Machine Learning Methods for Neural Data Analysis

Lecture 4: Spike Sorting

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STATS 220/320 (NBIO220, CS339N). Winter 2023.

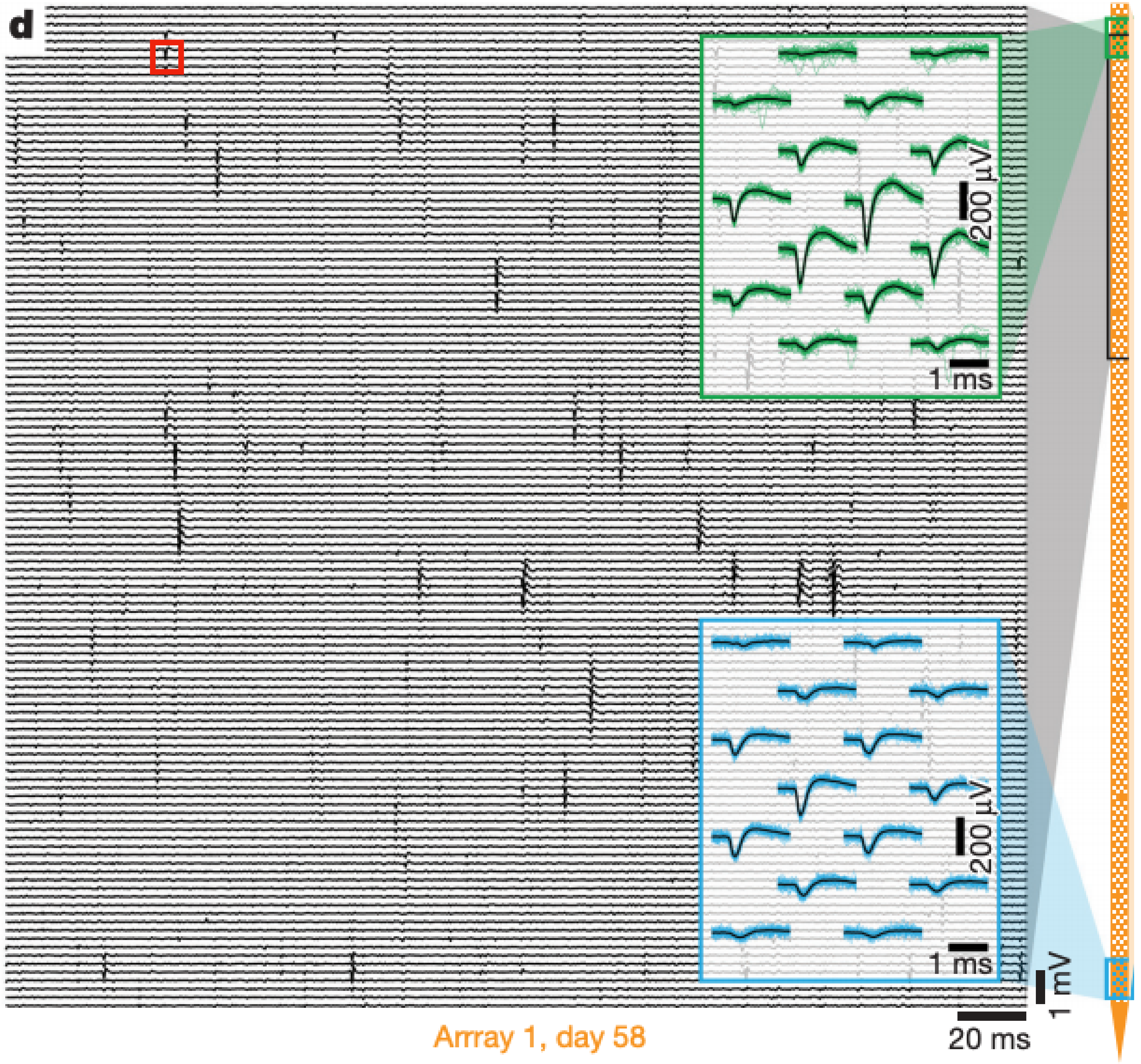
Announcements

- Course Website: https://slinderman.github.io/stats320
- Ed: I'll add auditors to Canvas and resync. If you're not on Ed yet, please let me know.
- Lab 0 will not graded, but it should be a good warm-up.
- Lab 1 is this Friday! We will implement the model in the **Spike Sorting by Deconvolution** notes.
  - Default plan is to come to this room, but stay tuned for announcements on Canvas/Ed!

Simple Spike Sorting

A simple probabilistic model

- Start with a zoomed-out view of average voltage in relatively large time bins (e.g. 2ms).
- Let N be the number of channels.
- Let T be the number of 2ms time bins.
- Let $x_{n,t}$ be the average voltage on channel n in time bin t.
- At this resolution, spikes can be contained to a single bin.



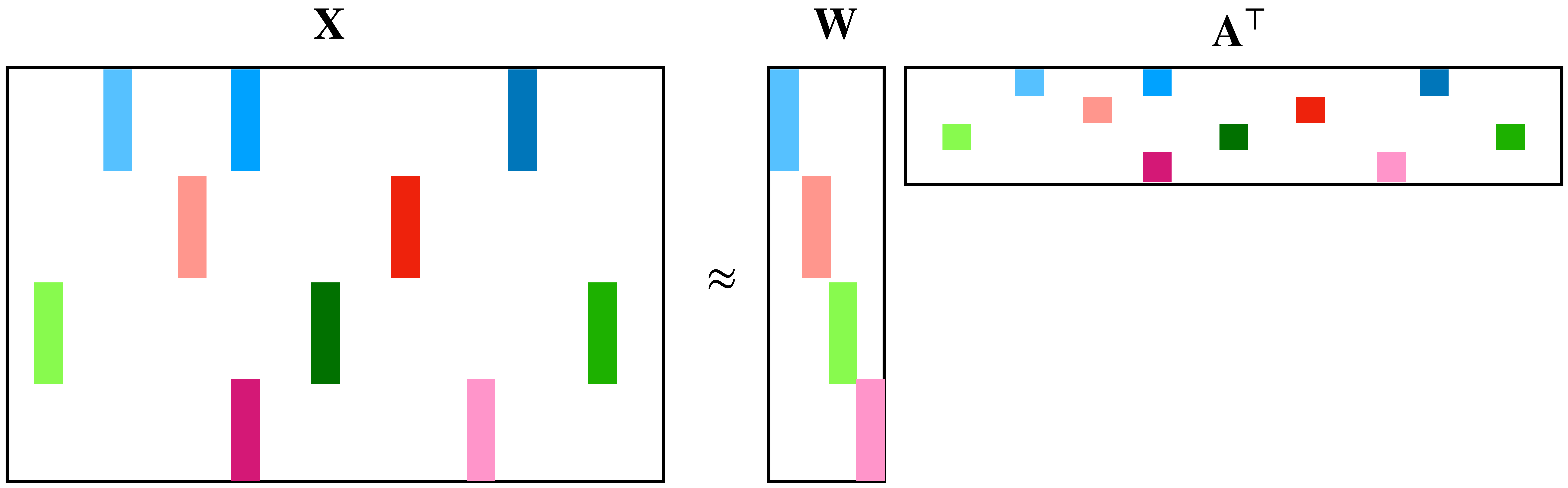
A simple probabilistic model

Assumptions

- There are K neurons. When neuron k spikes it produces a **waveform** $\mathbf{w}_k = (w_{k,1}, \ldots, w_{k,N}) \in \mathbb{R}^N$
- Let $\mathbf{a}_k = (a_{k,1}, \ldots, a_{k,T}) \in \mathbb{R}_+^T$ denote the time series of spike **amplitudes** for neuron k.
    - Since neurons spike only a few times a second, amplitudes are mostly zero.
    - Amplitudes are non-negative.
- If two neurons spike at the same, waveforms add.
- Voltage recordings have additive noise.

A simple probabilistic model

Matrix factorization perspective



A simple probabilistic model

Accounting for scale invariance

- Notice that the model is **invariant to rescaling.**
  - Multiple $\mathbf{a}_k$ by constant $c > 0$ and scale $\mathbf{w}_k$ by c^{-1}.
- We can remove this degree of freedom by forcing $\|\mathbf{w}_k\|_2 = 1$; e.g., with a **uniform prior** on the unit hypersphere,

$$\mathbf{w}_k \sim \mathrm{Unif}(\mathbb{S}_{N-1})$$

- where $\mathbb{S}_{N-1} = \left\{\mathbf{u} : \mathbf{u} \in \mathbb{R}^N \text{ and } \|\mathbf{u}\|_2 = 1\right\}$

A simple probabilistic model

Prior on amplitudes

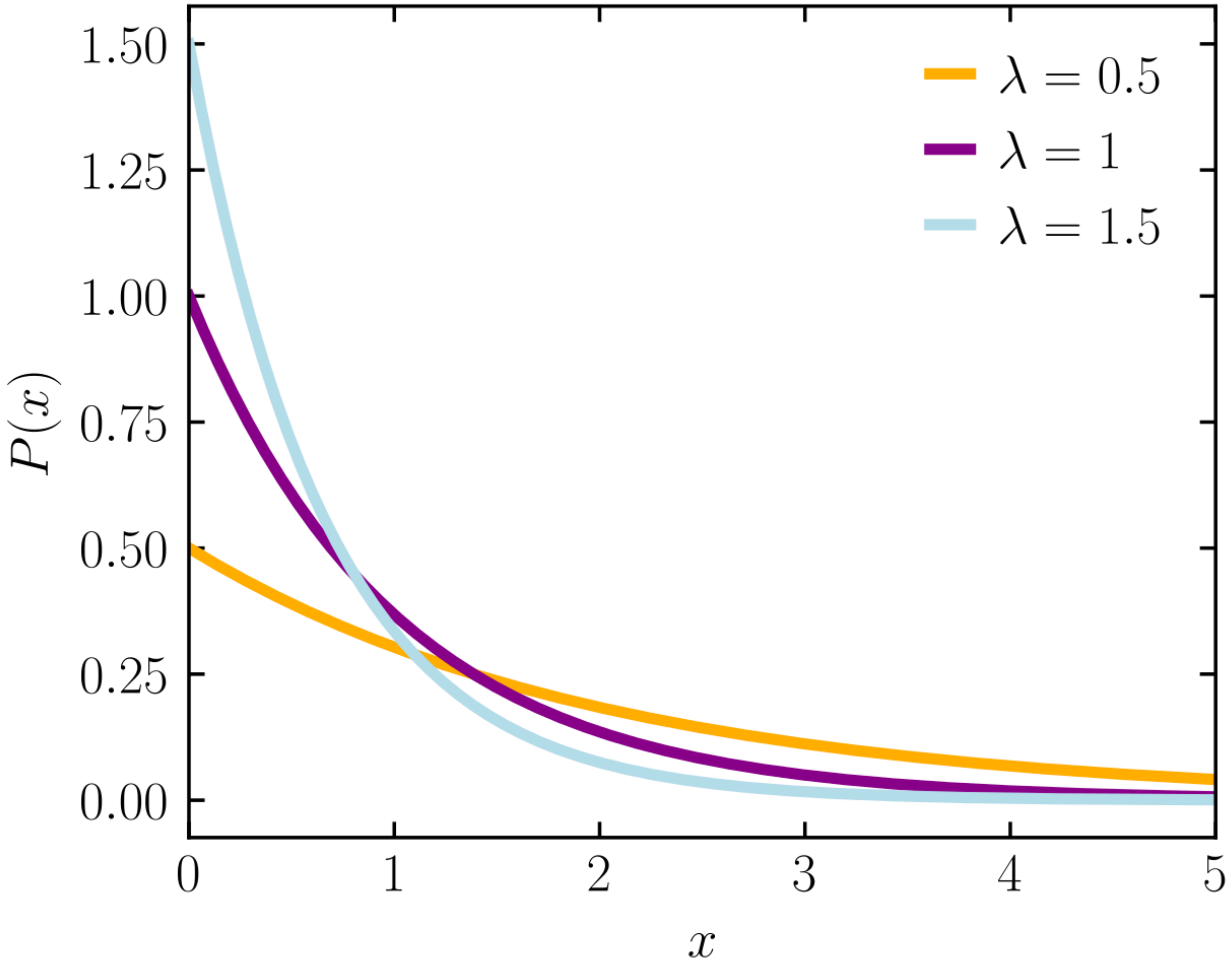
- To complete the model, we place an **exponential** prior on amplitudes,

$$a_{k,t} \sim \mathrm{Exp}(\lambda)$$

where λ is the inverse-scale (aka rate) parameter.

- It's pdf is $\mathrm{Exp}(x; \lambda) = \lambda e^{-\lambda x}$.

- As we will see, this prior will lead to **sparse** estimates.



https://en.wikipedia.org/wiki/Exponential_distribution

A simple probabilistic model

Noise model

- So far, $\mathbf{X} = \mathbf{W}\mathbf{A}^\top + \mathbf{E}$ where $\mathbf{E} = [[\epsilon_{n,t}]]$ is a matrix of "noise." How to model the noise?

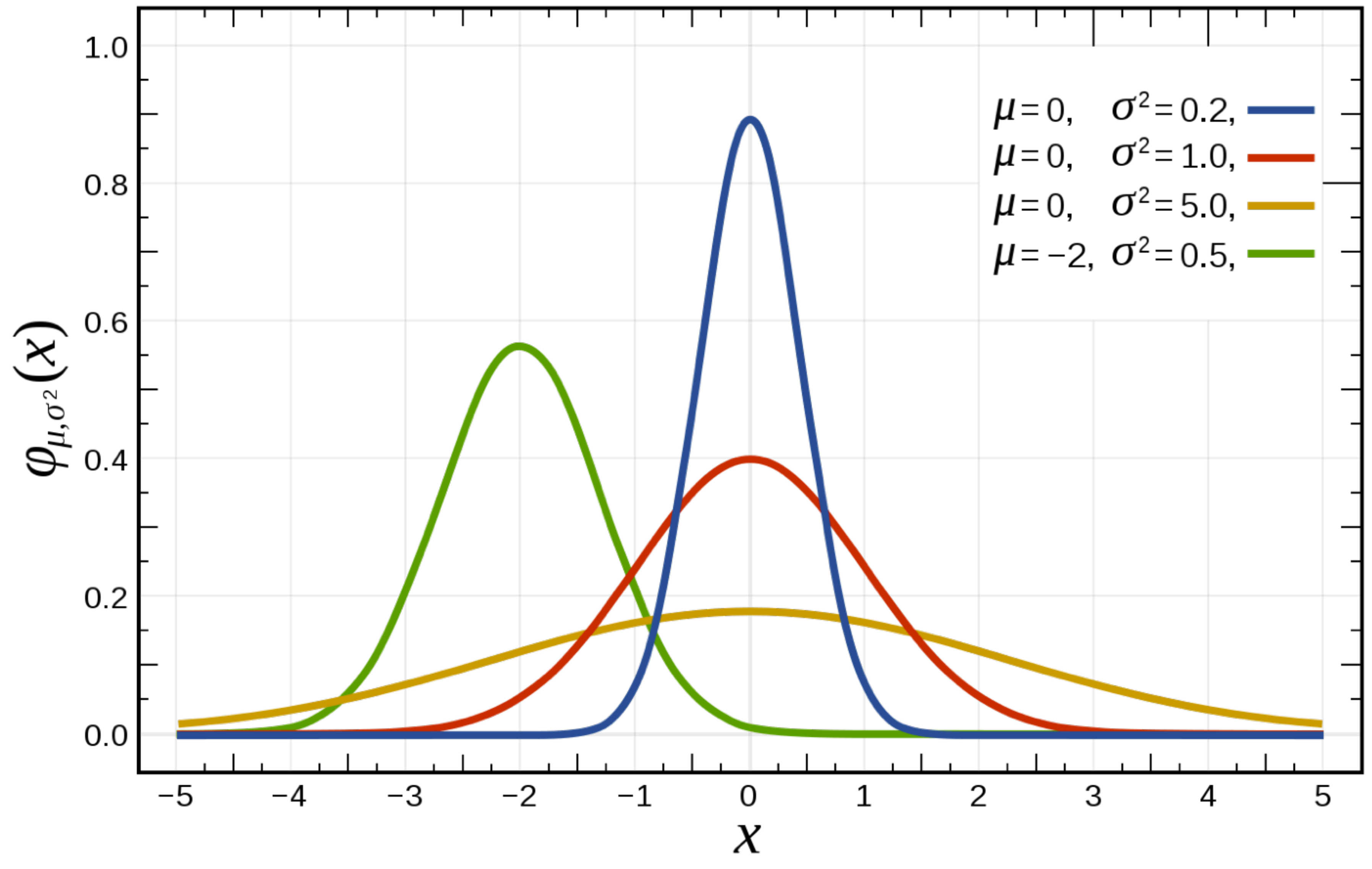
- Simple assumption: $\epsilon_{n,t} \sim \mathcal{N}(0,\sigma^2)$ where

$$\mathcal{N}(x; \mu, \sigma^2) = \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left\{ -\frac{1}{2\sigma^2}(x-\mu)^2 \right\}$$

  is the **Gaussian** or **normal distribution**.

- Linear transformations of Gaussians are still Gaussian!

$$x \sim \mathcal{N}(\mu, \sigma^2) \Rightarrow ax + b \sim \mathcal{N}(a\mu + b, a^2\sigma^2)\,.$$



https://en.wikipedia.org/wiki/Normal_distribution

A simple probabilistic model

The joint distribution

$$
\begin{aligned}
p(\mathbf{X}, \mathbf{W}, \mathbf{A}) &= p(\mathbf{X} \mid \mathbf{W}, \mathbf{A})\, p(\mathbf{W})\, p(\mathbf{A}) \\
&= \left[\prod_{n=1}^{N} \prod_{t=1}^{T} \mathcal{N}\left(x_{n,t} \mid \sum_{k=1}^{K} w_{k,n} a_{k,t}, \sigma^2 \right) \right] \\
&\quad \times \left[\prod_{k=1}^{K} \mathrm{Unif}(\mathbf{w}_k; \mathbb{S}_{N-1}) \right] \times \left[\prod_{k=1}^{K} \prod_{t=1}^{T} \mathrm{Exp}(a_{k,t}; \lambda) \right].
\end{aligned}
$$

This is called **semi-nonnegative matrix factorization (semi-NMF).**

Fitting the model

MAP estimation by coordinate ascent

- repeat until convergence:
  - for $k = 1, \ldots, K$:
    - Set $\mathbf{w}_k = \arg\max\, p(\mathbf{X}, \mathbf{W}, \mathbf{A})$ holding all else fixed
    - Set $\mathbf{a}_k = \arg\max\, p(\mathbf{X}, \mathbf{W}, \mathbf{A})$ holding all else fixed

Fitting the model
Optimizing the waveforms

Maximizing the joint probability wrt $\mathbf{w}_k$ is equivalent to maximizing the log joint probability,

$$\log p(\mathbf{X}, \mathbf{W}, \mathbf{A}) = \sum_{n=1}^{N} \sum_{t=1}^{T} \log \mathcal{N}\left(x_{n,t} \,\middle|\, \sum_{j=1}^{K} w_{j,n} a_{j,t}, \sigma^2\right)$$

$$= -\frac{1}{2\sigma^2} \sum_{n=1}^{N} \sum_{t=1}^{T} \left(x_{n,t} - \sum_{j=1}^{K} w_{j,n} a_{j,t}\right)^2 + c'$$

$$= -\frac{1}{2\sigma^2} \sum_{n=1}^{N} \sum_{t=1}^{T} \left(r_{n,t} - w_{k,n} a_{k,t}\right)^2 + c'$$

where $r_{n,t} = x_{n,t} - \sum_{j \neq k} w_{j,n} a_{j,t}$ is the **residual**.

Fitting the model

Optimizing the waveforms

It's easier to solve in vector form. Let $\mathbf{r}_t = (r_{1,t}, \ldots, r_{N,t})$. Then,

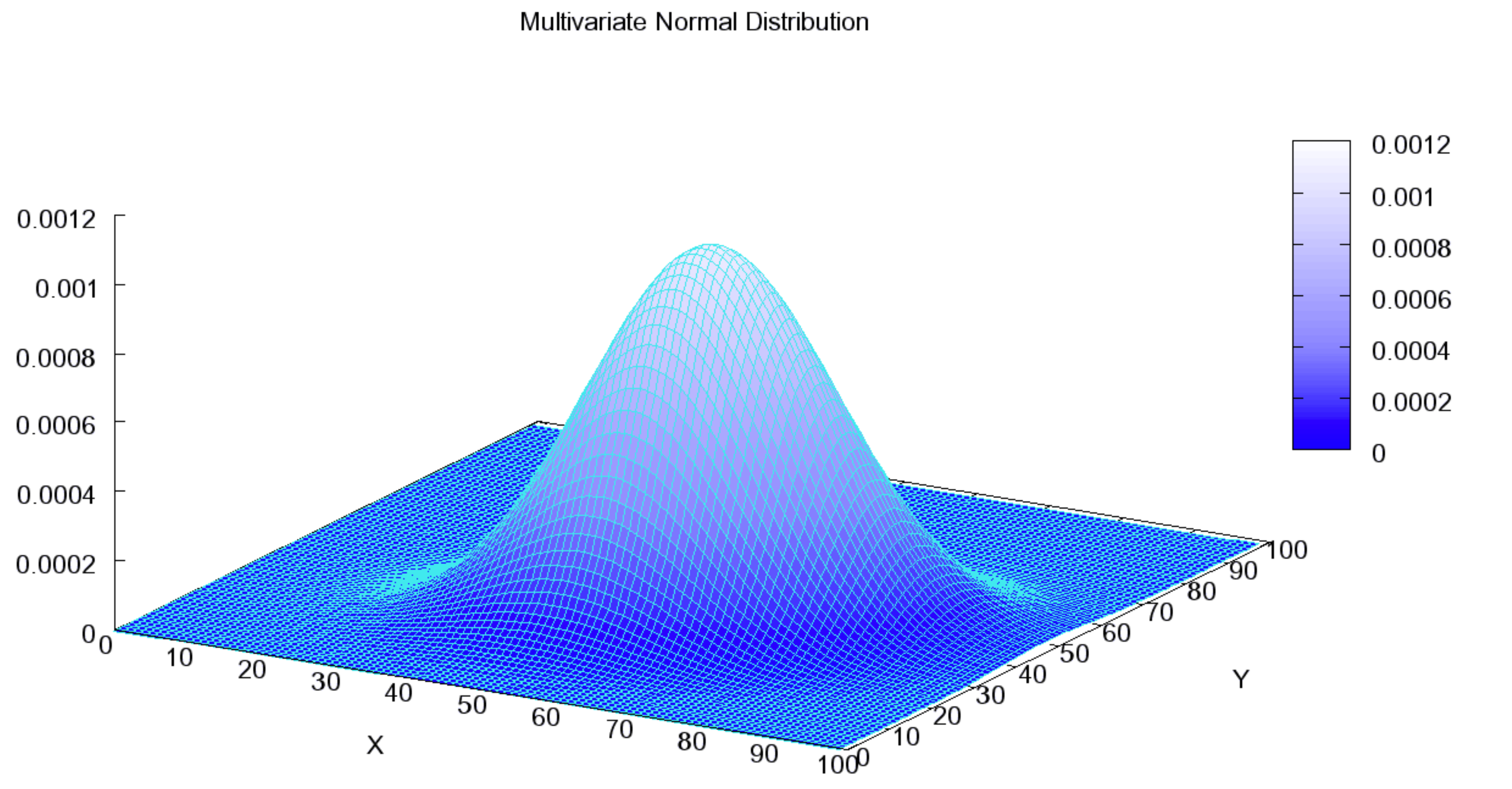
$$\log p(\mathbf{X}, \mathbf{W}, \mathbf{A}) = -\frac{1}{2\sigma^2} \sum_{t=1}^{T} (\mathbf{r}_t - \mathbf{w}_k a_{k,t})^\top (\mathbf{r}_t - \mathbf{w}_k a_{k,t}) + c'$$

$$= \sum_{t=1}^{T} \mathcal{N}(\mathbf{r}_t; \mathbf{w}_k a_{k,t}, \sigma^2 \mathbf{I}) + c'$$

where $\mathcal{N}(\mathbf{x}; \boldsymbol{\mu}, \boldsymbol{\Sigma})$ is the **multivariate normal distribution**.

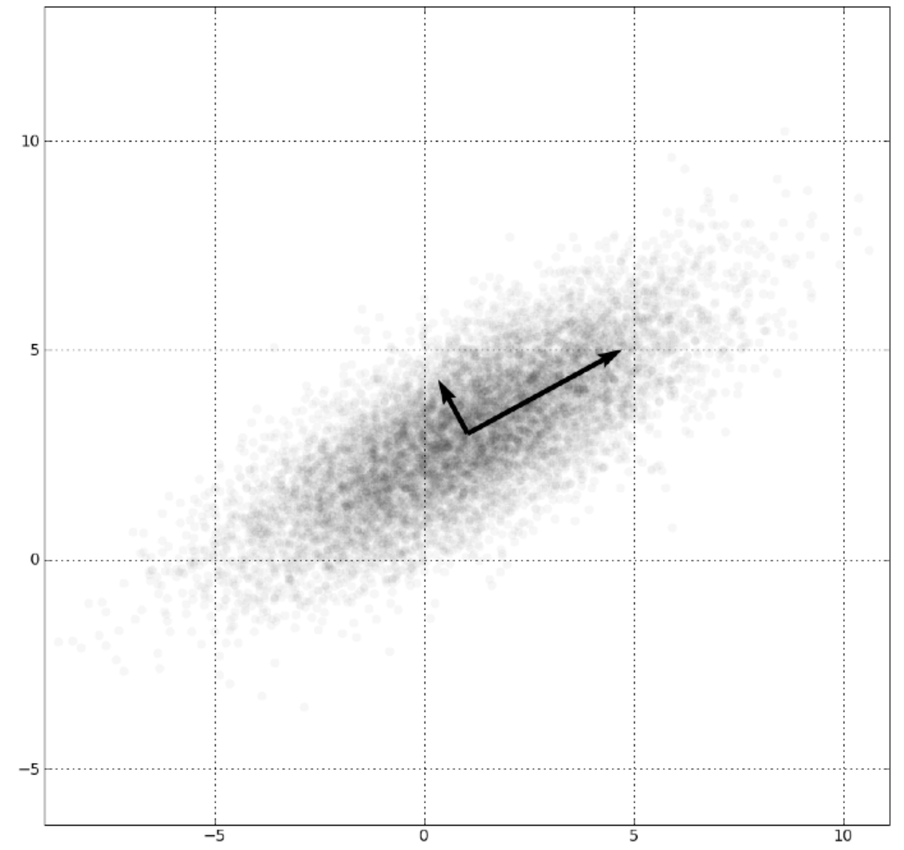
Fitting the model

The multivariate normal distribution



The multivariate normal density for $\mathbf{x} \in \mathbb{R}^D$ is,

$$\mathcal{N}(\mathbf{x}; \boldsymbol{\mu}, \boldsymbol{\Sigma}) = (2\pi)^{-\frac{D}{2}} |\boldsymbol{\Sigma}|^{-\frac{1}{2}} \exp\left\{-\frac{1}{2}(\mathbf{x}-\boldsymbol{\mu})^\top \boldsymbol{\Sigma}^{-1}(\mathbf{x}-\boldsymbol{\mu})\right\}$$



where $\boldsymbol{\mu} \in \mathbb{R}^D$ is the **mean** and $\boldsymbol{\Sigma} \in \mathbb{R}^{D \times D}_{\succeq 0}$ is the (positive definite) **covariance matrix.**

When $\boldsymbol{\Sigma} = \sigma^2 \mathbf{I}$, we call it a **spherical Gaussian** distribution.

https://en.wikipedia.org/wiki/Multivariate_normal_distribution

Fitting the model

Optimizing the waveforms

Returning to the optimization

$$
\begin{aligned}
\log p(\mathbf{X}, \mathbf{W}, \mathbf{A}) &= \sum_{t=1}^{T} \mathcal{N}(\mathbf{r}_t; \mathbf{w}_k a_{k,t}, \sigma^2 \mathbf{I}) + c' \\
&= -\frac{1}{2\sigma^2} \sum_{t=1}^{T} (\mathbf{r}_t - \mathbf{w}_k a_{k,t})^\top (\mathbf{r}_t - \mathbf{w}_k a_{k,t}) + c' \\
&= \frac{1}{\sigma^2} \sum_{t=1}^{T} \left(\mathbf{r}_t^\top \mathbf{w}_k a_{k,t} - \frac{a_{k,t}^2}{2} \mathbf{w}_k^\top \mathbf{w}_k \right) + c''
\end{aligned}
$$

Note: $\mathbf{w}_k^\top \mathbf{w}_k = 1$ by the constraint $\mathbf{w}_k \in \mathbb{S}_{N-1}$.

Fitting the model

Optimizing the waveforms

$$
\begin{aligned}
\mathbf{w}_k^\star &= \text{arg} \max_{\mathbf{w}_k \in \mathbb{S}_{N-1}} \left(\sum_{t=1}^{T} a_{k,t} \mathbf{r}_t \right)^\top \mathbf{w}_k \\
&= \text{arg} \max_{\mathbf{w}_k \in \mathbb{S}_{N-1}} \left\langle \sum_{t=1}^{T} a_{k,t} \mathbf{r}_t, \mathbf{w}_k \right\rangle \\
&= \text{arg} \max_{\mathbf{w}_k \in \mathbb{S}_{N-1}} \left\langle \mathbf{R}\mathbf{a}_k, \mathbf{w}_k \right\rangle \\
&\propto \mathbf{R}\mathbf{a}_k \,.
\end{aligned}
$$

where $\mathbf{R} \in \mathbb{R}^{N \times T}$ is the matrix of residuals with columns $[\mathbf{r}_1, \ldots, \mathbf{r}_T]$.

Fitting the model

Optimizing the amplitudes

As a function of $a_{k,t}$, the log joint probability is,

$$\log p(\mathbf{X}, \mathbf{W}, \mathbf{A}) = \frac{\mathbf{r}_t^\top \mathbf{w}_k a_{k,t}}{\sigma^2} - \frac{a_{k,t}^2}{2\sigma^2} - \lambda a_{k,t} + c'$$

This is a **quadratic optimization subject to a non-negativity constraint.**

Fitting the model

Generic solution

Assume $\alpha > 0$. Solve

$$\arg\max_{x \geq 0} \quad f(x) = -\frac{\alpha}{2}x^2 + \beta x + \gamma,$$

Fitting the model

Optimizing the amplitudes

By pattern matching to our problem, we have

$$a_{k,t}^{\star} = \max\left\{0, \sigma^2\left(\frac{\mathbf{r}_t^\top \mathbf{w}_k}{\sigma^2} - \lambda\right)\right\} = \max\left\{0, \mathbf{r}_t^\top \mathbf{w}_k - \lambda\sigma^2\right\}$$

$\mathbf{r}_t^\top \mathbf{w}_k$, is the **projection** of the residual onto the waveform for neuron k.

$\lambda\sigma^2$ the **threshold** that projection must exceed to designate a spike in amplitude.

The final algorithm

MAP estimation by coordinate ascent

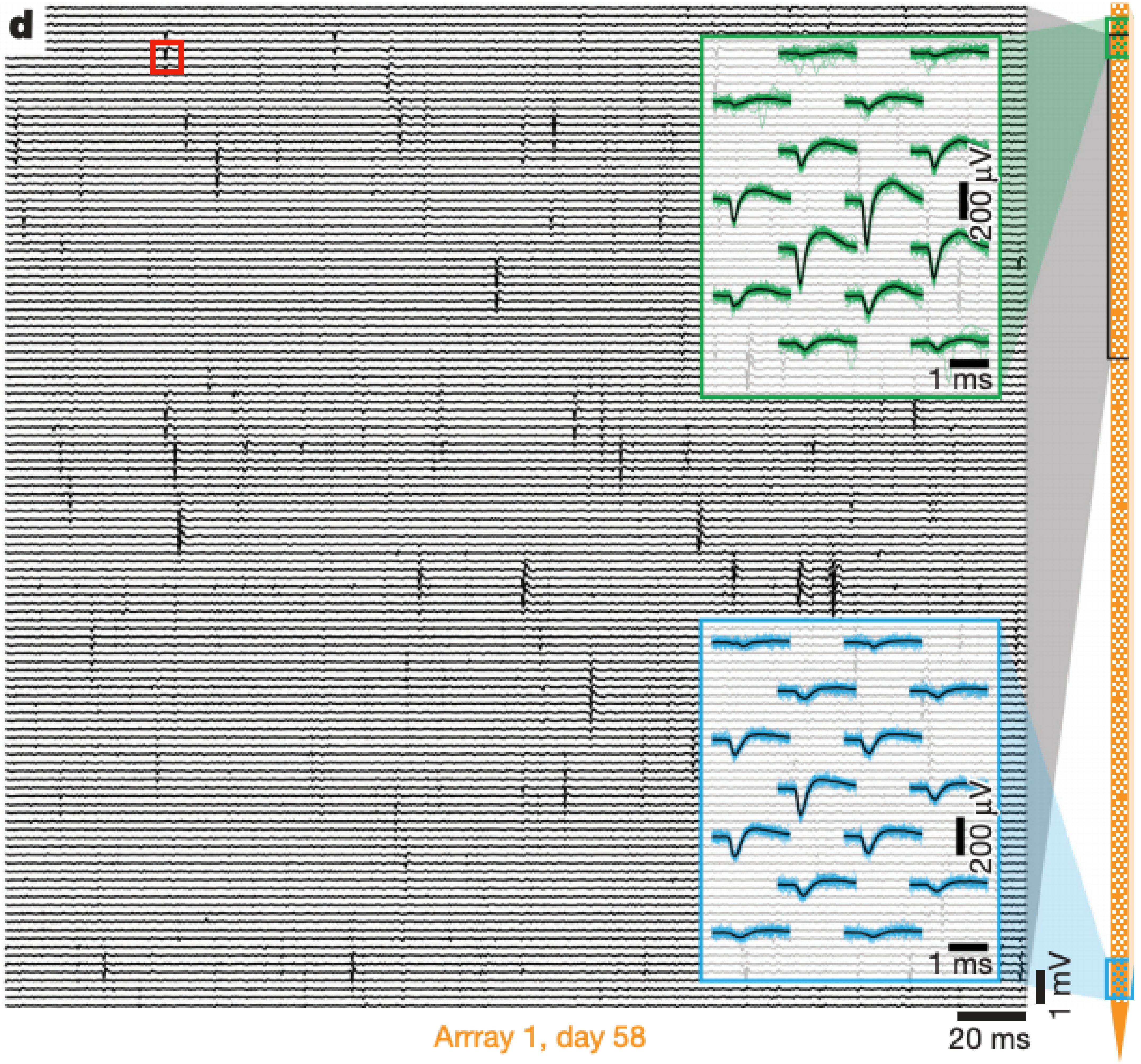
- repeat until convergence:
  - for $k = 1, \ldots, K$:
    - Compute the residual $\mathbf{R} = \mathbf{X} - \sum_{j \neq k} \mathbf{w}_j \mathbf{a}_j^\top$
    - Set $\mathbf{w}_k \propto \mathbf{R}\mathbf{a}_k$
    - Set $\mathbf{a}_k = \max\{0, \mathbf{R}^\top \mathbf{w}_k - \lambda\sigma^2\}$

Note: You don't have to recompute the residual from scratch each iteration.

Spike Sorting by Deconvolution

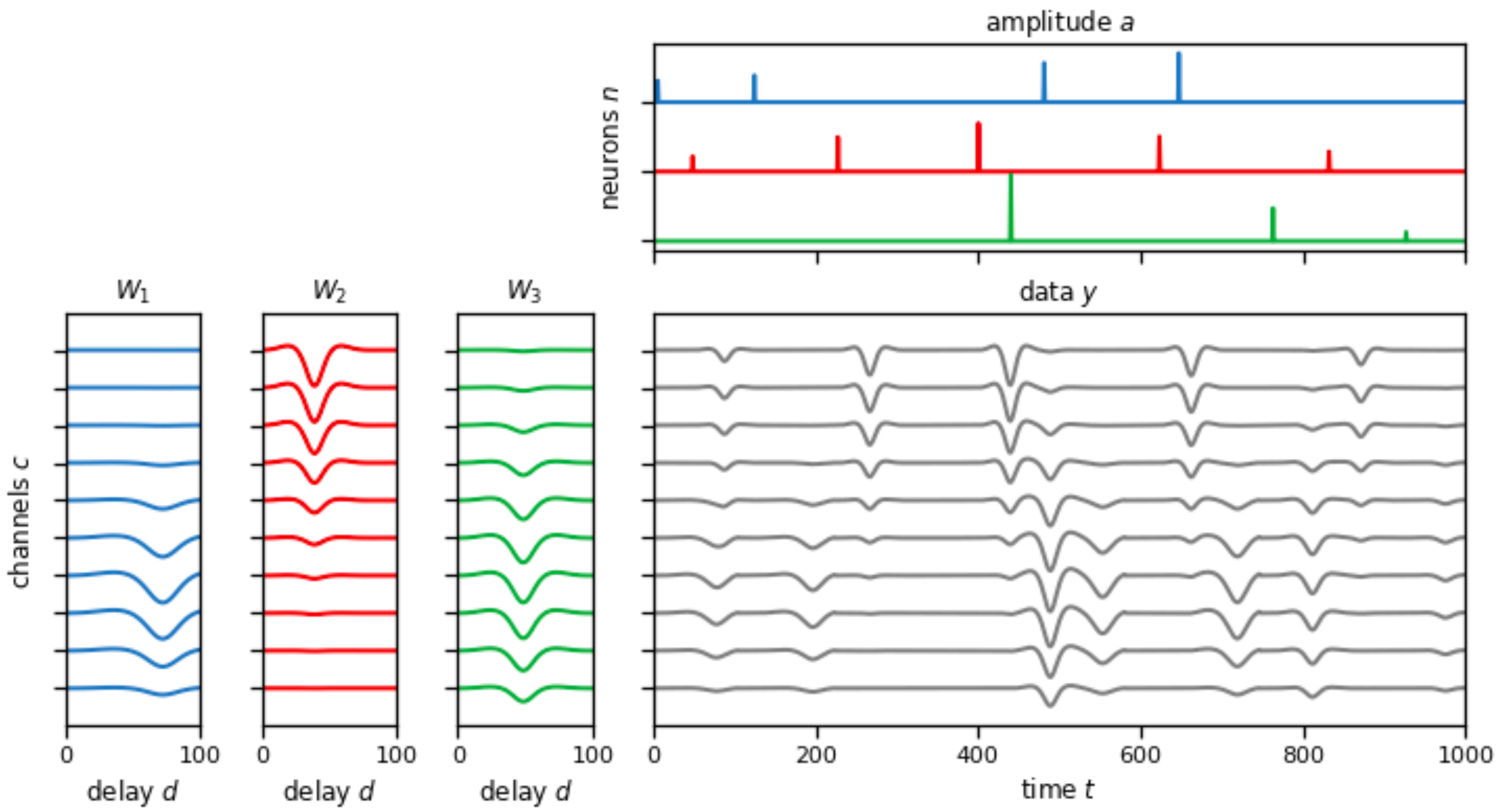
Improving upon the simple model

- Our simple model was a good warm-up, but **downsampling** to 2ms bins **isn't very practical**.
- In reality, the average voltage over a spike can be ≈ 0, so **you might miss spikes altogether**!
- Next, we'll extend the simple model with a more realistic one using **convolutions**.
- The resulting model will be very similar to **Kilosort** [Pachitariu et al., 2023]



10,000ft view

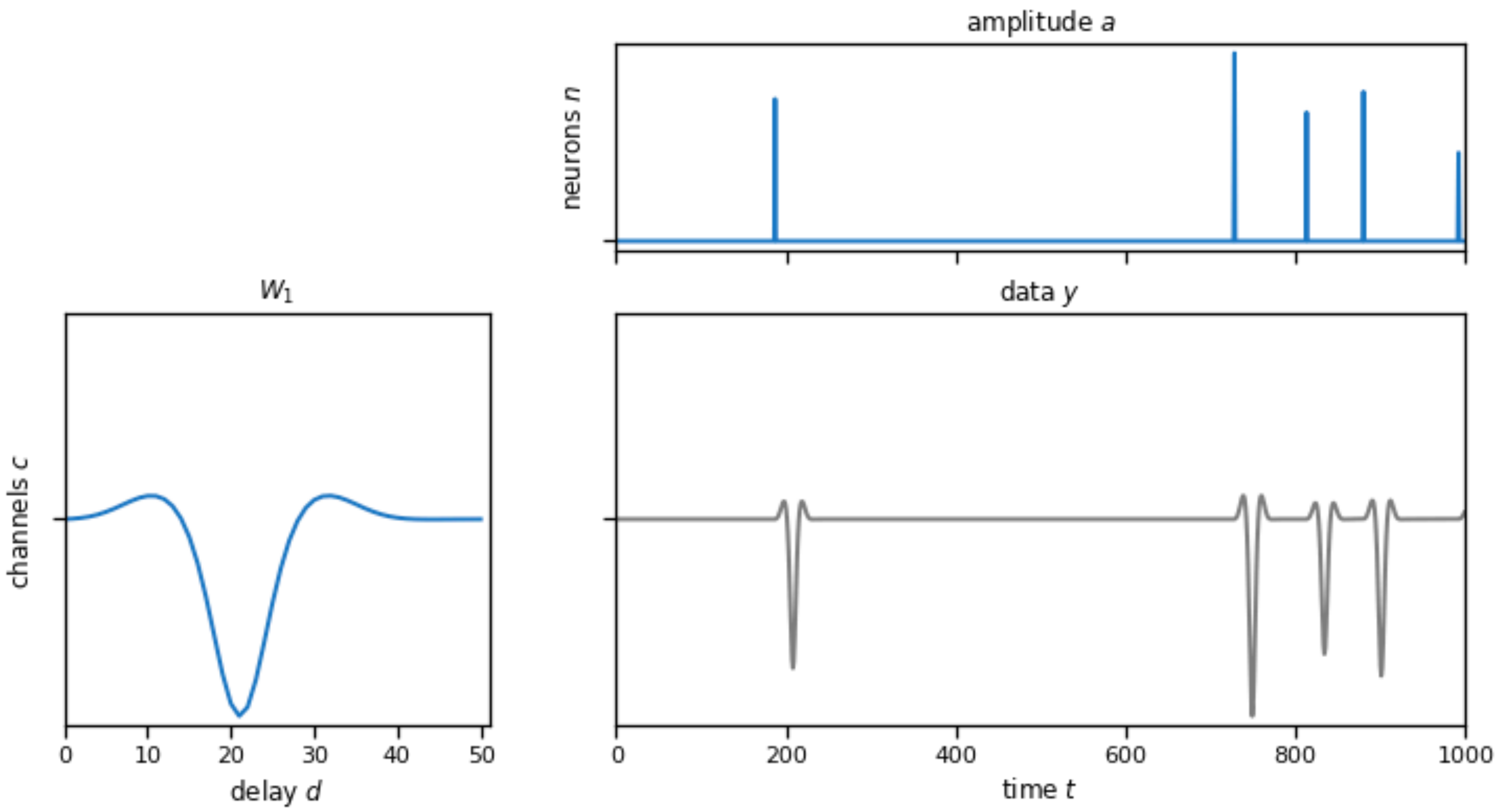
- **Idea:** each time a neuron spikes, it adds a scaled copy of its template to the measured voltage.
- Formally, we model the data as a **sum of convolutions** of templates and amplitudes for each neuron, plus noise.



Convolution

In one dimension

- **Convolution** is an operation that takes in a signal $a(t)$ and a filter $w(t)$ and outputs
$$y(t) = [a \circledast w](t) = \int a(t-\tau)w(\tau)\,\mathrm{d}\tau.$$
- In **discrete time** this becomes,
$$y_t = [a \circledast w]_t = \sum_{d=-\infty}^{\infty} a_{t-d} w_d$$
- **Causal** filters are constrained so that $w_d = 0$ for $d < 0$. Then y_t is only influenced by $a_{1:t}$.
- Our filters will also have **bounded support** so that $w_d = 0$ for $d \geq D$. Then y_t is only influenced by $a_{t-D+1:t}$.
- In our case, the signal is the time series of spike amplitudes, and the filter is the waveform template. Every time there's a spike, we plop down a scaled template.



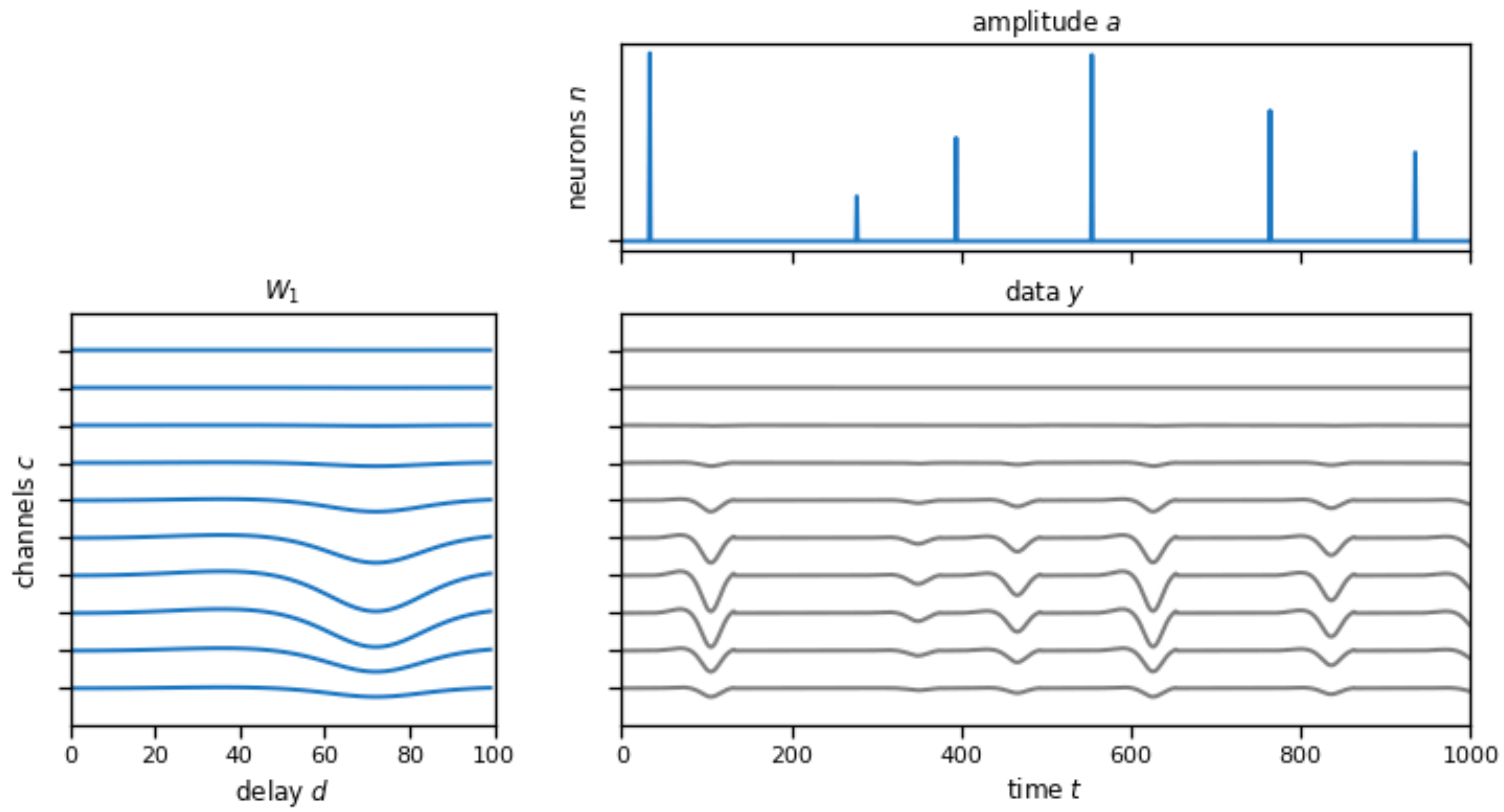
Convolution

With multiple output channels

- We need to convolve the amplitude signal with **multiple filters** in parallel, **one for each channel** of the voltage recording.

$$\mathbf{y}_t = \begin{pmatrix} [a \circledast w_1]_t \\ \vdots \\ [a \circledast w_N]_t \end{pmatrix} = \begin{pmatrix} \sum_{d=1}^{D} a_{t-d} w_{1,d} \\ \vdots \\ \sum_{d=1}^{D} a_{t-d} w_{N,d} \end{pmatrix}$$

- (I'm going to index d from $1, \ldots, D$ because the notation is a bit simpler.)



Convolution

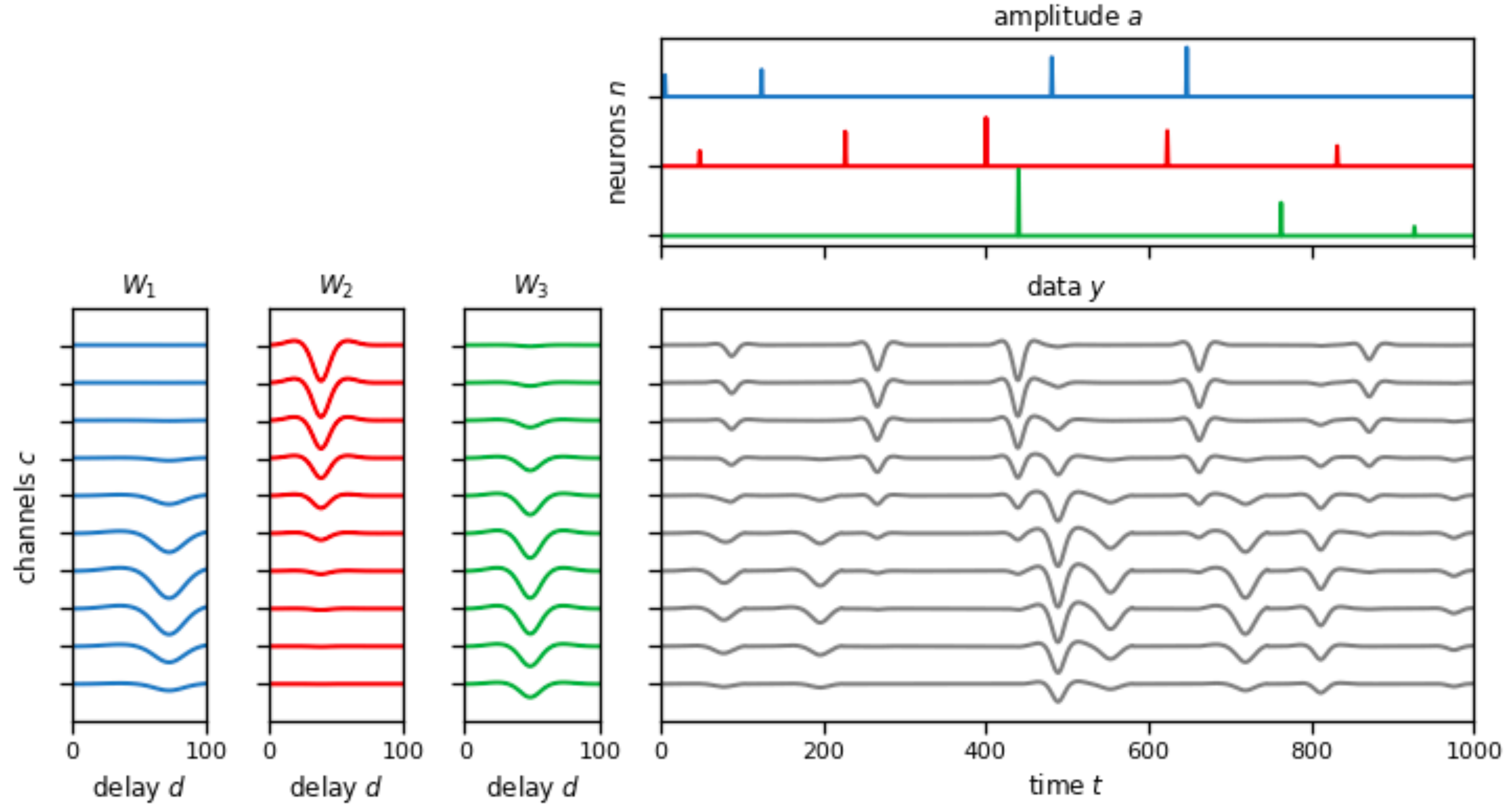
With multiple input & output channels

- Finally, we need to sum convolutions of multiple input signals, **one for each neuron** in the model.

$$\mathbf{X} = \mathbf{A} \circledast \mathbf{W}$$

by which we mean

$$x_{n,t} = \sum_{k=1}^{K} \sum_{d=1}^{D} a_{k,t-d} w_{k,n,d}.$$



Cross-Correlation

In one dimension

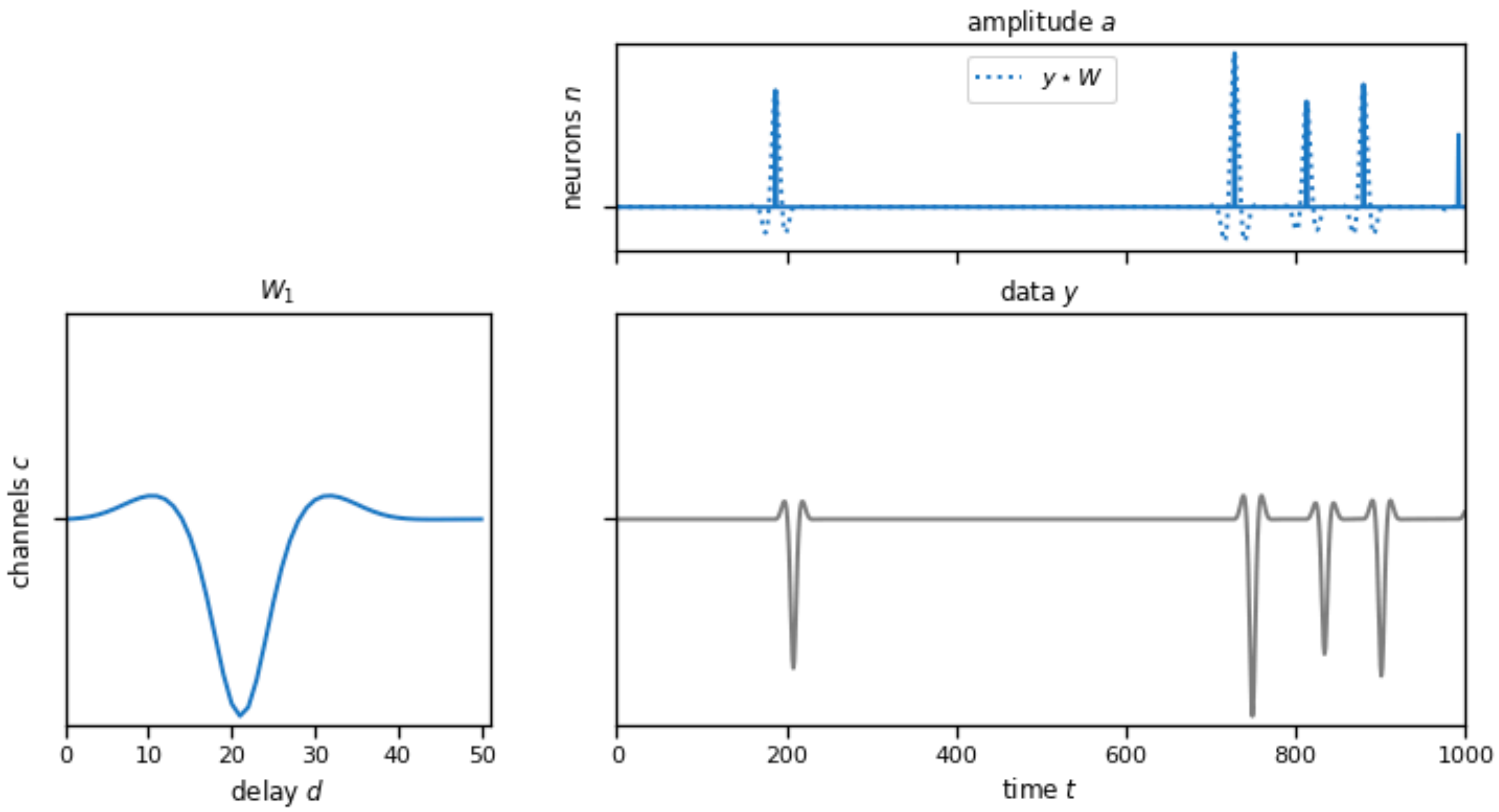
- Cross-correlation essentially goes in reverse.
- In signal processing, the cross-correlation is a sliding dot product of data $y(t)$ and template $w(t)$, which produces a new function $[y \star w](t)$.
- For discrete time, real-valued inputs,

$$[y \star w]_t = \sum_{d=-\infty}^{\infty} y_{t+d} w_d.$$

- With a change of variables, we see that cross-correlation is equivalent to convolution with a time-reversed filter $\overleftarrow{w}$:

$$[y \star w]_t = \sum_{d=\infty}^{-\infty} y_{t-d} w_{-d} = [y \circledast \overleftarrow{w}]_t.$$

- (Note: the definition of cross-correlation is not unique. This definition is consistent with `np.correlate` but opposite of Wikipedia.)



Cross-Correlation

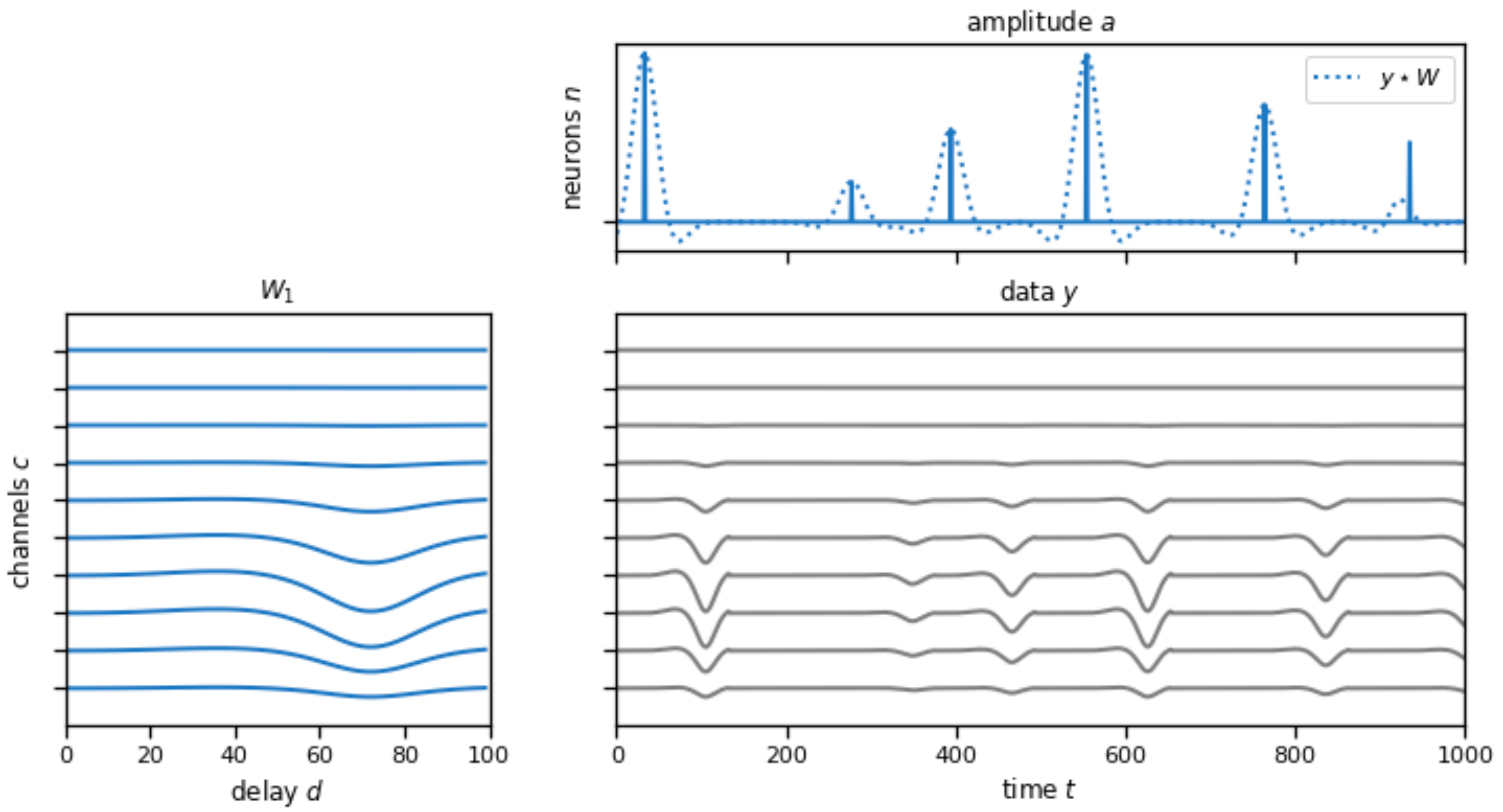
With multiple channels

- As before, we can extend this definition to handle multiple channels

$$[\mathbf{Y} \star \mathbf{W}]_t = \sum_{n=1}^{N} \sum_{d=-\infty}^{\infty} y_{n,t+d} w_{n,d}.$$

- The cross-correlation measures the similarity of the data and the template at each point in time.

- The **auto-correlation** is the cross-correlation of a signal with itself.



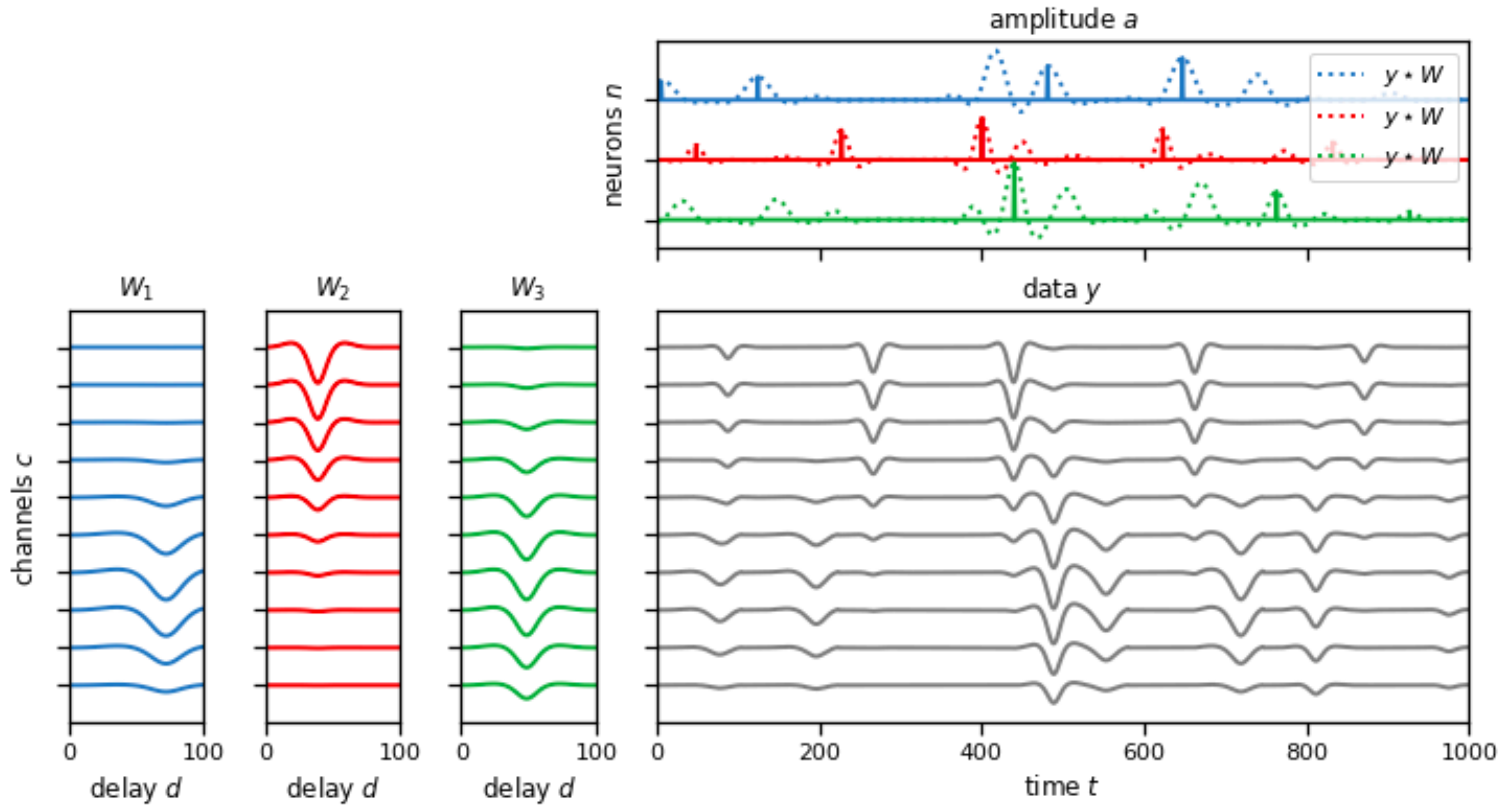
Cross-Correlation

With multiple input & output channels

As before, we can extend this definition to handle multiple channels

$$[Y \star W]_t = \begin{pmatrix} [Y \star W_1]_t \\ \vdots \\ [Y \star W_K]_t \end{pmatrix}$$

$$= \begin{pmatrix} \sum_{n=1}^{N} \sum_{d=-\infty}^{\infty} y_{n,t+d} w_{1,n,d} \\ \vdots \\ \sum_{n=1}^{N} \sum_{d=-\infty}^{\infty} y_{n,t+d} w_{K,n,d} \end{pmatrix}$$



Convolution and Cross-Correlation in Pytorch

- PyTorch (and other deep learning libraries) have fast, **GPU-backed implementations** of convolutions.
- **What they call convolution is actually cross-correlation!**
- But remember, we can always get convolution by cross-correlating with the flipped filter.
- For discrete time signals, you have to play with **padding** to handle **edge effects**.
- By default, these functions operate on **mini-batches** of inputs, so you need to add an extra leading dimension to your signal.
- There are **lots of other options** to read about (strides, dilations, groups), but we won't use them this week.

`torch.nn.functional.conv1d(`*`input, weight, bias=None, stride=1, padding=0, dilation=1, groups=1`*`)` → Tensor

Applies a 1D convolution over an input signal composed of several input planes.

This operator supports TensorFloat32.

See `Conv1d` for details and output shape.

• NOTE

In some circumstances when using the CUDA backend with CuDNN, this operator may select a nondeterministic algorithm to increase performance. If this is undesirable, you can try to make the operation deterministic (potentially at a performance cost) by setting `torch.backends.cudnn.deterministic = True`. Please see the notes on Reproducibility for background.

Parameters

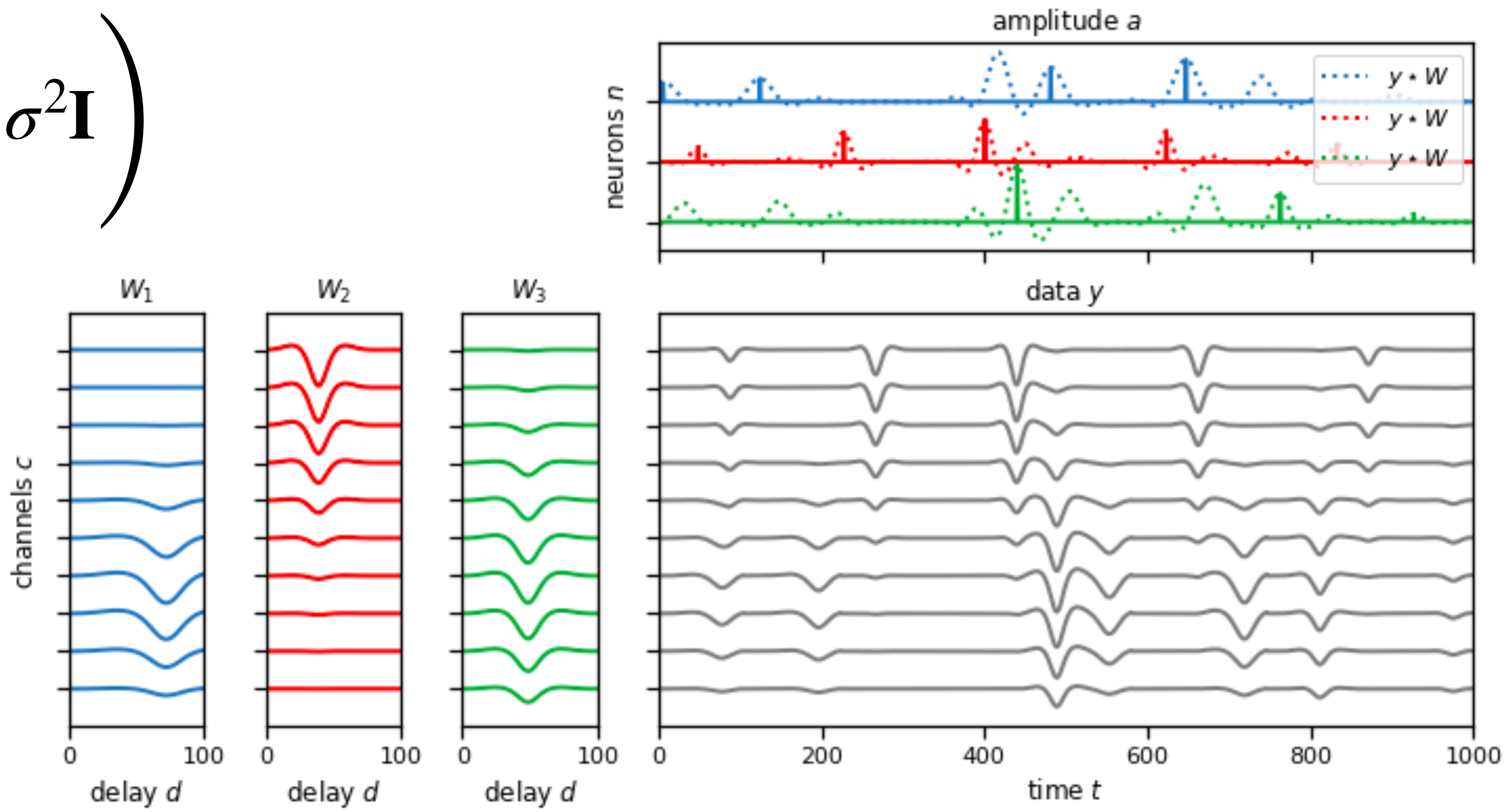
- **input** – input tensor of shape $(\text{minibatch}, \text{in\_channels}, iW)$
- **weight** – filters of shape $(\text{out\_channels}, \frac{\text{in\_channels}}{\text{groups}}, kW)$
- **bias** – optional bias of shape (out_channels). Default: `None`
- **stride** – the stride of the convolving kernel. Can be a single number or a one-element tuple *(sW,)*. Default: 1
- **padding** – implicit paddings on both sides of the input. Can be a single number or a one-element tuple *(padW,)*. Default: 0
- **dilation** – the spacing between kernel elements. Can be a single number or a one-element tuple *(dW,)*. Default: 1
- **groups** – split input into groups, in_channels should be divisible by the number of groups. Default: 1

Spike sorting by deconvolution

Probabilistic Model
Likelihood

- Assume each spike is a noisy, scaled version of the template of the neuron that generated it.

$$p(\mathbf{X} \mid \mathbf{A}, \mathbf{W}) = \prod_{t=1}^{T} \mathcal{N}\left(\mathbf{x}_t \mid \sum_{k=1}^{K} [\mathbf{a}_k \circledast \mathbf{W}_k]_t, \sigma^2 \mathbf{I}\right)$$



Probabilistic Model

Prior on spike amplitudes

- Assume the spike amplitudes are drawn from an exponential distribution.

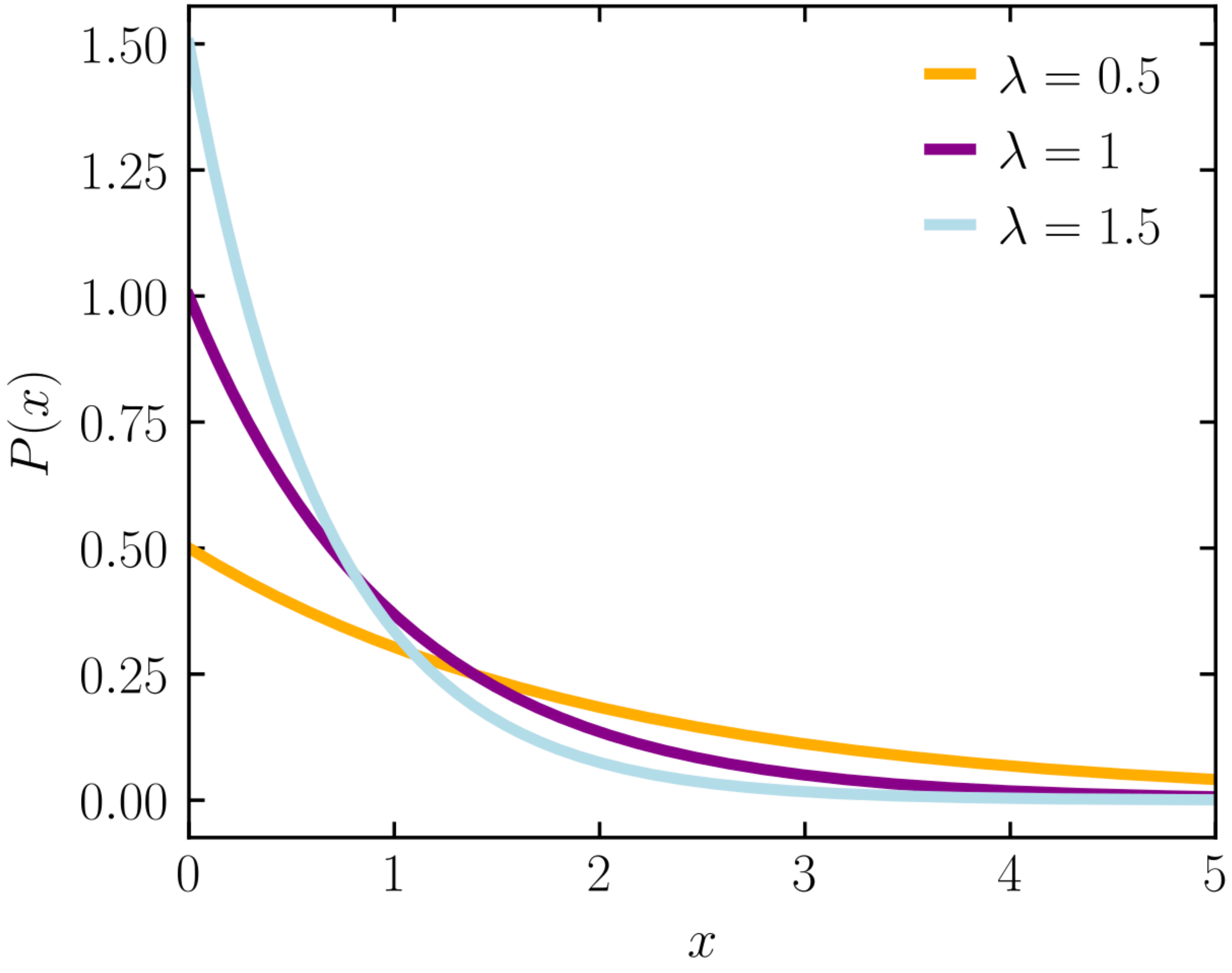
$$a_{k,t} \sim \mathrm{Exp}(\lambda)$$

- This simple prior will lead to sparse amplitudes, but it does not encode any dependencies between time steps.

- Ideally, we would also like to prohibit two spikes within D samples of each other.

- We'll use a heuristic solution in this week's lab.

pdf of exponential distribution



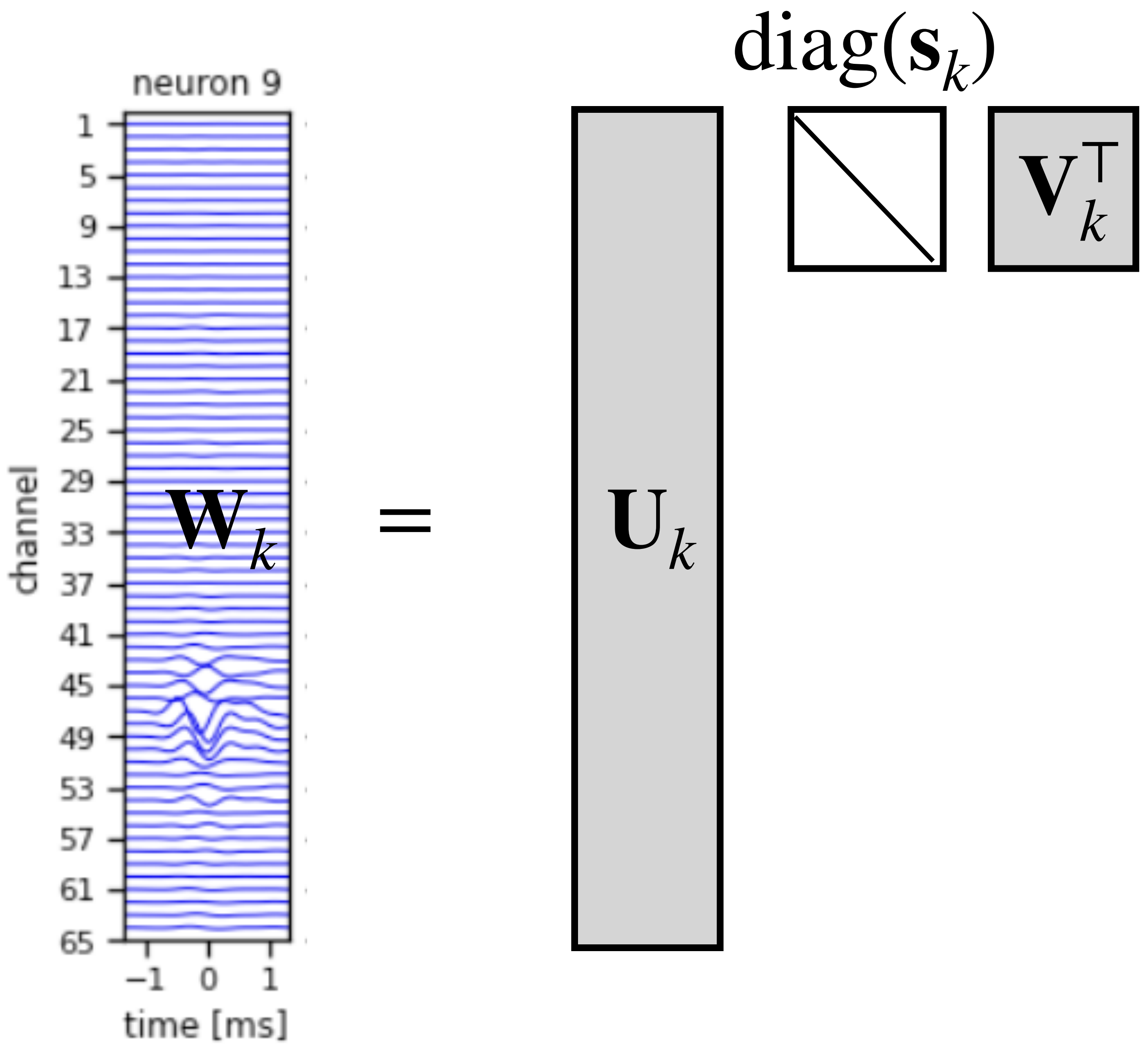
https://en.wikipedia.org/wiki/Exponential_distribution

Probabilistic Model

Scale invariance via Frobenius norm constraint

- What is the generalization of the unit-norm constraint $\mathbf{w}_k \in \mathbb{S}_{N-1}$ to matrices?

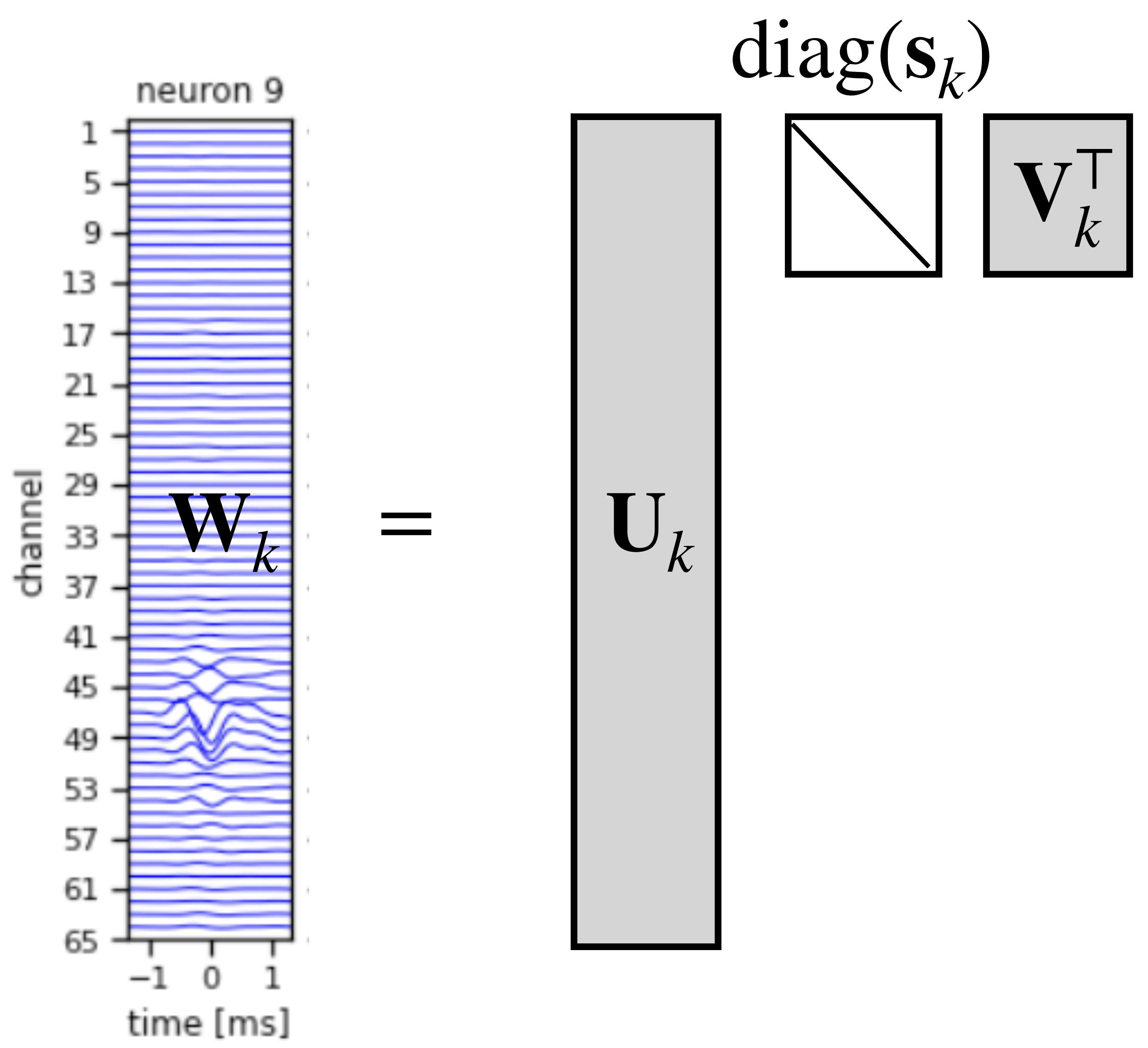
- Assume the matrix $\mathbf{W}_k \in \mathbb{R}^{N \times D}$ has unit **Frobenius norm** $||\mathbf{W}_k||_\mathrm{F} = 1$.



Probabilistic Model

Aside: The Frobenius norm and the SVD

- The Frobenius norm is the ℓ_2 norm of the flattened matrix,
$$\|\mathbf{W}\|_F^2 = \sum_{n=1}^{N} \sum_{d=1}^{D} w_{n,d}^2 = \mathrm{vec}(\mathbf{W})^\top \mathrm{vec}(\mathbf{W}) = \|\mathrm{vec}(\mathbf{W})\|_2^2$$



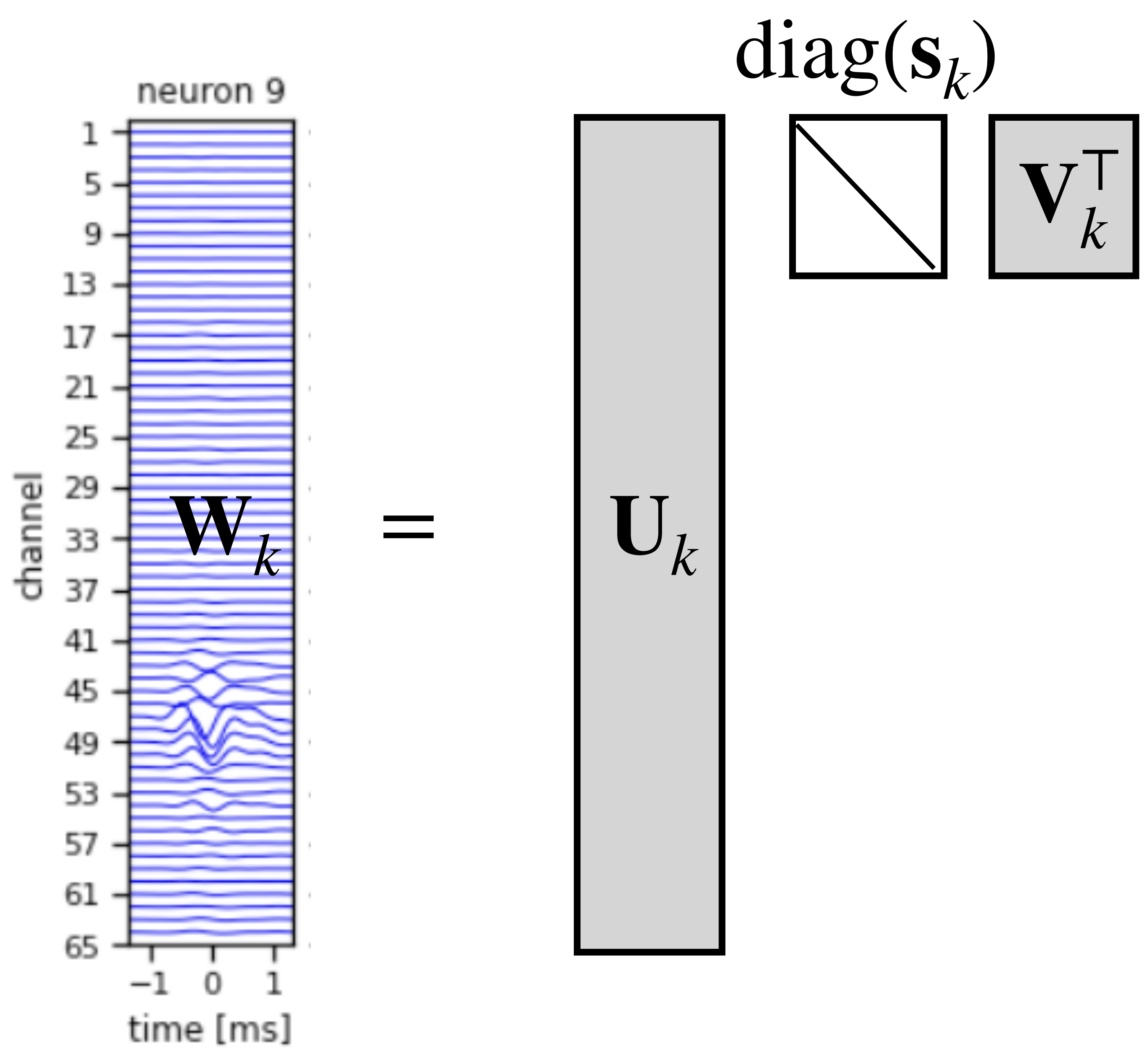
- We can also write it as a trace,
$$\|\mathbf{W}\|_F = \sqrt{\mathrm{Tr}(\mathbf{W}^\top \mathbf{W})}$$

- Or in terms of the singular values,
$$\|\mathbf{W}\|_\mathrm{F} = \|\mathbf{s}\|_2$$

Probabilistic Model

Scale invariance via Frobenius norm constraint

- What is the generalization of the unit-norm constraint $\mathbf{w}_k \in \mathbb{S}_{N-1}$ to matrices?
- Assume the matrix $\mathbf{W}_k \in \mathbb{R}^{N \times D}$ has unit **Frobenius norm** $||\mathbf{W}_k||_\mathrm{F} = 1$.
- This is equivalent to constraining the **singular values** to be normalized $||\mathbf{s}_k||_2 = 1$.



Probabilistic Model

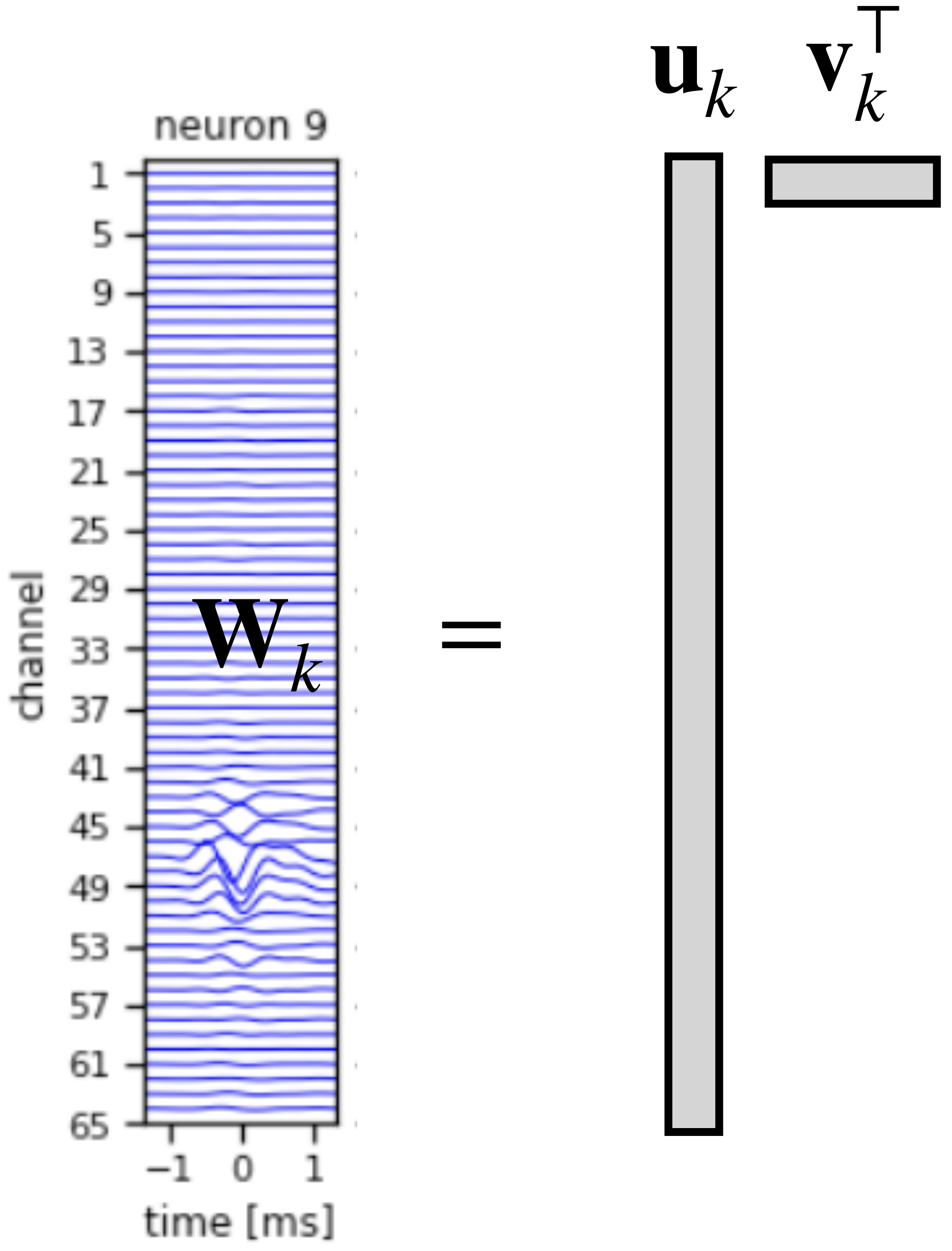
Low-rank constraint

- This view suggests a further assumption: constraint the **rank** of the templates as well.

- If we constrain it to be rank 1 (i.e., only one nonzero singular value), then

$$\mathbf{W}_k = \mathbf{u}_k \mathbf{v}_k^\top$$

where $\mathbf{u}_k \in \mathbb{S}_{N-1}$ is the **spatial footprint** and $\mathbf{v}_k \in \mathbb{S}_{D-1}$ is the **temporal profile**.



MAP estimation

Maximum a posteriori estimation

Coordinate ascent

- Initialize templates $\mathbf{W}$ and set $\mathbf{A} = 0$.
- Iterate until convergence:
  - For neuron $k = 1, \ldots, K$:

    a. Optimize **amplitudes** a_k for neuron k.

    b. Optimize **templates** $\mathbf{W}_k$ for neuron k.

[In each case, maximize log joint probability wrt one variable, holding others fixed.]

Maximum a posteriori estimation

Optimizing the amplitudes

As a function of $\mathbf{a}_k$,

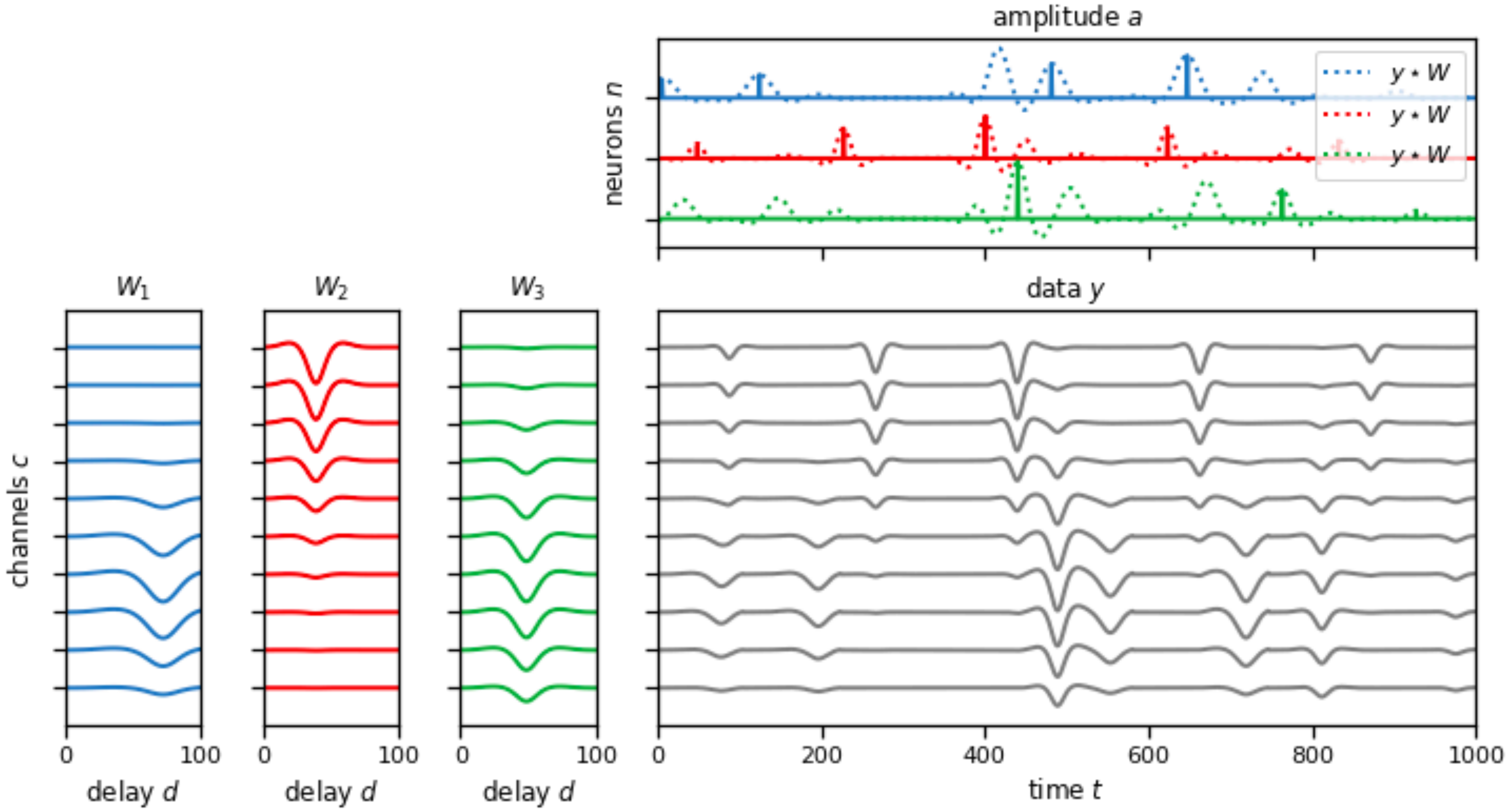
$$\log p(\mathbf{X}, \mathbf{W}, \mathbf{A}) =$$

$$= \log p(\mathbf{X} \mid \mathbf{A}, \mathbf{W}) + \log p(\mathbf{a}_k; \lambda)$$

$$= -\frac{1}{2\sigma^2} \|\mathbf{R} - \mathbf{a}_k \circledast \mathbf{W}_k\|_{\mathrm{F}}^2 + \log p(\mathbf{a}_k) + \mathrm{c}$$

where $\mathbf{R} \in \mathbb{R}^{N \times T}$ is the residual for neuron n, defined as

$$\mathbf{R} = \mathbf{X} - \sum_{j \neq k} [\mathbf{a}_j \circledast \mathbf{W}_j]$$



Maximum a posteriori estimation

Optimizing the amplitudes

Expanding the square

$$
\begin{aligned}
\log p(\mathbf{X}, \mathbf{W}, \mathbf{A}) &= -\frac{1}{2\sigma^2}\|\mathbf{R} - \mathbf{a}_k \circledast \mathbf{W}_k\|_\mathrm{F}^2 + \log p(\mathbf{a}_k) + \mathrm{c} \\
&= \underbrace{-\frac{1}{2\sigma^2}\|\mathbf{a}_k \circledast \mathbf{W}_k\|_\mathrm{F}^2}_{\mathscr{L}_2(\mathbf{a}_k)} + \underbrace{\frac{1}{\sigma^2}\langle \mathbf{R}, \mathbf{a}_K \circledast \mathbf{W}_k \rangle_\mathrm{F}}_{\mathscr{L}_1(\mathbf{a}_k)} + \log p(\mathbf{a}_k) + \mathrm{c}\,.
\end{aligned}
$$

where $\mathbf{r}_t \in \mathbb{R}^N$ is the t-th column of the residual $\mathbf{R}$.

Maximum a posteriori estimation

Optimizing the amplitudes

Further expanding the quadratic term,

$$
\begin{aligned}
\mathscr{L}_2(\mathbf{a}_k) &= -\frac{1}{2\sigma^2}\|\mathbf{a}_k \circledast \mathbf{W}_k\|_F^2 \\
&= -\frac{1}{2\sigma^2}\sum_{t=1}^{T}\sum_{n=1}^{N}\left(\sum_{d=1}^{D} a_{k,t-d}^2 w_{k,n,d}^2 + 2\sum_{d=1}^{D}\sum_{d'=1}^{d-1} a_{k,t-d}a_{k,t-d'}w_{k,n,d}w_{k,n,d'}\right) \\
&\approx -\frac{1}{2\sigma^2}\sum_{t=1}^{T} a_{k,t}^2\|\mathbf{W}_k\|_F^2 \\
&= -\frac{1}{2\sigma^2}\sum_{t=1}^{T} a_{k,t}^2
\end{aligned}
$$

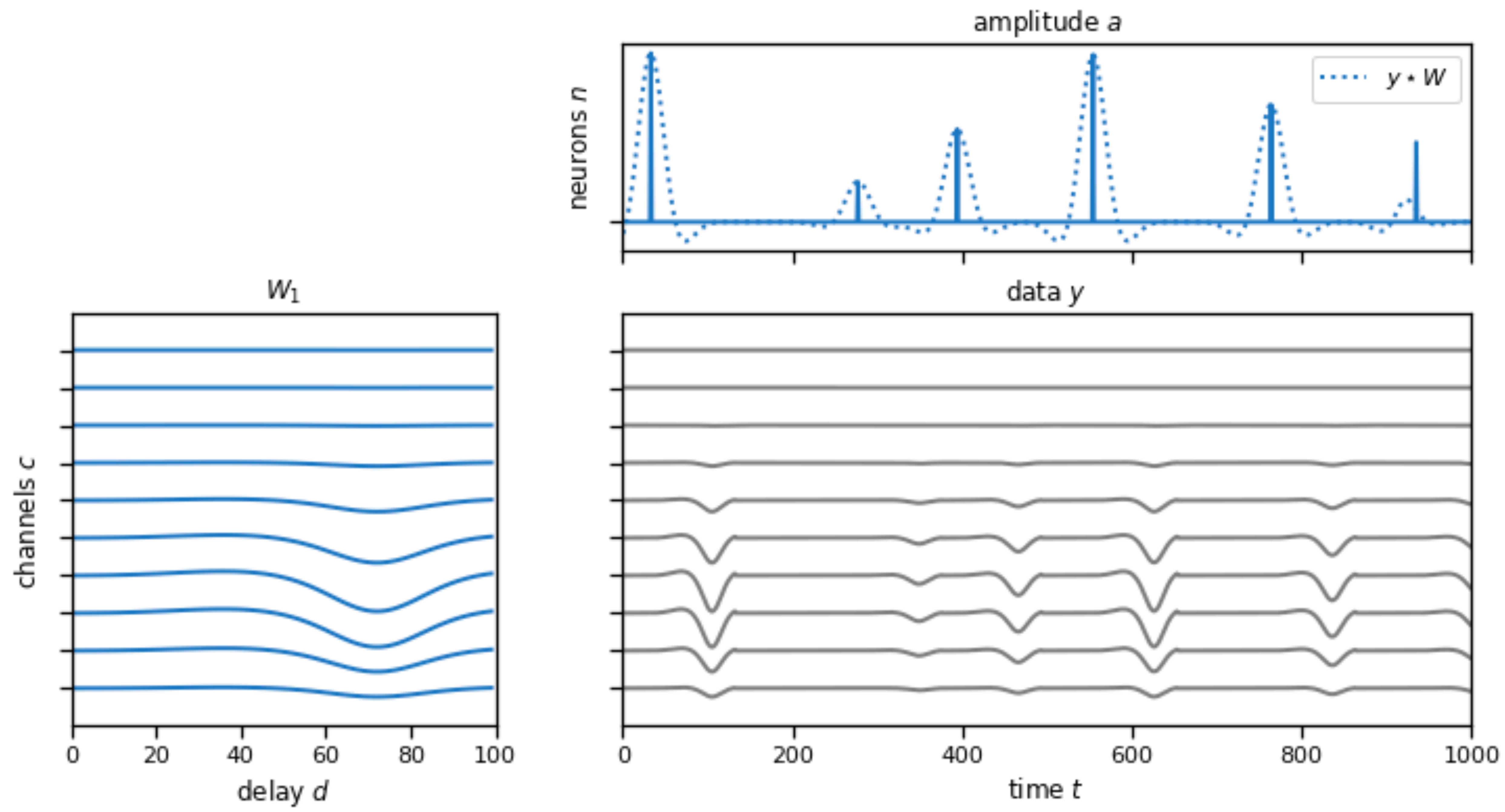
with equality when nonzero entries (i.e. “spikes”) of $\mathbf{a}_k$ are separated by at least D samples.

Maximum a posteriori estimation

Optimizing the amplitudes

Now take the linear term…

$$
\begin{aligned}
\mathscr{L}_1(\mathbf{a}_k) &= \frac{1}{\sigma^2}\langle \mathbf{R}, \mathbf{a}_k \circledast \mathbf{W}_k \rangle \\
&= \frac{1}{\sigma^2}\sum_{t=1}^{T}\sum_{n=1}^{N} r_{n,t}[\mathbf{a}_k \circledast \mathbf{w}_{k,n}]_t \\
&= \frac{1}{\sigma^2}\sum_{t=1}^{T}\sum_{n=1}^{N}\sum_{d=1}^{D} a_{k,t-d} r_{n,t} w_{k,n,d} \\
&= \frac{1}{\sigma^2}\sum_{t=1}^{T} a_{k,t} \sum_{n=1}^{N}\sum_{d=1}^{D} r_{n,t+d} w_{k,n,d} \\
&= \frac{1}{\sigma^2}\sum_{t=1}^{T} a_{k,t} [\mathbf{R} \star \mathbf{W}_k]_t
\end{aligned}
$$



where $[\mathbf{R} \star \mathbf{W}_k]_t$ is the cross-correlation of the residual and the template for neuron k.

Maximum a posteriori estimation

Optimizing the amplitudes

Putting it all together

$$\mathscr{L}(\mathbf{a}_k) = \sum_{t=1}^{T} \left[-\frac{1}{2\sigma^2} a_{k,t}^2 + \frac{1}{\sigma^2} \mu_{k,t} a_{k,t} - \lambda a_{k,t} \right] + \text{c},$$

which separates into a sum of quadratic objective functions for each time t.

Maximum a posteriori estimation

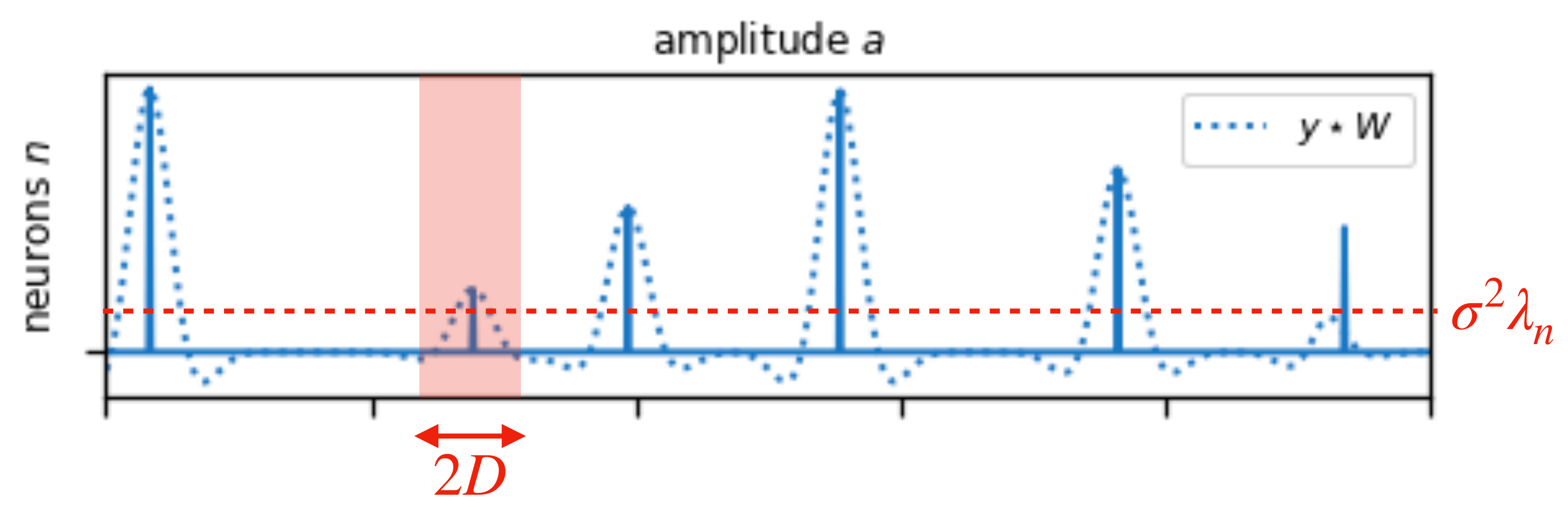
Completing the square and solving for the optimal amplitudes

- Like before, the maximum, subject to non-negativity constraints, is obtained at

$$a_{k,t} = \max\left\{0, \mu_{k,t} - \sigma^2\lambda\right\}$$

- However, we also want spikes to be well-separated; i.e. $a_{k,t} > 0 \implies a_{k,t+d} = 0$ for $d = 1, \ldots, D$.

- We'll enforce this with a **simple heuristic**: use `find_peaks` to select local maxima of this "score" signal.



Maximum a posteriori estimation

Optimizing the templates

As a function of $\mathbf{W}_k$

$$\log p(\mathbf{X}, \mathbf{A}, \mathbf{W}) = \frac{1}{2\sigma^2} \sum_{t=1}^{T} \langle a_{k,t} \mathbf{R}_t, \mathbf{W}_k \rangle + c'$$

$$= \frac{1}{2\sigma^2} \left\langle \sum_{t=1}^{T} a_{k,t} \mathbf{R}_t, \mathbf{W}_k \right\rangle + c'$$

where

$$\mathbf{R}_t = \begin{bmatrix} r_{1,t} & \cdots & r_{1,t+D} \\ \vdots & & \vdots \\ r_{n,t} & \cdots & r_{n,t+D} \end{bmatrix}$$

is a slice of the residual matrix (`R[:,t:t+D]` in code).

Maximum a posteriori estimation

Optimizing the templates

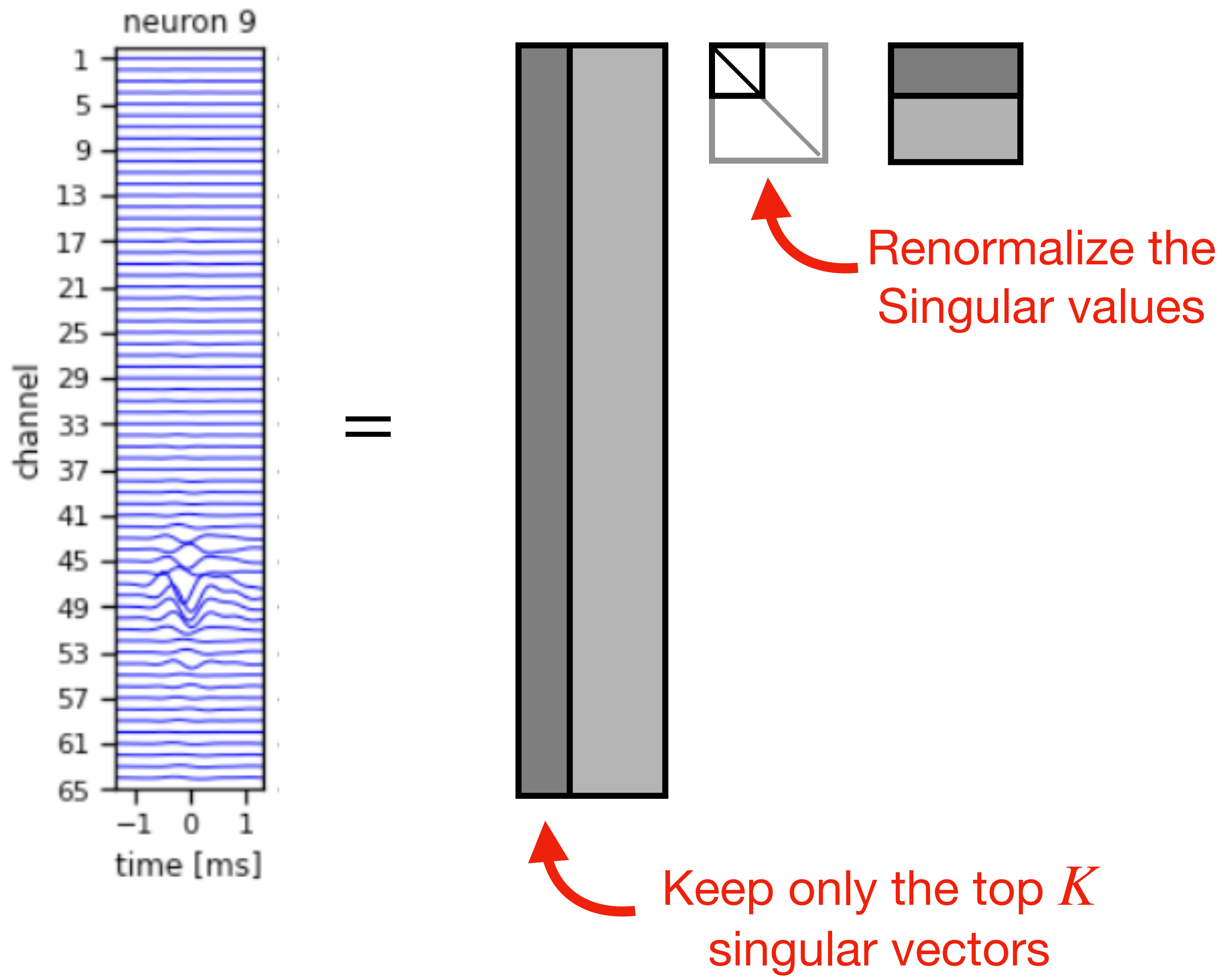
We want to maximize this log joint probability over the space of low-rank, unit-norm matrices,

$$\mathbf{W}_k^\star = \arg \max_{\mathbf{W}_k \in \mathbb{S}_R^{N,D}} \left\langle \sum_{t=1}^{T} a_{k,t} \mathbf{R}_t, \mathbf{W}_k \right\rangle$$

The solution is to set the waveform matrix "proportional to" the weighted sum of residual matrices by taking its SVD and renormaling the singular values.

$$\mathbf{W}_k^\star = \sum_{r=1}^{R} \bar{s}_r \mathbf{u}_r \mathbf{v}_r^\top \quad \text{where} \quad \bar{s}_r = \frac{s_r}{\sqrt{\sum_{r'=1}^{R} s_{r'}^2}}.$$

$$\sum_{t=1}^{T} a_{k,t} \mathbf{R}_t = \mathbf{U}_k \; \mathrm{diag}(\mathbf{s}_k) \; \mathbf{V}_k^\top$$



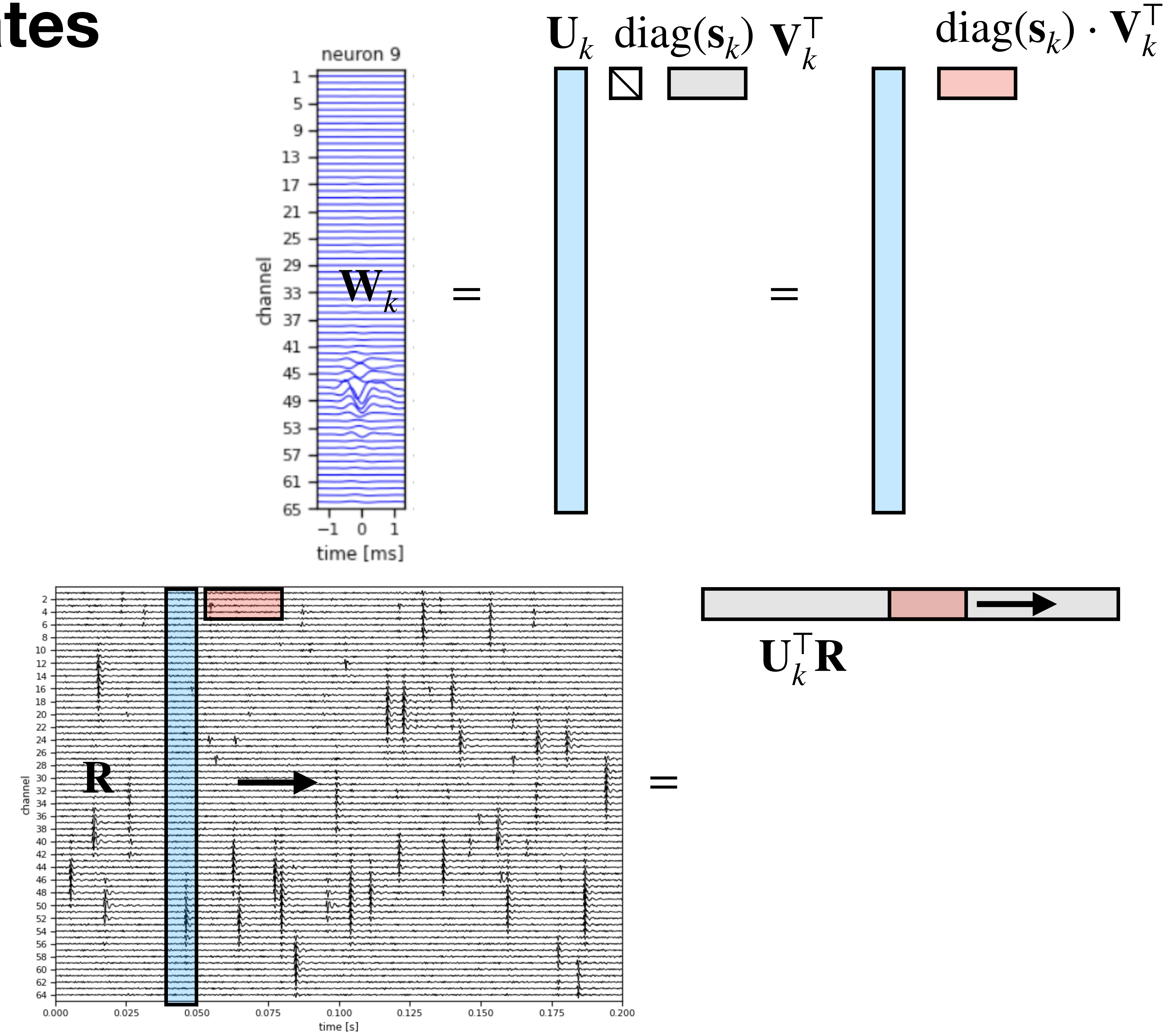
More efficient computation

Leveraging the low-rank templates

We can compute the "scores" for amplitude updates more efficiently by leveraging the low-rank templates,

$$
\begin{aligned}
[\mathbf{R} \star \mathbf{W}_k]_t &= \sum_{n=1}^{N} \sum_{d=1}^{D} r_{n,t+d} w_{k,n,d} \\
&= \sum_{d=1}^{D} \mathbf{r}_{t+d}^\top \mathbf{w}_{k,:,d} \\
&= \sum_{d=1}^{D} \mathbf{r}_{t+d}^\top \mathbf{U}_k \mathbf{S}_k \mathbf{v}_{k,:,d} \\
&= \sum_{d=1}^{D} (\mathbf{U}_k^\top \mathbf{r}_{t+d})^\top [\mathbf{S}_k \mathbf{V}_k^\top]_{:,d} \\
&= [(\mathbf{U}_k^\top \mathbf{R}) \star (\mathbf{S}_k \mathbf{V}_k^\top)]_t
\end{aligned}
$$

In other words, we cross-correlate the projected residual.



Conclusion

- We developed a basic spike sorting model that was good for building intuition, but not very practical.
- We developed a new model for the voltage in terms of a superposition of templates convolved with spike amplitudes for each neuron.
  - Along the way, we learned about convolution and cross-correlation.
- We derived a **coordinate ascent algorithm** for *maximum a posteriori* (MAP) inference.
- **Next time**: you'll implement the algorithm in lab! You'll learn a bit of PyTorch for implementing the convolutions and cross-correlations, then test it out on the GPU.

Further reading

- **Simple Spike Sorting** and **Spike Sorting by Deconvolution** course notes.
- Convolution and cross-correlation:
    - Chapter 9 of *The Deep Learning Book* (deeplearningbook.org/contents/convnets.html)
    - Start reading up on PyTorch convolutions! https://pytorch.org/docs/stable/generated/torch.nn.functional.conv1d.html
- Spike sorting:
    - Pachitariu, Marius, Shashwat Sridhar, and Carsen Stringer. "Solving the spike sorting problem with Kilosort." bioRxiv (2023).
        - The model we presented is a slightly modified version of *Kilosort*