

Generalized Linear Models (GLM)

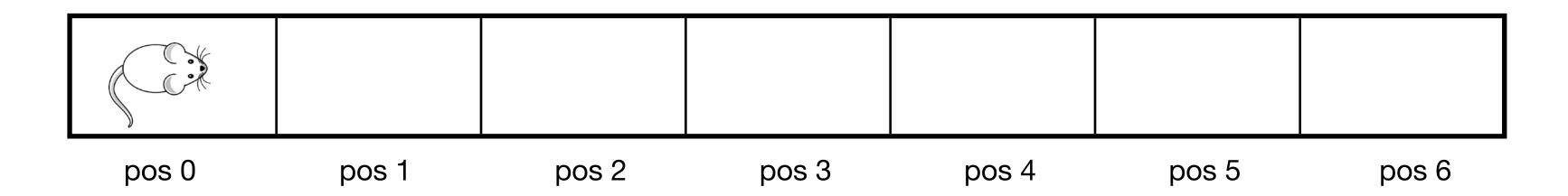
A conceptual introduction to GLM

Roadmap

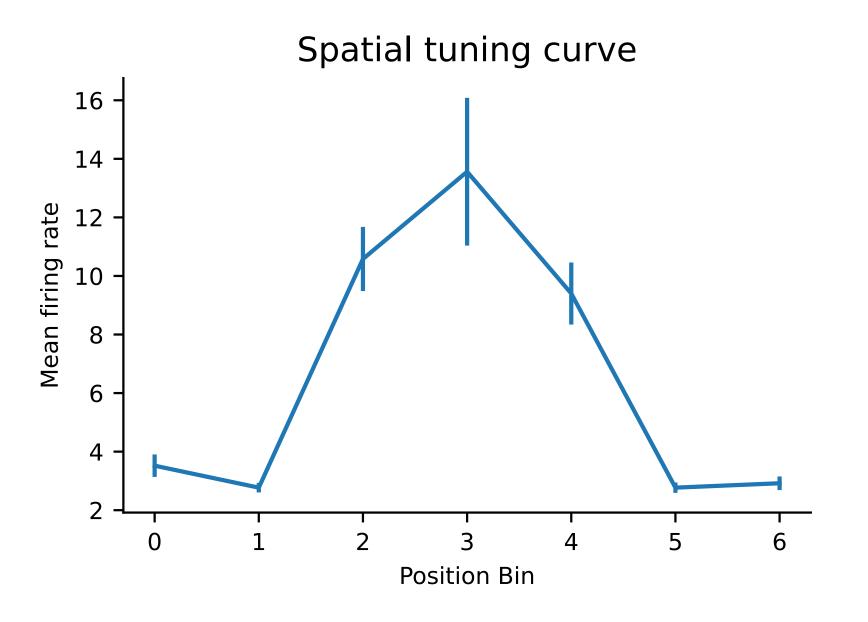
- Why models?
- What are GLMs?
- Why GLMs?
- What can I do with a GLM?
- What features can/should I use?
- Feature construction with Basis
- Overfitting
- Summary
- Today's roadmap

Why models? A hook

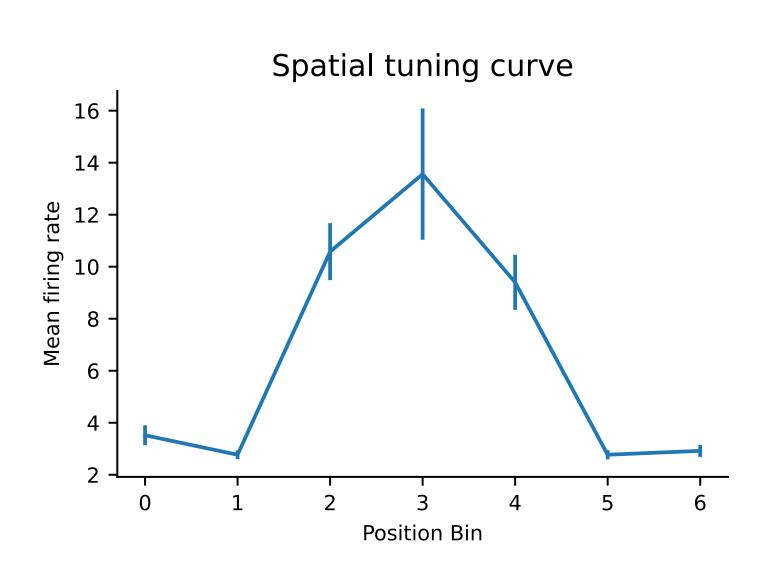
linear maze



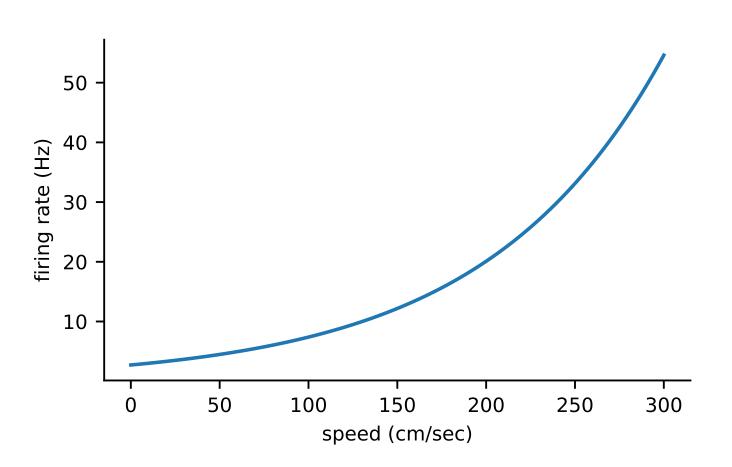
is this neuron encoding the mouse position?



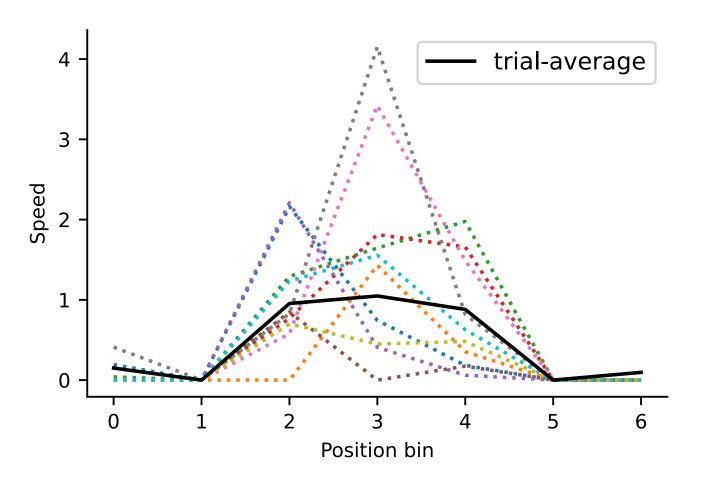
Why models? A hook



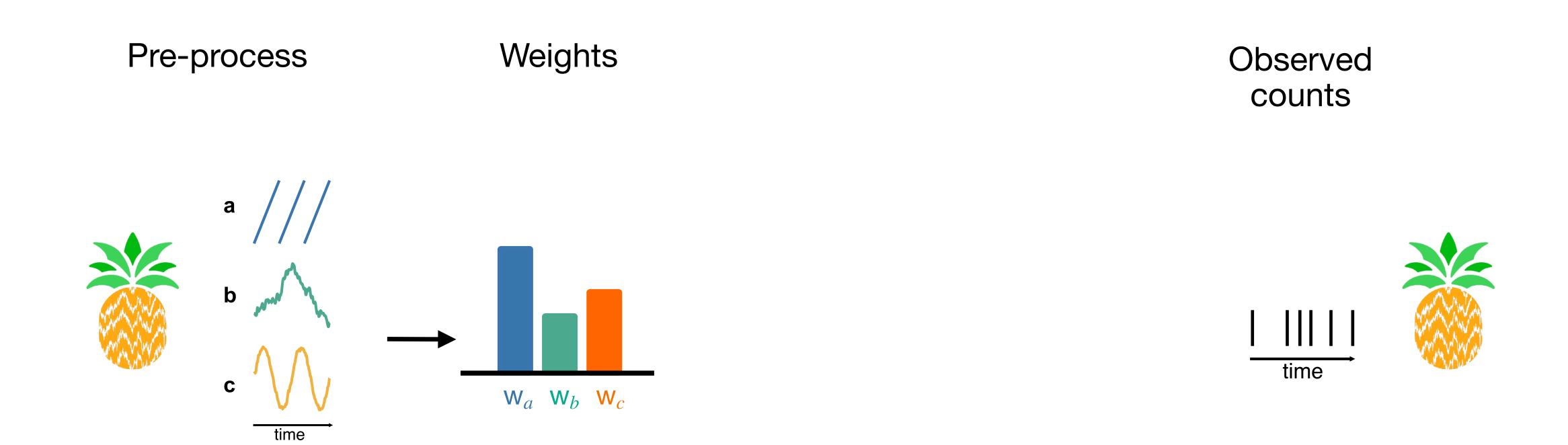
..actually, not!



position and speed are correlated

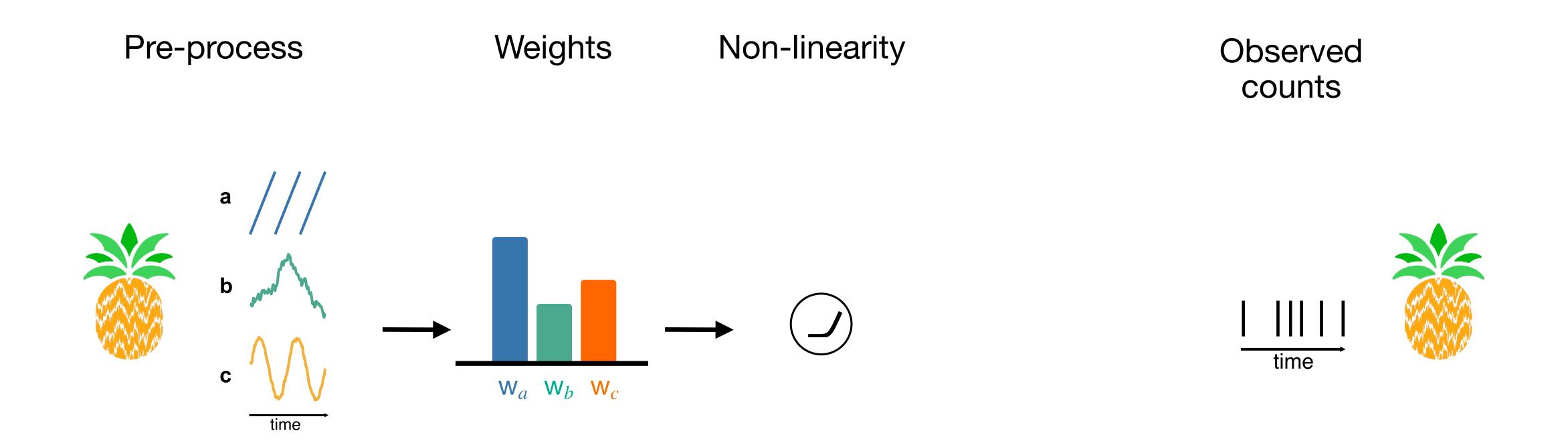


tuning functions don't tell you the whole story need better models!



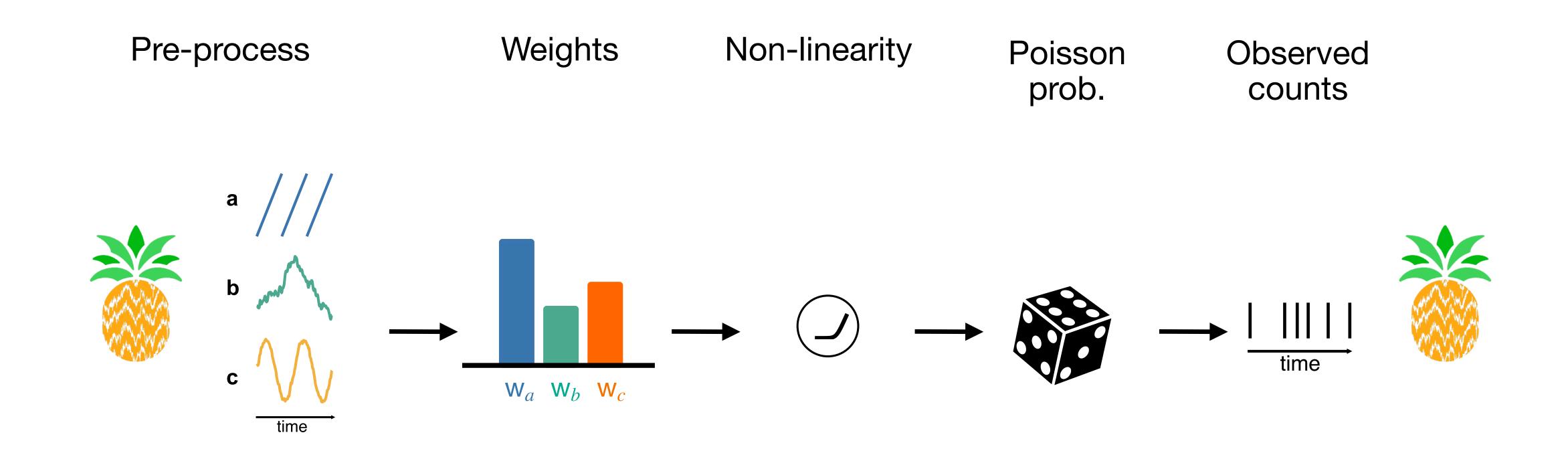
scale the inputs by some weights

$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$



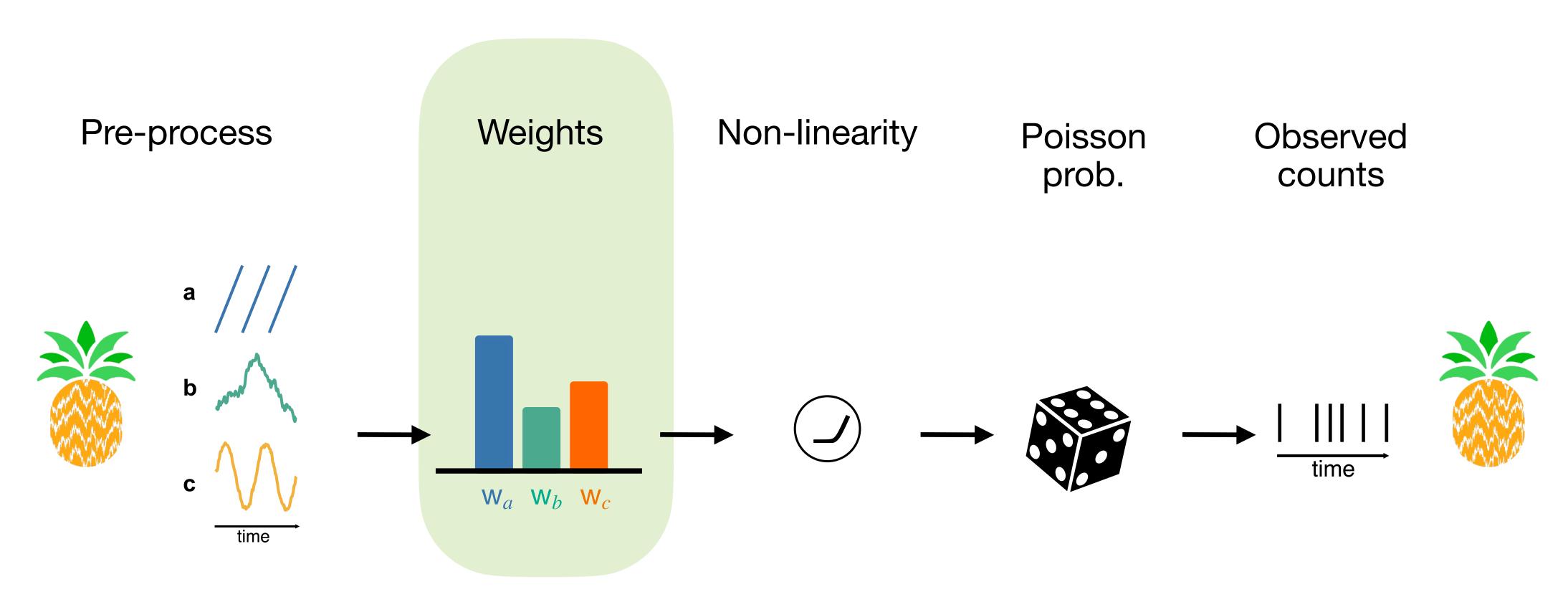
non-linearity to make the result positive

firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)



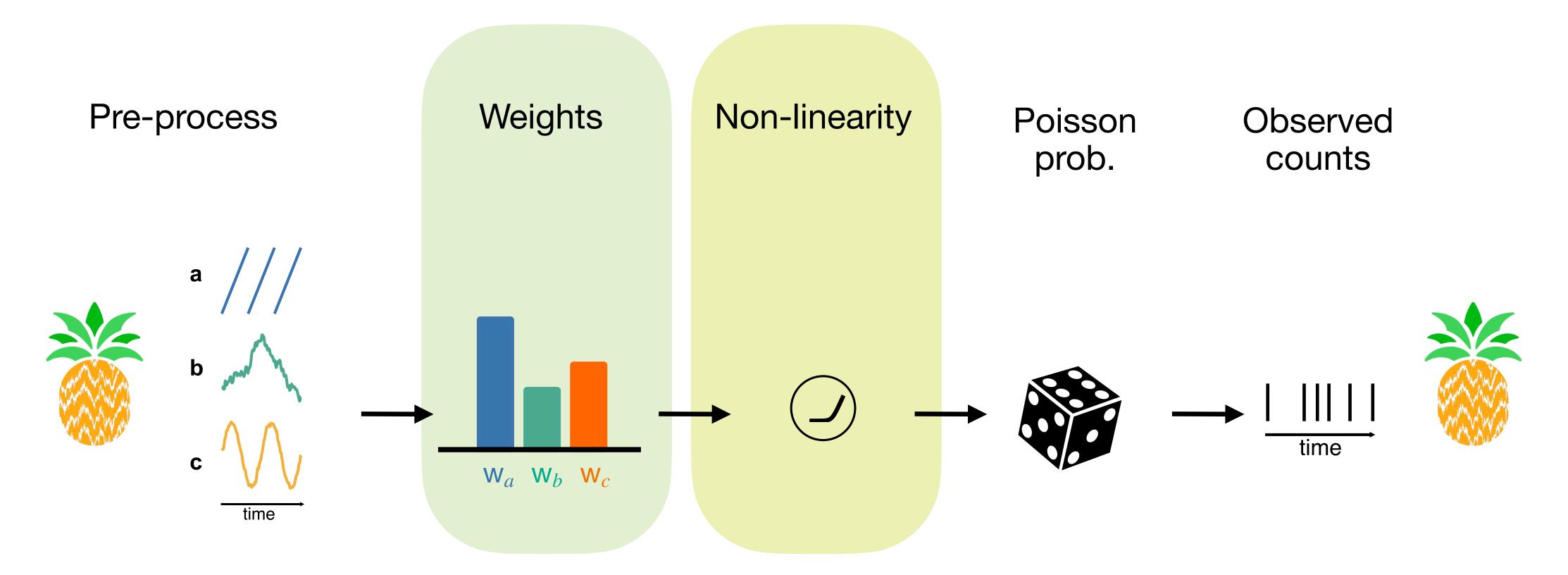
firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)

Linear



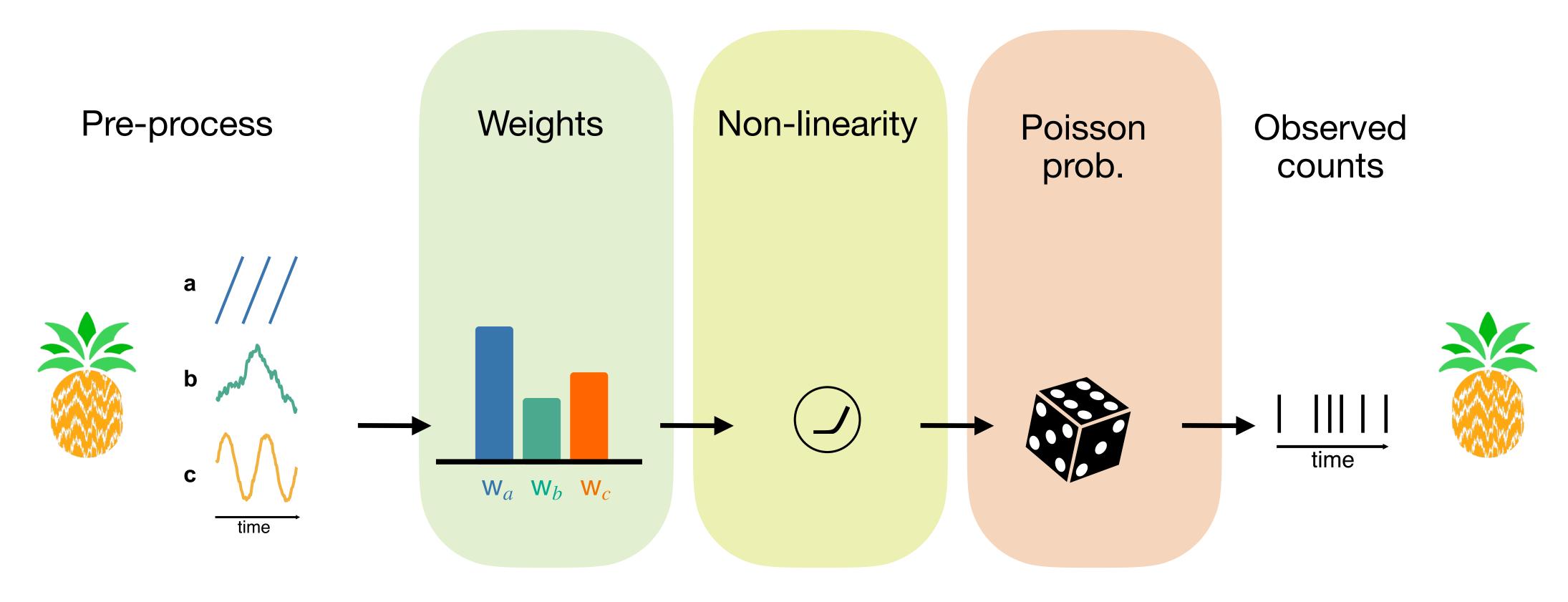
firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)

Linear - NonLinear

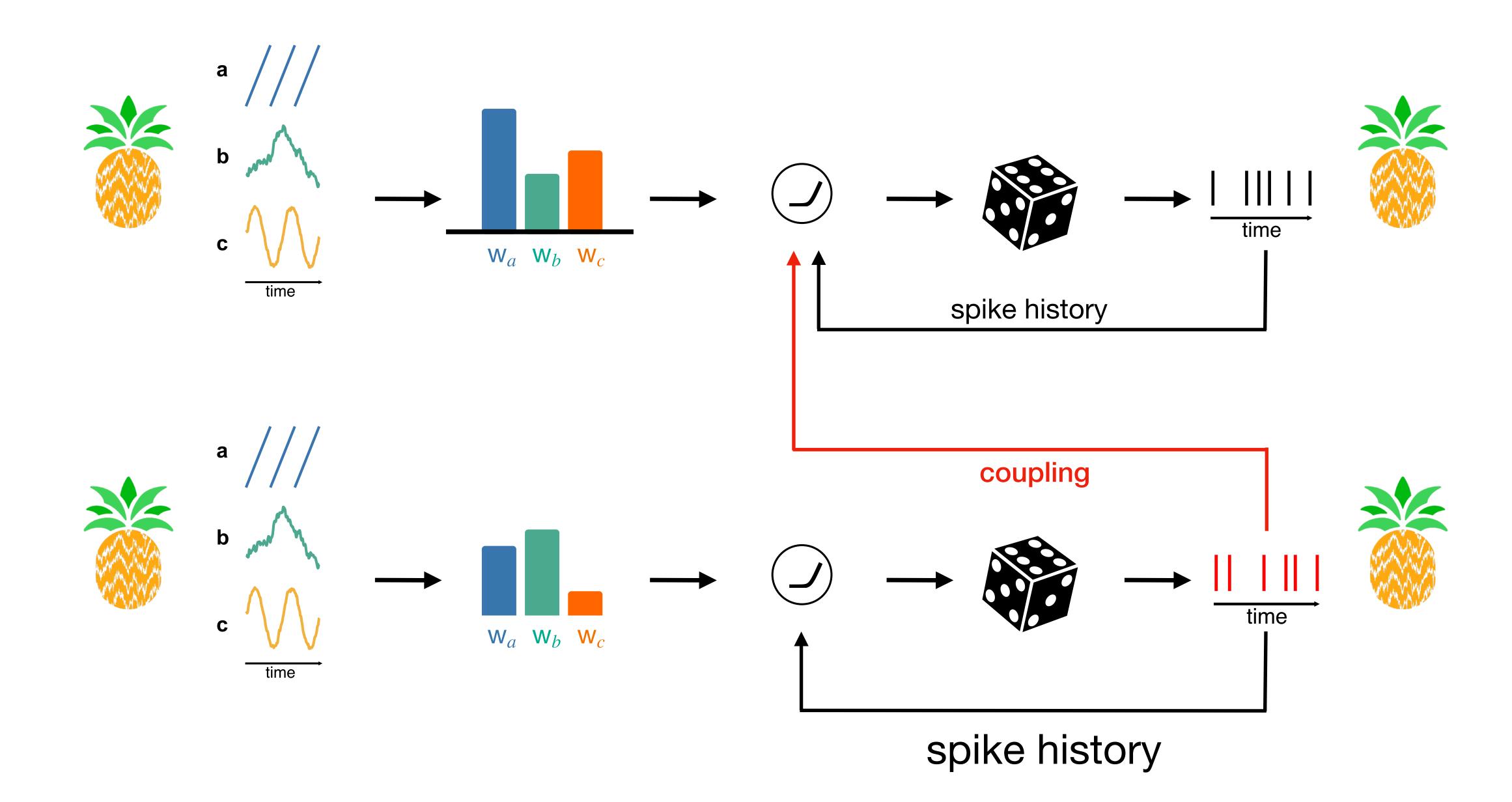


firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)

Linear - NonLinear - Poisson (LNP)



firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)



firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)

• a, b, c are called features or predictors

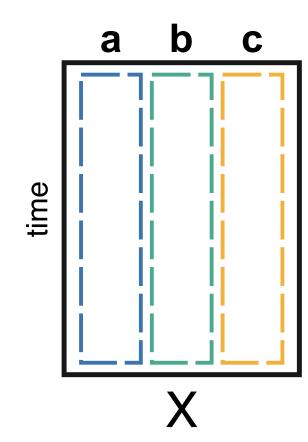
firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)

- a, b, c are called features or predictors
- \mathbf{w}_a , \mathbf{w}_b , \mathbf{w}_c are called weights or coefficients

firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)

- a, b, c are called features or predictors
- \mathbf{w}_a , \mathbf{w}_b , \mathbf{w}_c are called weights or coefficients
- Features are concatenated to form the design or feature matrix X = [a, b, c]

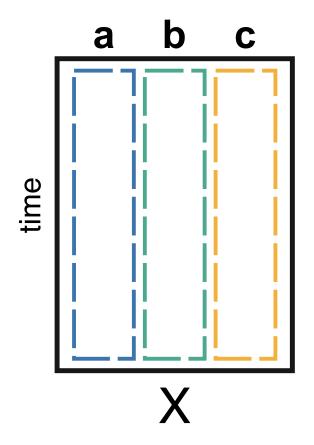
Design matrix



firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)

- · a, b, c are called features or predictors
- \mathbf{w}_a , \mathbf{w}_b , \mathbf{w}_c are called weights or coefficients
- Features are concatenated to form the design or feature matrix X = [a, b, c]
- The **likelihood** is the probability of observing spike counts given some features and weights.

Design matrix



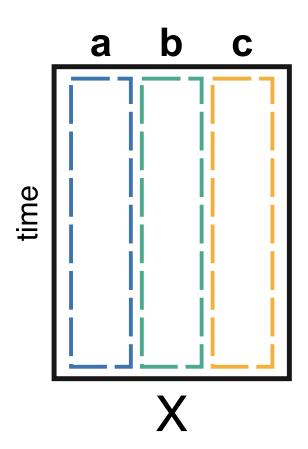
Likelihood

probability(spike count = $k \mid \mathbf{X}, \mathbf{w}$)

firing rate = exp(
$$\mathbf{a} \cdot \mathbf{w}_a + \mathbf{b} \cdot \mathbf{w}_b + \mathbf{c} \cdot \mathbf{w}_c$$
)

- a, b, c are called features or predictors
- \mathbf{w}_a , \mathbf{w}_b , \mathbf{w}_c are called weights or coefficients
- Features are concatenated to form the design or feature matrix X = [a, b, c]
- The **likelihood** is the probability of observing spike counts given some features and weights.
- The likelihood is a function of the weights because counts and features are fixed.

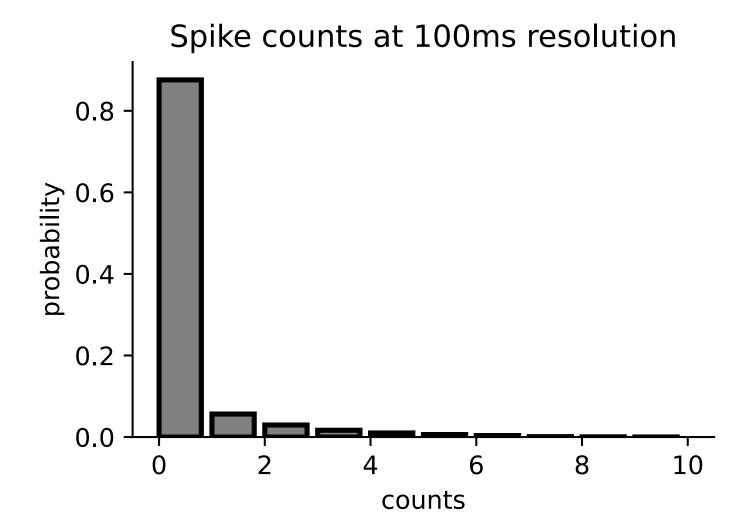
Design matrix



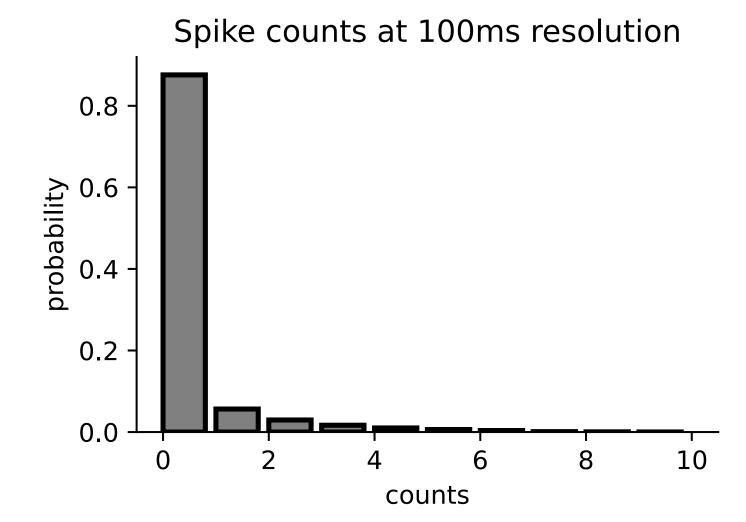
Likelihood

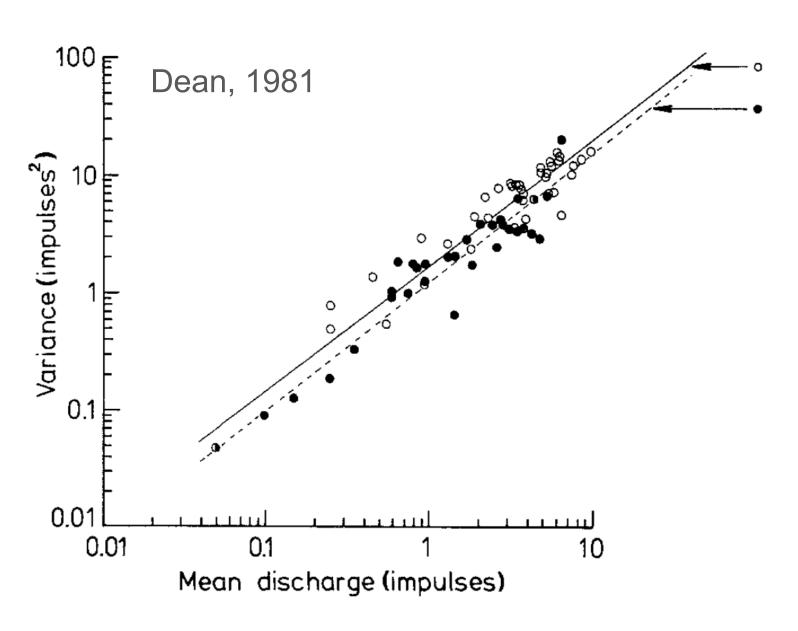
probability(spike count = $k \mid \mathbf{X}, \mathbf{w}$)

- 1. Why not linear regression? which assumes normality
 - A. Spike counts are non-Gaussian

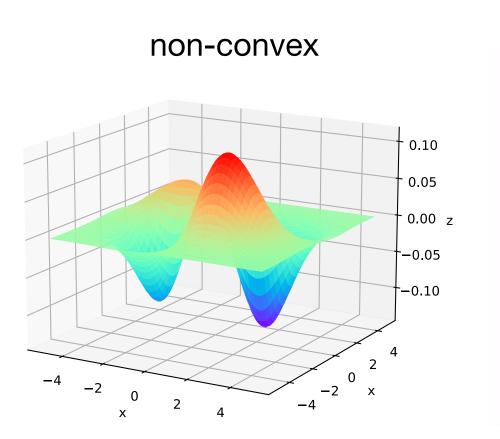


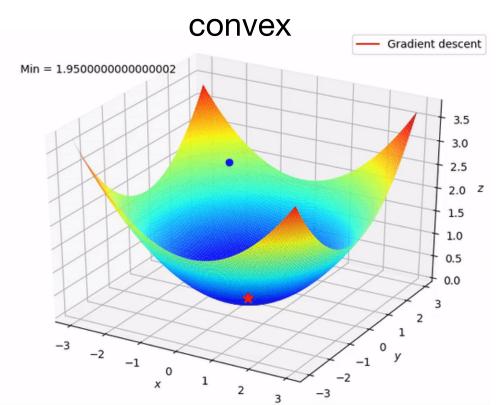
- 1. Why not linear regression? which assumes normality
 - A. Spike counts are non-Gaussian
 - B. Neural activity variance is non-constant



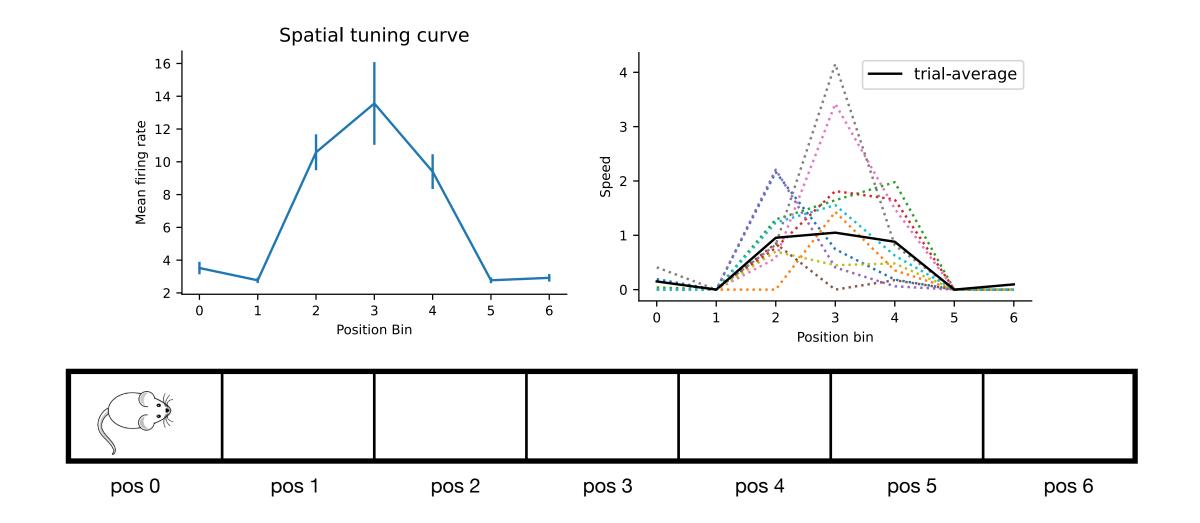


- 1. Why not linear regression? which assumes normality
 - A. Spike counts are non-Gaussian
 - B. Neural activity variance is non-constant
- 2. GLM are as **easy to fit** as linear regression convex, unique optimal solution





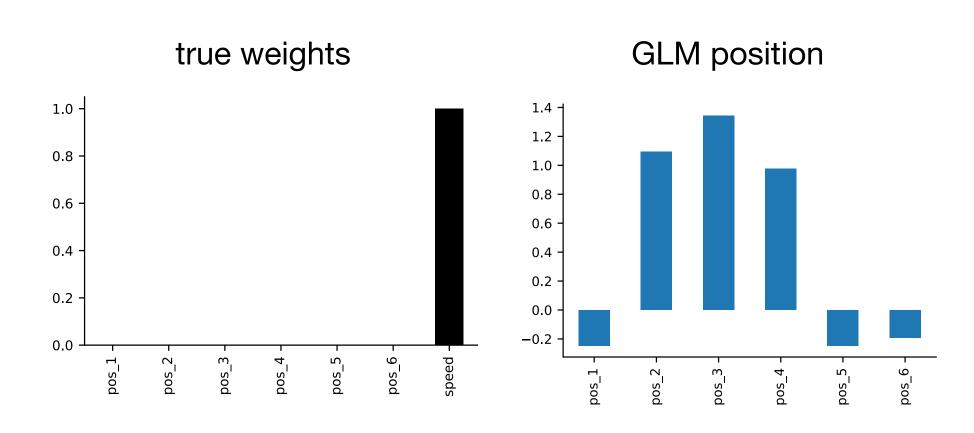
- 1. Why not linear regression? which assumes normality
 - A. Spike counts are non-Gaussian
 - B. Neural activity variance is non-constant
- 2. GLM are as **easy to fit** as linear regression convex, unique optimal solution
- 3. GLM are flexible model multiple inputs jointly



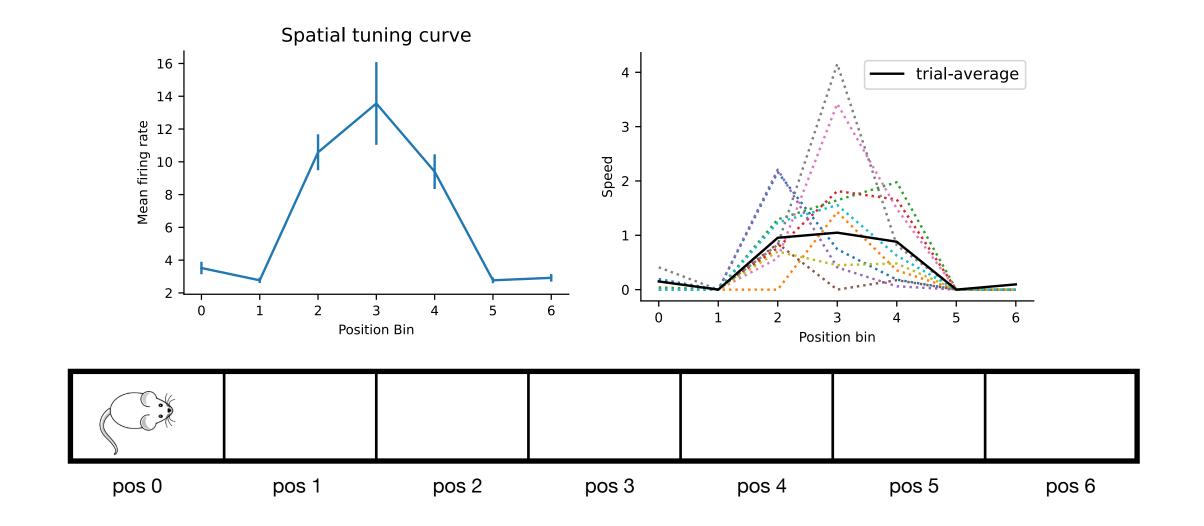
Firing rate model:

firing rate =
$$\exp(w_0 \cdot pos_0(t) + ... + w_6 \cdot pos_6(t))$$

$$pos_i(t) = \begin{cases} 1 & \text{if mouse is in position } i \text{ at time} t \\ 0 & \text{otherwise} \end{cases}$$



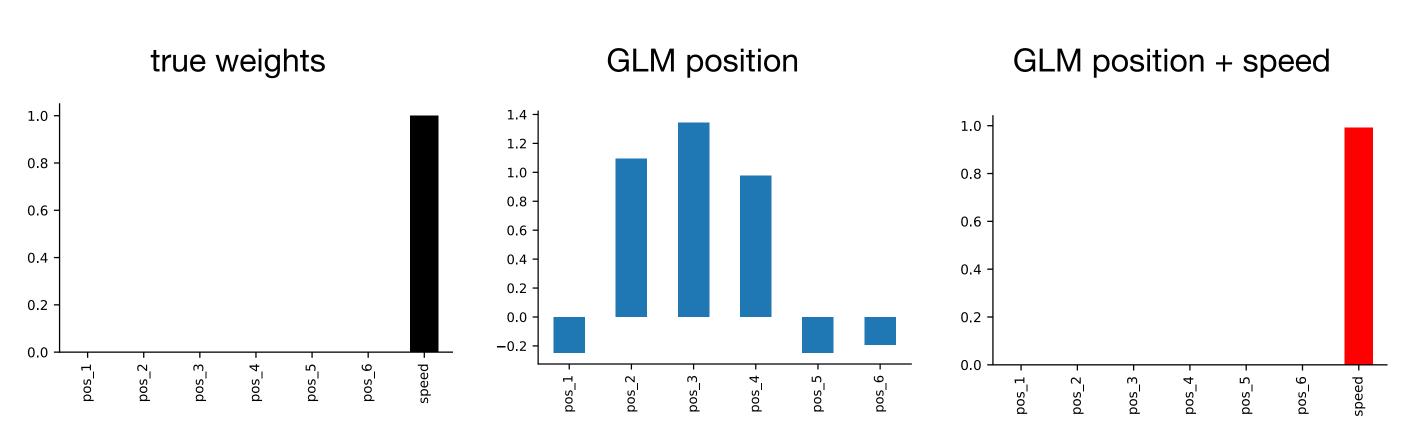
- 1. Why not linear regression? which assumes normality
 - A. Spike counts are non-Gaussian
 - B. Neural activity variance is non-constant
- 2. GLM are as **easy to fit** as linear regression convex, unique optimal solution
- 3. GLM are **flexible** model multiple inputs jointly



Firing rate model:

firing rate =
$$\exp(w_0 \cdot \text{pos}_0(t) + \dots + w_6 \cdot \text{pos}_6(t) + w_s \cdot \text{speed}(t))$$

$$pos_i(t) = \begin{cases} 1 & \text{if mouse is in position } i \text{ at time} t \\ 0 & \text{otherwise} \end{cases}$$



1. Model responses to high dimensional inputs images, videos, 2D/3D positions...

Pillow at al., 2008
Retina Macaques

Hardcastle et al., 2018
MEC mice

Gardner et al. 2019 *MEC rats*

Park et al. 2019 LIP Macaques

Weber & Pillow 2017 simulations

Peyrache et al., 2018 ADN mice

1. Model responses to high dimensional inputs images, videos, 2D/3D positions...

2. Non-linear responses

place cells, head-direction, grid cells

Pillow at al., 2008
Retina Macaques

Hardcastle et al., 2018
MEC mice

Gardner et al. 2019 MEC rats

Park et al. 2019 LIP Macaques

Weber & Pillow 2017 simulations

Peyrache et al., 2018 ADN mice

1. Model responses to high dimensional inputs images, videos, 2D/3D positions...

- 2. Non-linear responses place cells, head-direction, grid cells
- 3. Functional connectivity and other time-dependent effects

Pillow at al., 2008
Retina Macaques

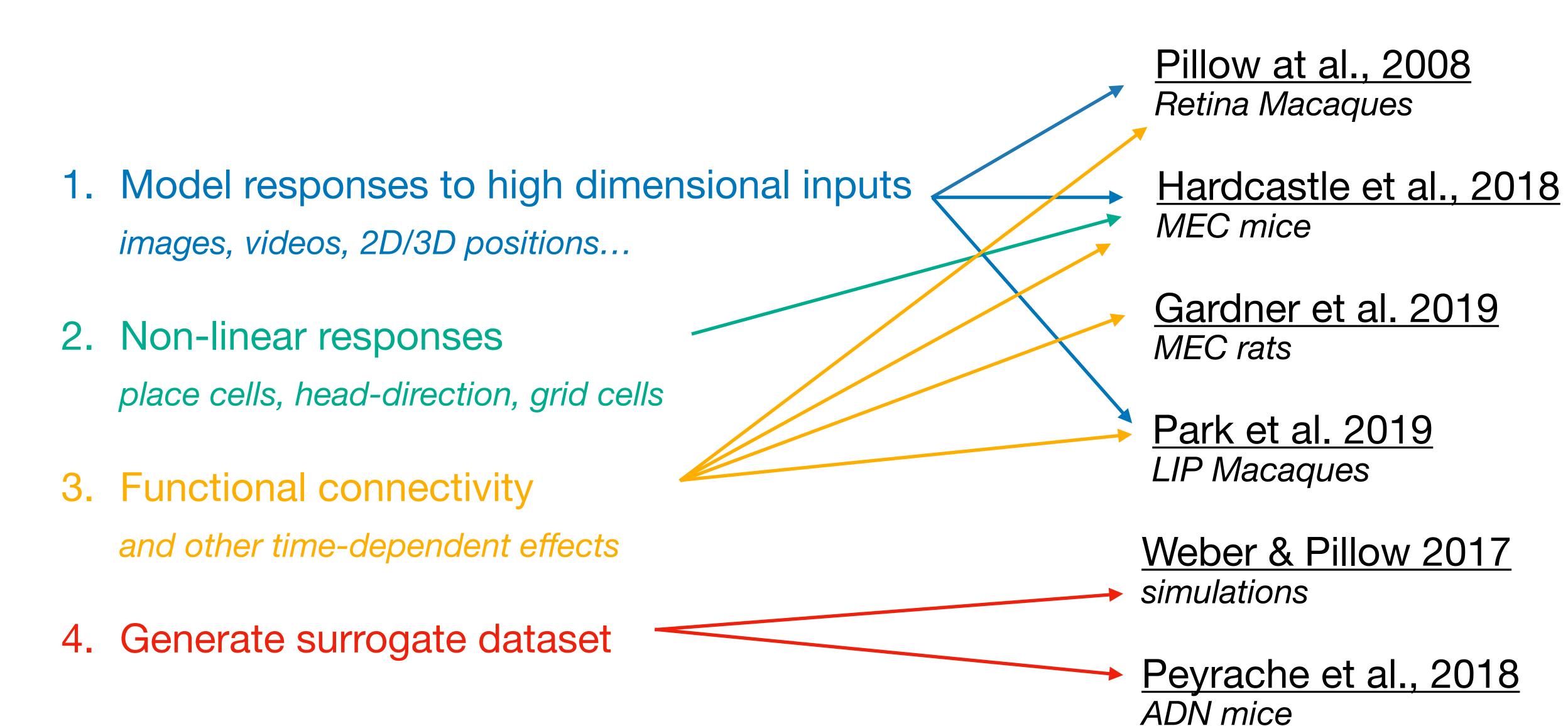
Hardcastle et al., 2018
MEC mice

Gardner et al. 2019 MEC rats

Park et al. 2019 LIP Macaques

Weber & Pillow 2017 simulations

Peyrache et al., 2018 ADN mice



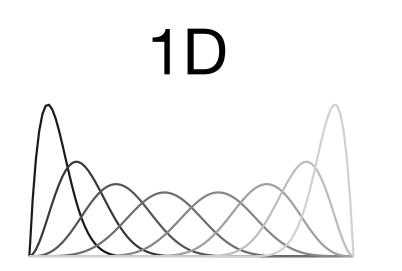
What features can/should I use?

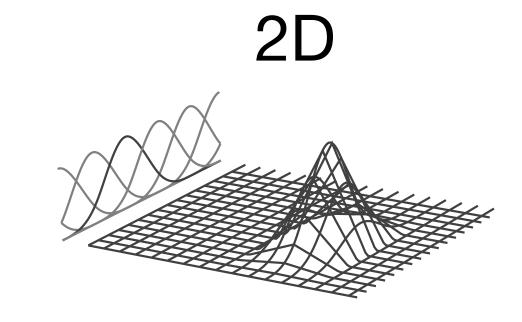
- It's up to the scientist!
- Choosing features is a way to formulate hypothesis about the neural encoding.
- Any fixed (not learned) transformation of your data is valid* (counting, binning, projecting into Principal Components, filtering, squaring ...)

^{*}as long as the resulting time axis matches that of the spike counts

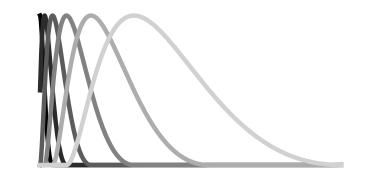
NeMoS provides the basis module for feature construction

- NeMoS provides the basis module for feature construction
- Basis are fixed non-linearities

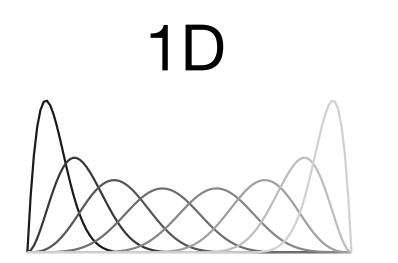


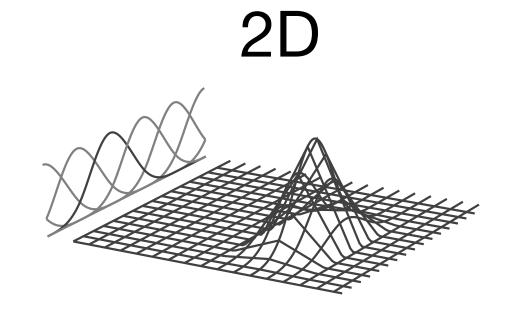


log-stretched

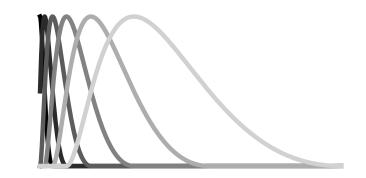


- NeMoS provides the basis module for feature construction
- Basis are fixed non-linearities
- Assume that firing rate varies smoothly/ gradually

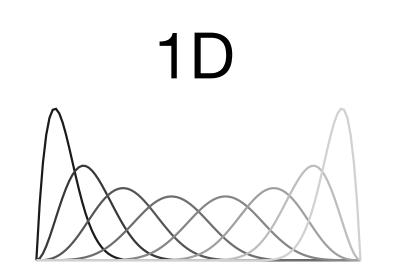


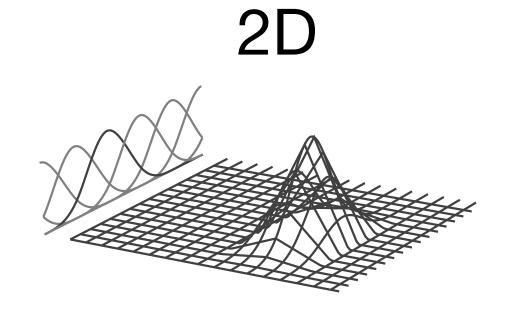


log-stretched

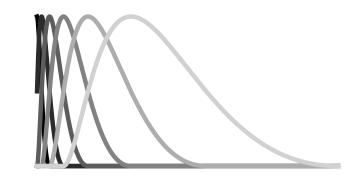


- NeMoS provides the basis module for feature construction
- Basis are fixed non-linearities
- Assume that firing rate varies smoothly/ gradually
- Used for:
 - 1. Reducing dimensionality
 - 2. Non-linear firing rate modulation
 - 3. Time dependent effects

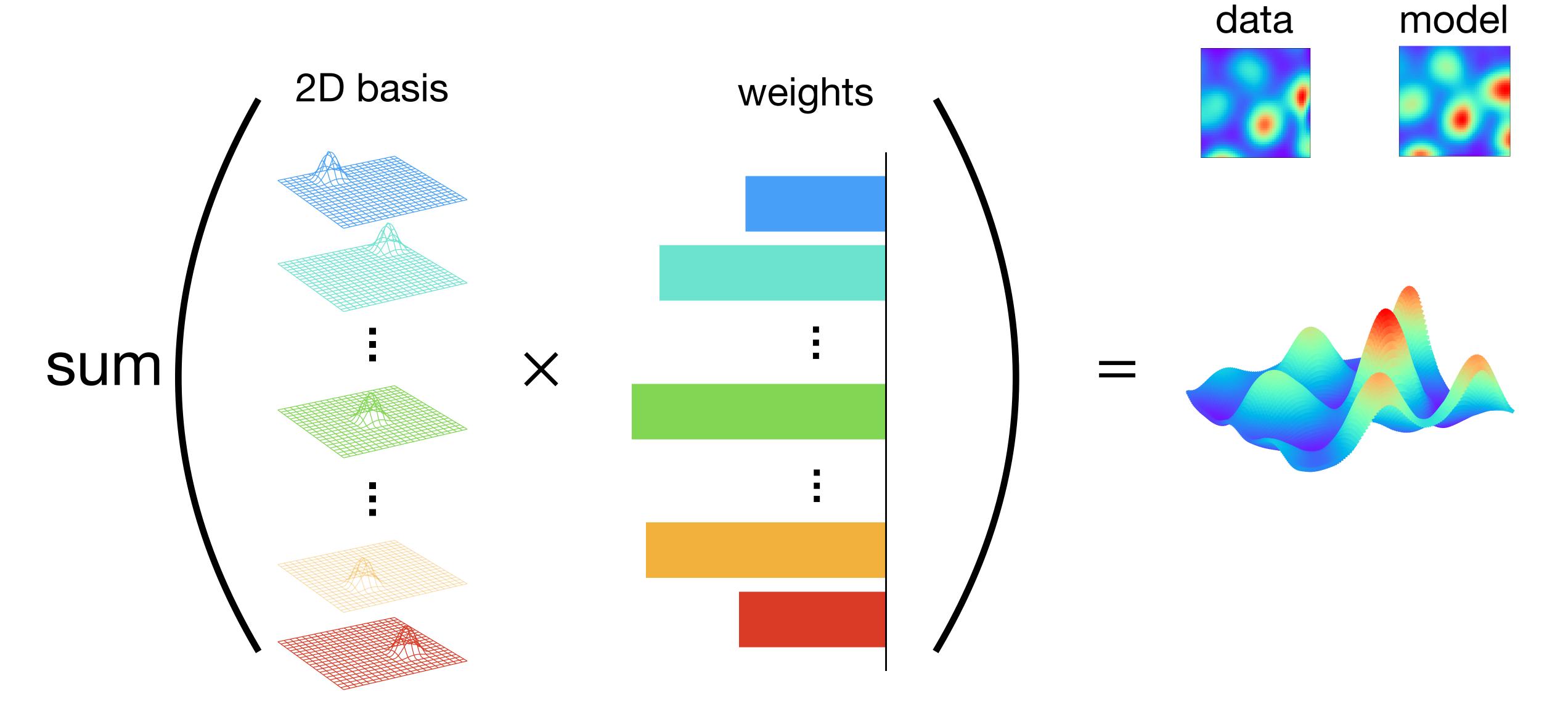




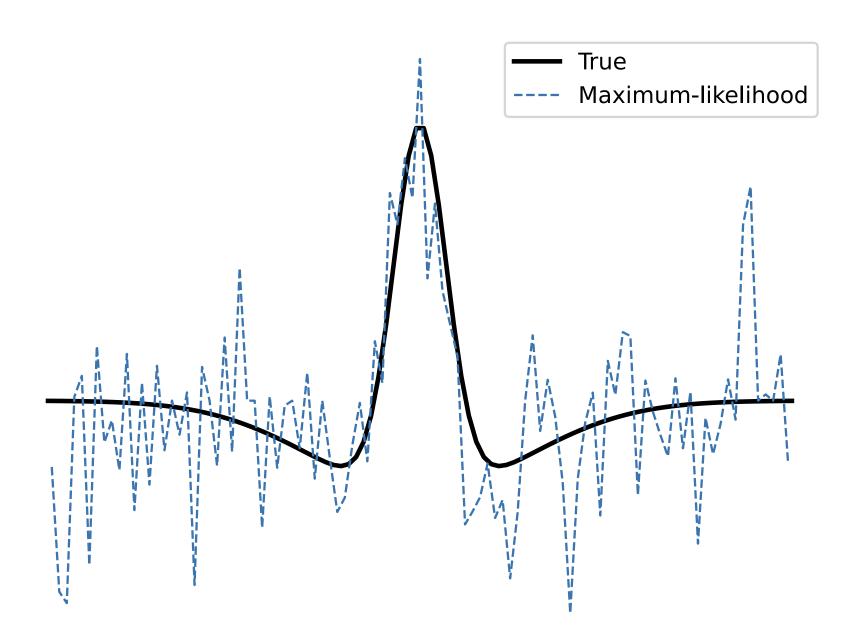
log-stretched



An Example: Grid Cell Modeling

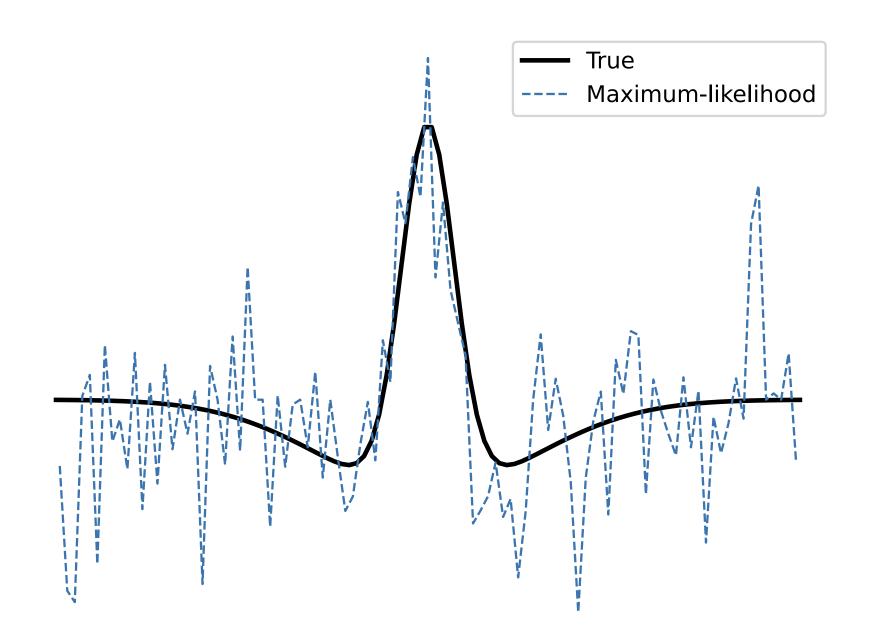


Maximum-Likelihood: $\max \log p(\text{counts} \mid \mathbf{X}, \mathbf{w})$



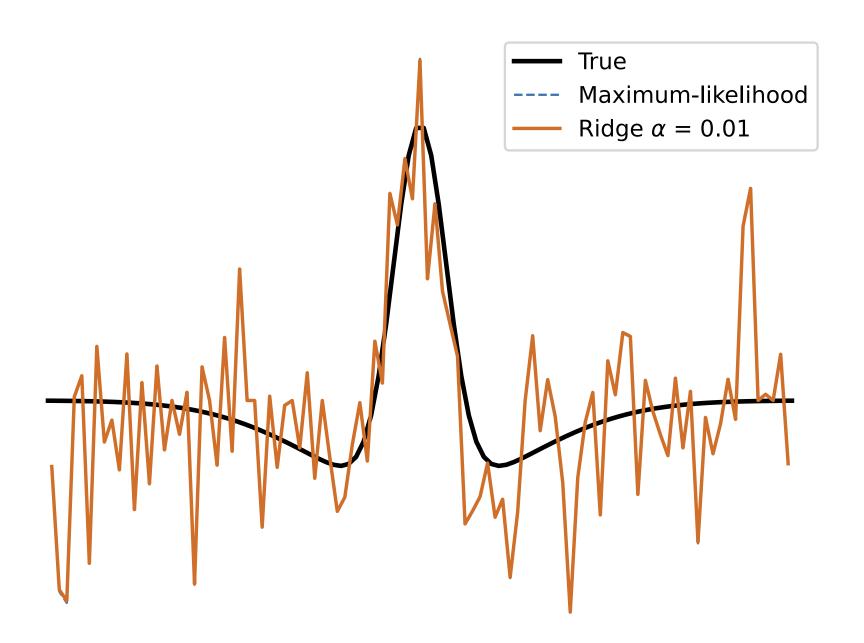
Maximum-Likelihood: $\max \log p(\text{counts} | \mathbf{X}, \mathbf{w})$

W



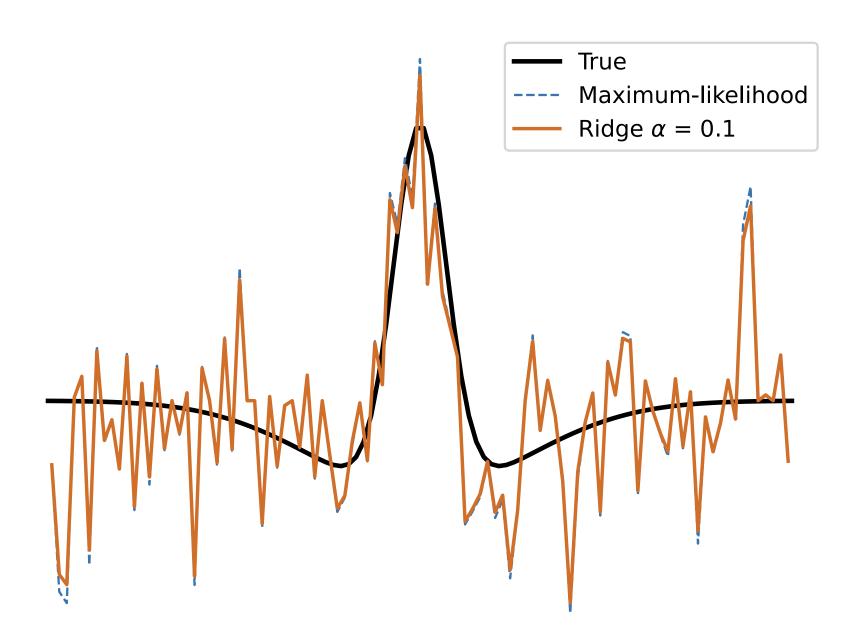
Maximum-Likelihood: $\max \log p(\text{counts} | \mathbf{X}, \mathbf{w})$

W



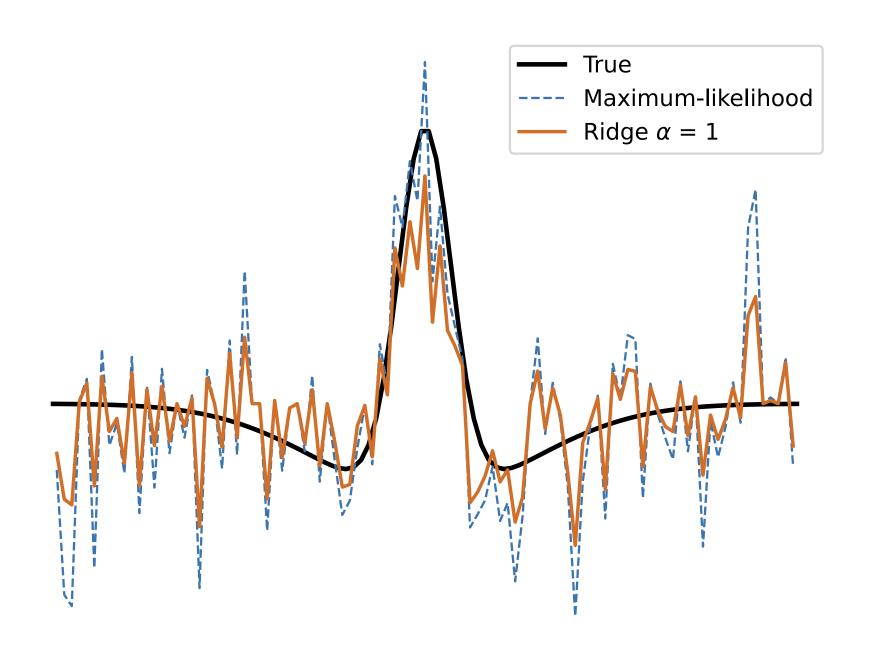
Maximum-Likelihood: $\max \log p(\text{counts} | \mathbf{X}, \mathbf{w})$

W



Maximum-Likelihood: $\max \log p(\text{counts} | \mathbf{X}, \mathbf{w})$

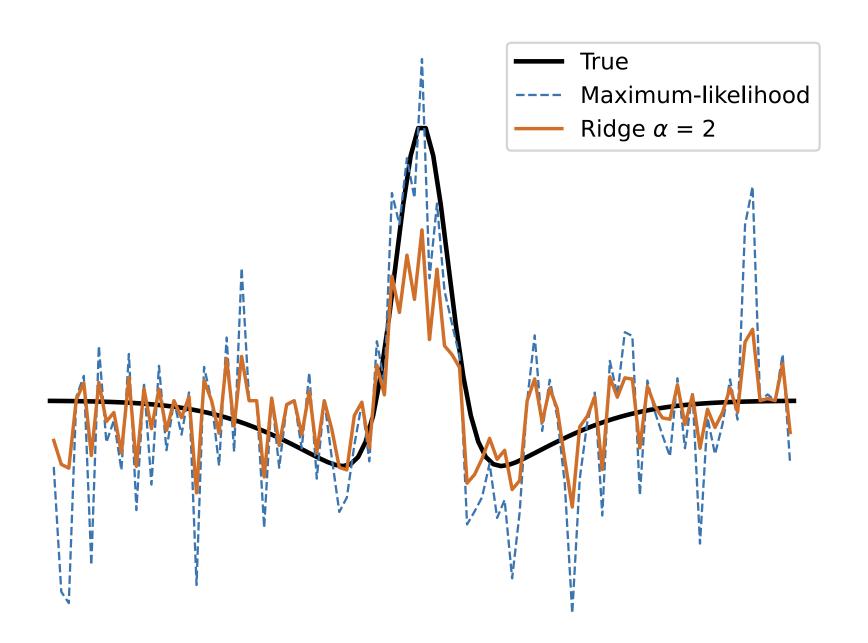
W



Maximum-Likelihood: $\max \log p(\text{counts} | \mathbf{X}, \mathbf{w})$

W

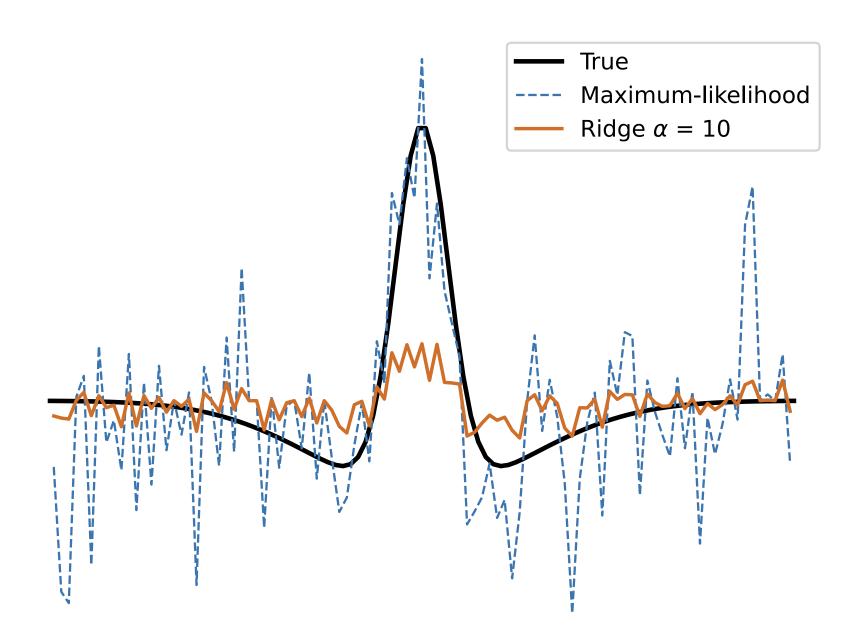
Ridge (L2): $\max_{\mathbf{w}} \log p(\text{counts} \mid \mathbf{X}, \mathbf{w}) - \alpha (w_1^2 + \ldots + w_n^2)$



Maximum-Likelihood: $\max \log p(\text{counts} | \mathbf{X}, \mathbf{w})$

W

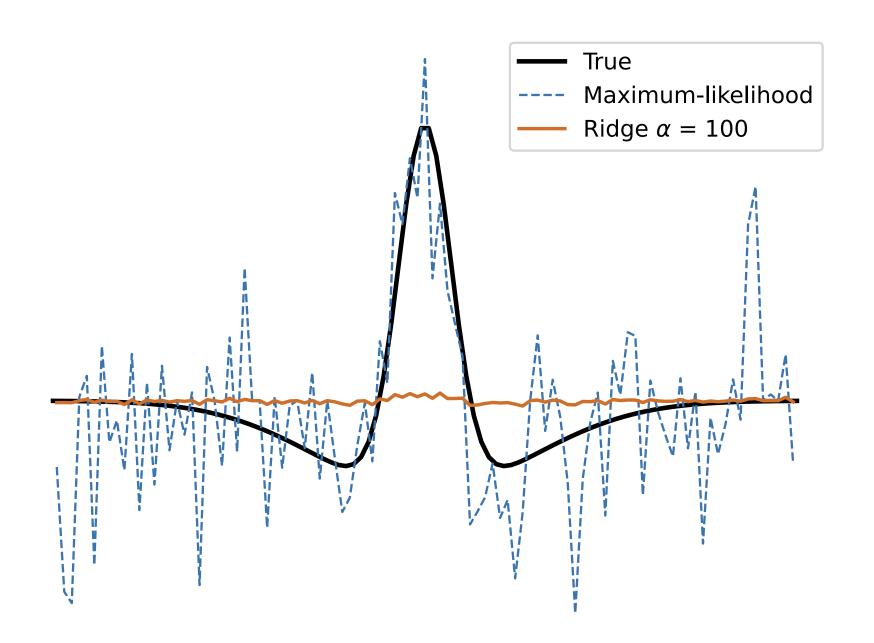
Ridge (L2): $\max_{\mathbf{w}} \log p(\text{counts} \mid \mathbf{X}, \mathbf{w}) - \alpha (w_1^2 + \ldots + w_n^2)$



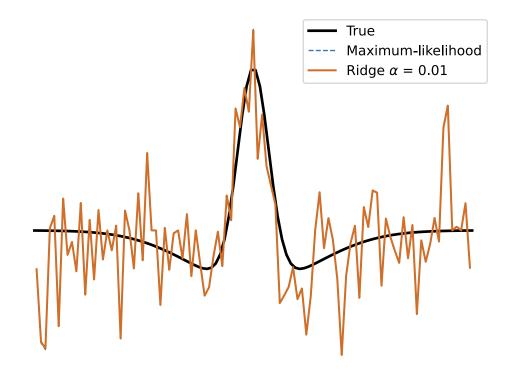
Maximum-Likelihood: $\max \log p(\text{counts} | \mathbf{X}, \mathbf{w})$

W

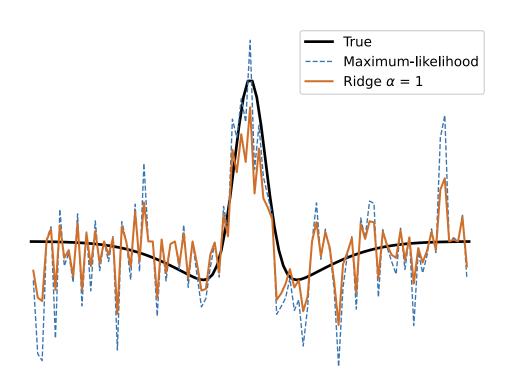
Ridge (L2): $\max_{\mathbf{w}} \log p(\text{counts} \mid \mathbf{X}, \mathbf{w}) - \alpha (w_1^2 + \ldots + w_n^2)$



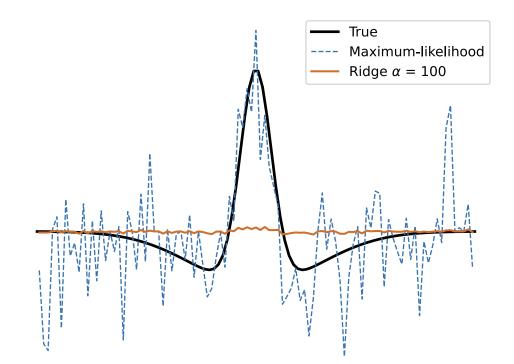
$$\alpha = 0.01$$



$$\alpha = 1$$



$$\alpha = 100$$



How do you select α ?

• Cross-validation: learn the weights on a subset of your data, test the model on another subset.

Other regularization approaches in NeMoS:

- Lasso (L1): Shrink coefficients to zero, enforcing sparsity. Feature selection.
- Group Lasso: Shrink groups of coefficients to zero.
 Group feature selection.

• Tuning functions do not fully characterize neural encoding.

- Tuning functions do not fully characterize neural encoding.
- GLMs retain many of the advantageous properties of linear regression (easy to fit, unique solution)

- Tuning functions do not fully characterize neural encoding.
- GLMs retain many of the advantageous properties of linear regression (easy to fit, unique solution)
- Better suited for non-normally distributed data.

- Tuning functions do not fully characterize neural encoding.
- GLMs retain many of the advantageous properties of linear regression (easy to fit, unique solution)
- Better suited for non-normally distributed data.
- Rich framework: model jointly many features, flexible design, regularization...

- 1. Current injection notebook:
 - Fit an LNP model to intracellular recordings from the Allen Brain Map.
 - Capture temporal effects using NeMoS' basis.

- 1. Current injection notebook:
 - Fit an LNP model to intracellular recordings from the Allen Brain Map.
 - Capture temporal effects using NeMoS' basis.

- 2. Head direction notebook:
 - Functional connectivity analysis of neurons in the anterodorsal thalamic nucleus (ADn).

- 1. Current injection notebook:
 - Fit an LNP model to intracellular recordings from the Allen Brain Map.
 - Capture temporal effects using NeMoS' basis.

- 2. Head direction notebook:
 - Functional connectivity analysis of neurons in the anterodorsal thalamic nucleus (ADn).

3. Advanced topics: regularization and model selection.

- 1. Current injection notebook:
 - Fit an LNP model to intracellular recordings from the Allen Brain Map.
 - Capture temporal effects using NeMoS' basis.

- 2. Head direction notebook:
 - Functional connectivity analysis of neurons in the anterodorsal thalamic nucleus (ADn).

3. Advanced topics: regularization and model selection.

4. Work on your own data (or keep going with your favorite notebook).