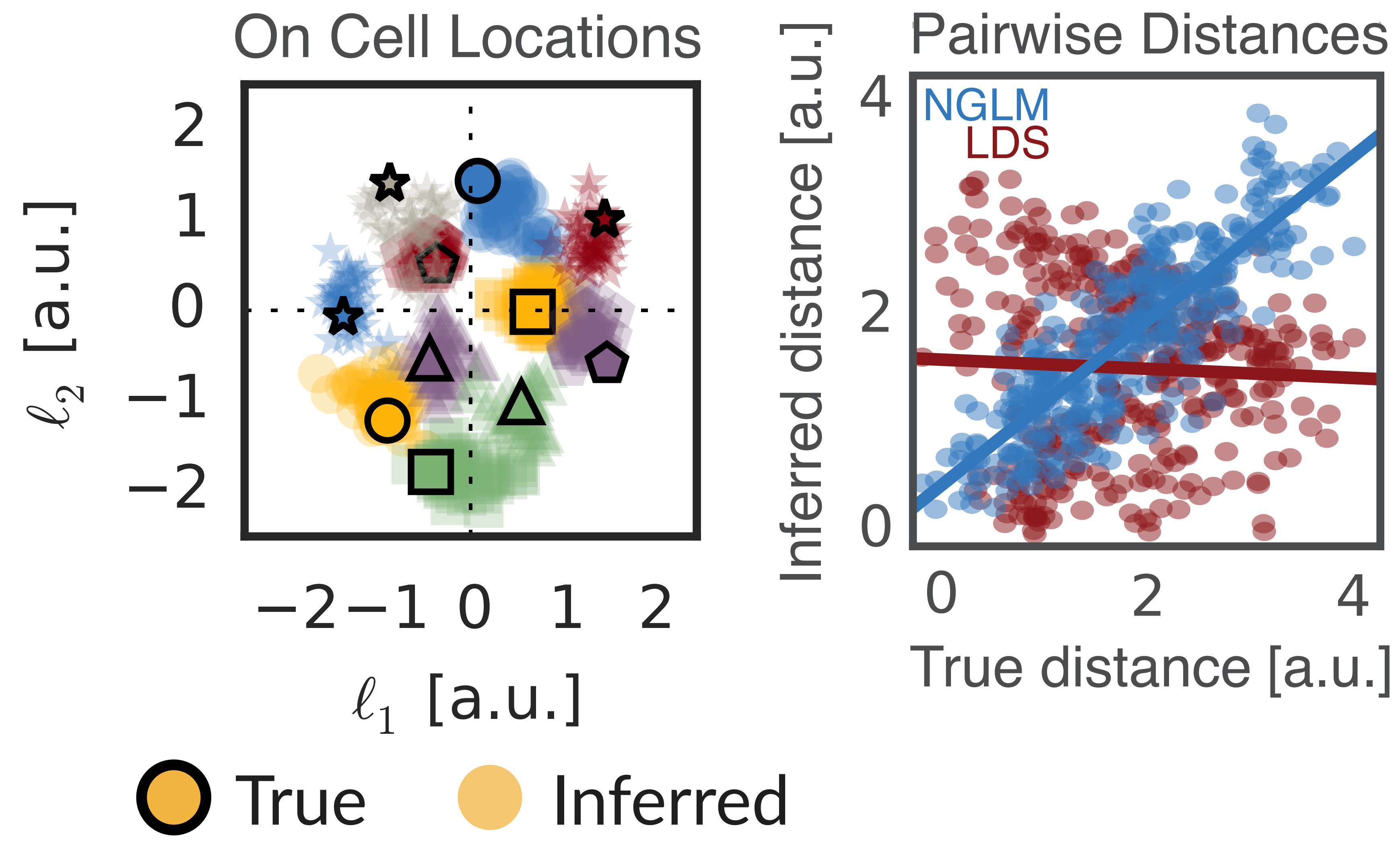
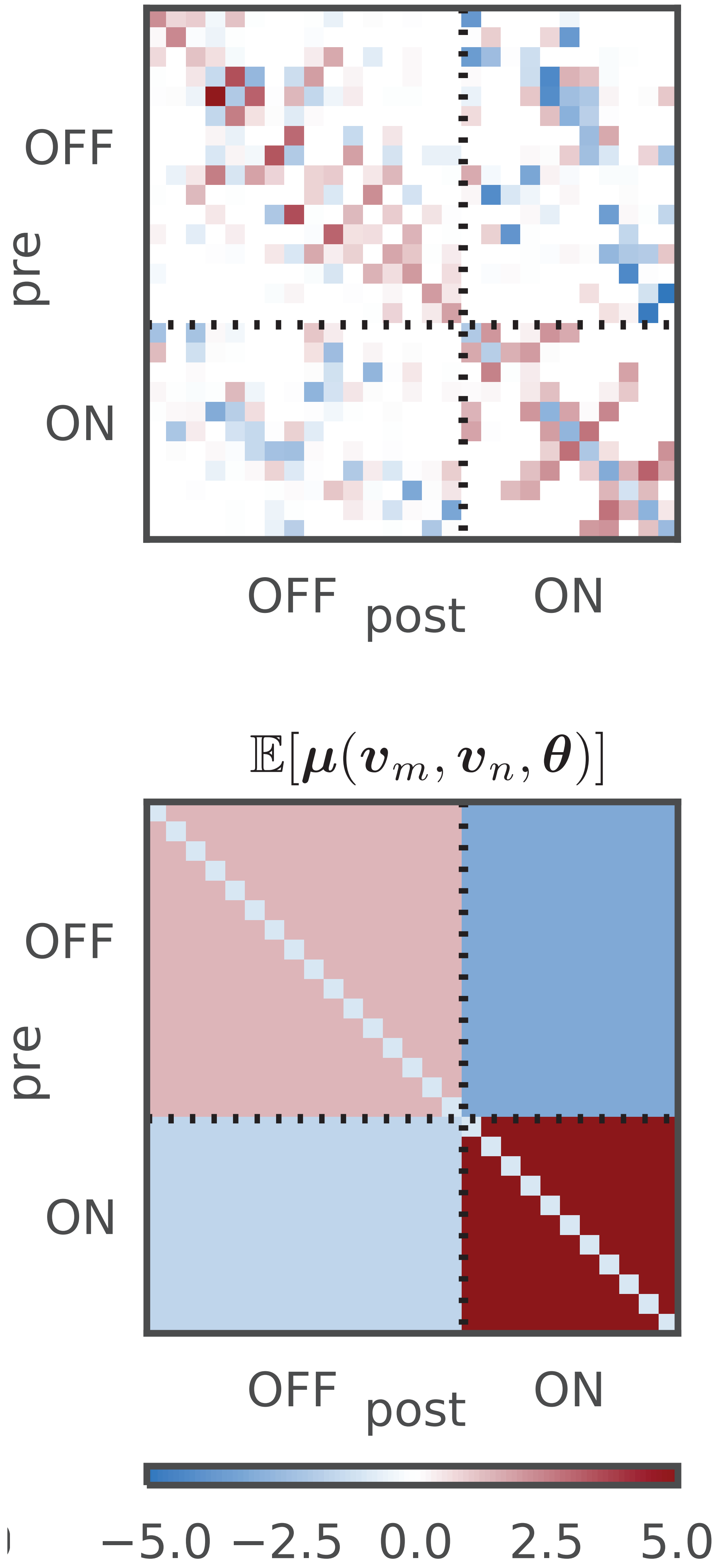




Inferring cell types



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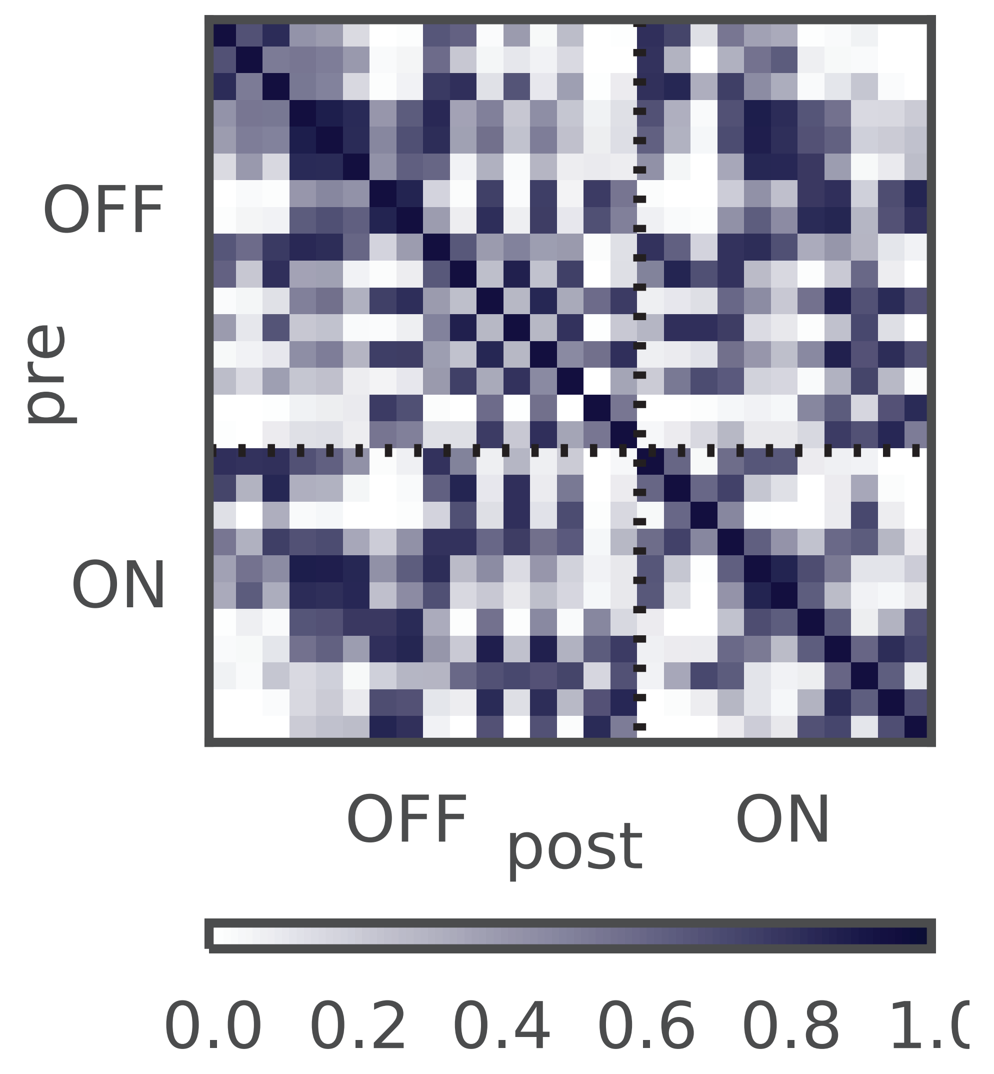

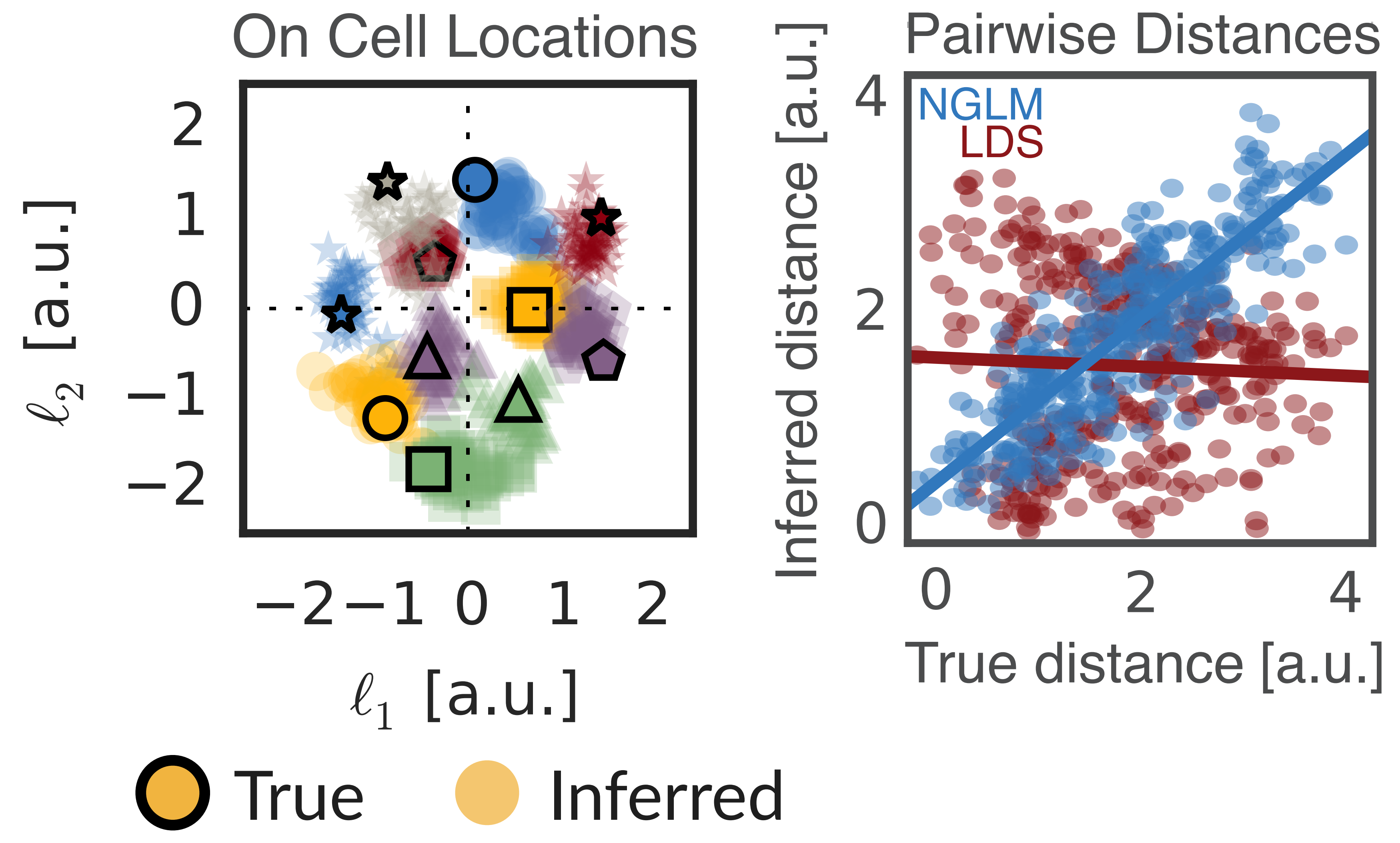

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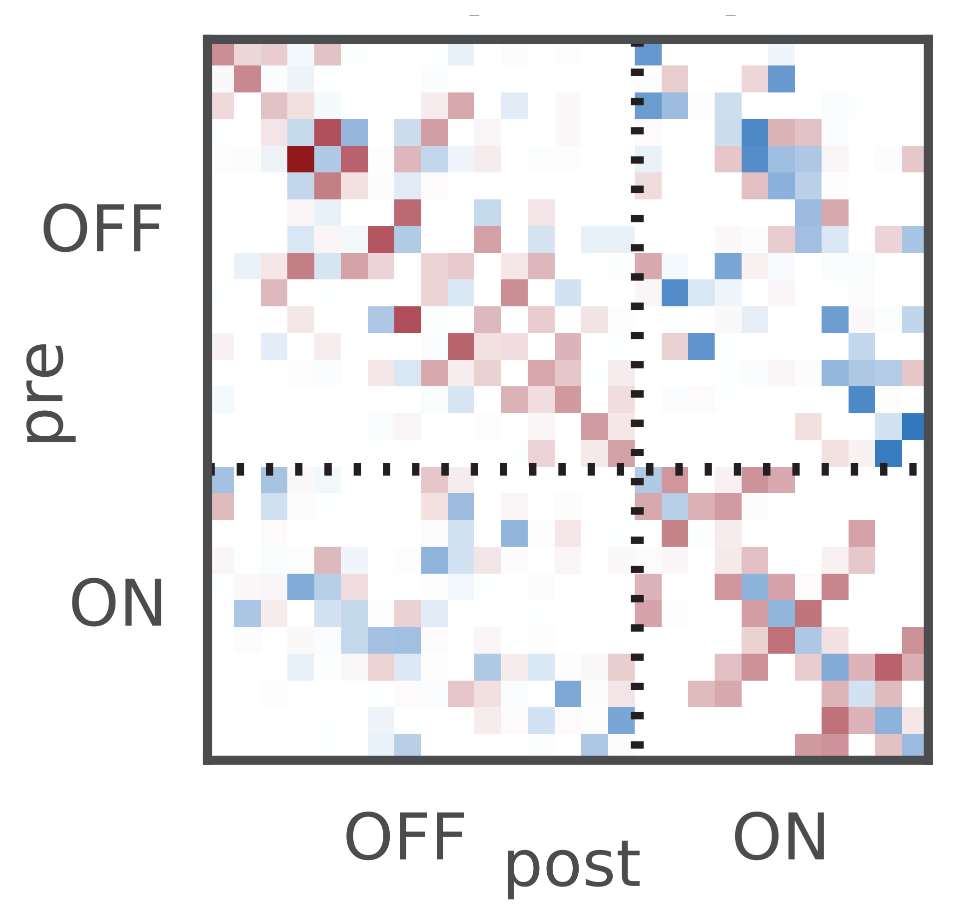
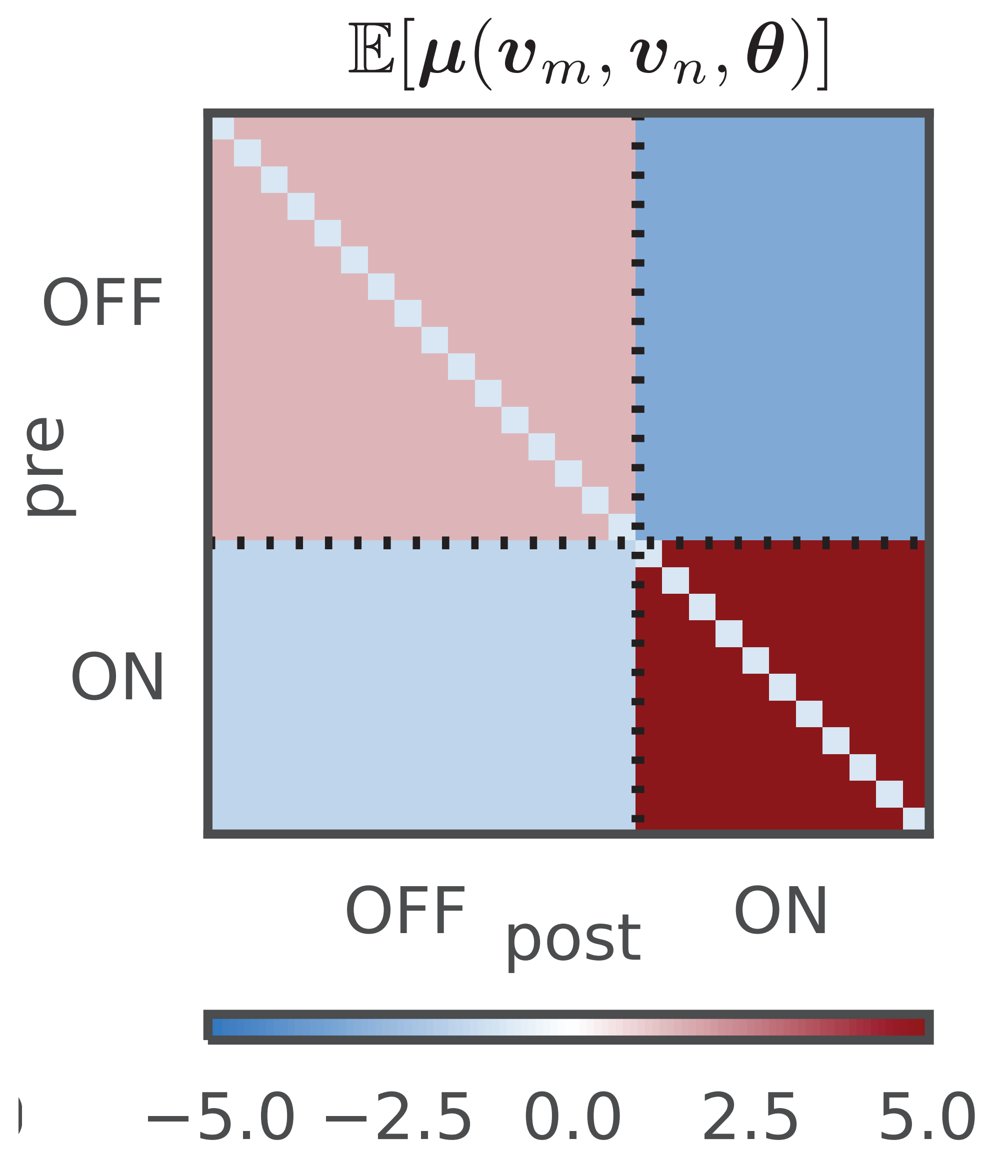
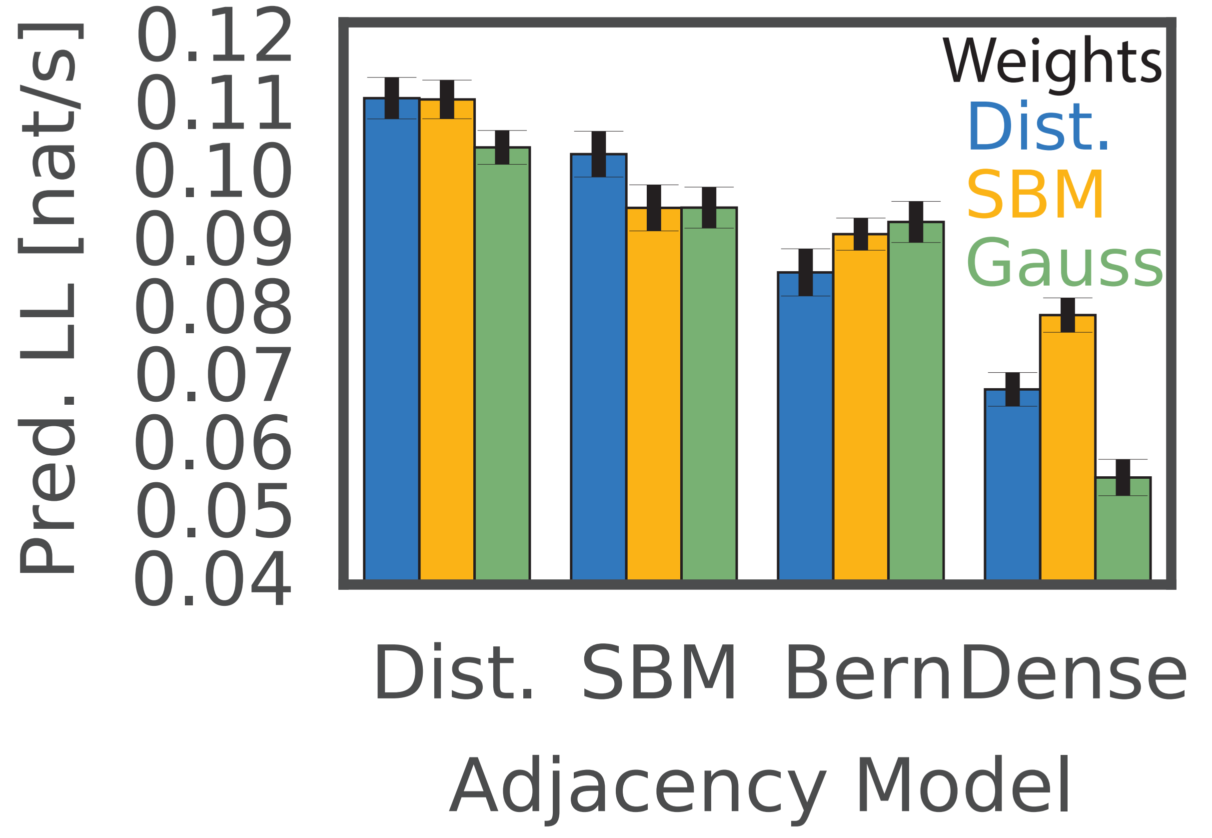




Model comparison



Linderman, Adams, Pillow (*NeurIPS*, 2016)

Encoding models of RGC responses

Going deeper

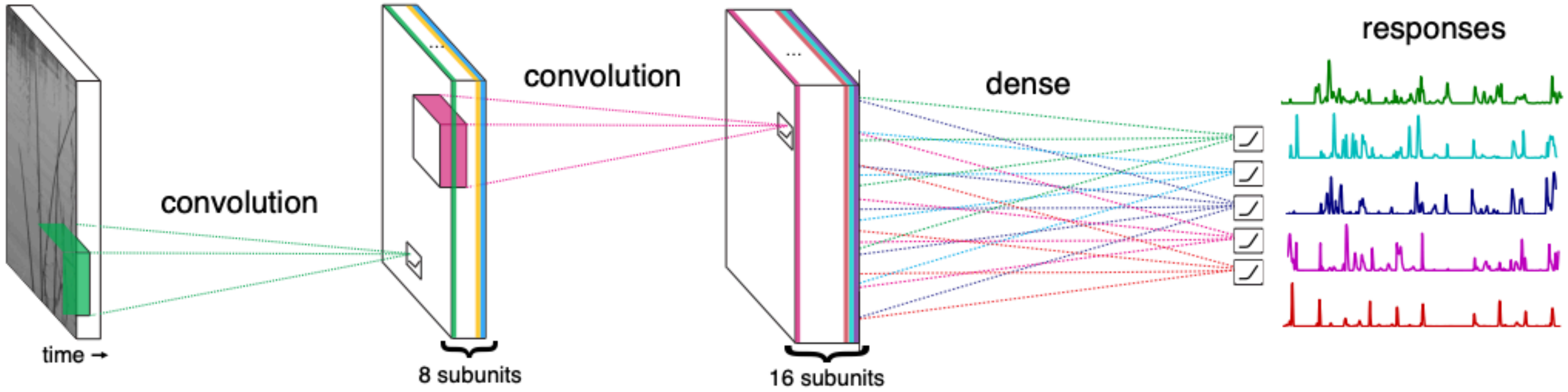


Figure 1: A schematic of the model architecture. The stimulus was convolved with 8 learned spatiotemporal filters whose activations were rectified. The second convolutional layer then projected the activity of these subunits through spatial filters onto 16 subunit types, whose activity was linearly combined and passed through a final soft rectifying nonlinearity to yield the predicted response.

McIntosh et al (*NeurIPS*, 2016)

Conclusion

- **Encoding models** predict the conditional distribution of neural responses to sensory stimuli.
    - Note, however, that we could have done the same thing by conditioning on (lagged) motor outputs instead.
- **Generalized linear models** are an effective means of modeling these conditional distributions.
- **Deep neural networks**, e.g. CNNs, essentially add multiple nonlinear layers to obtain features for estimating the conditional mean, rather than assuming its linear in the stimulus.

Further reading

- Dayan, Peter, and Laurence F. Abbott. Theoretical neuroscience: computational and mathematical modeling of neural systems. Computational Neuroscience Series, 2001.
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