

Uni- and Multivariate Analysis of Dendritic Ca²⁺ Data

In a Stimulus Detection Task

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July 17, 2017

BCCN Berlin

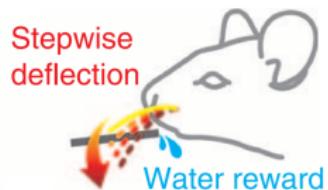
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2. Goal
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4. Multivariate SMV Analysis
5. Population Coding

Introduction

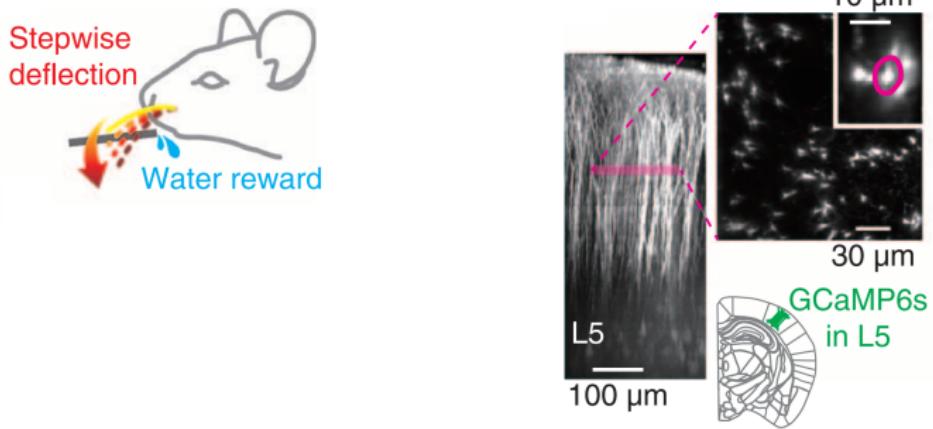
The Experiment

Takahashi et al. 2016



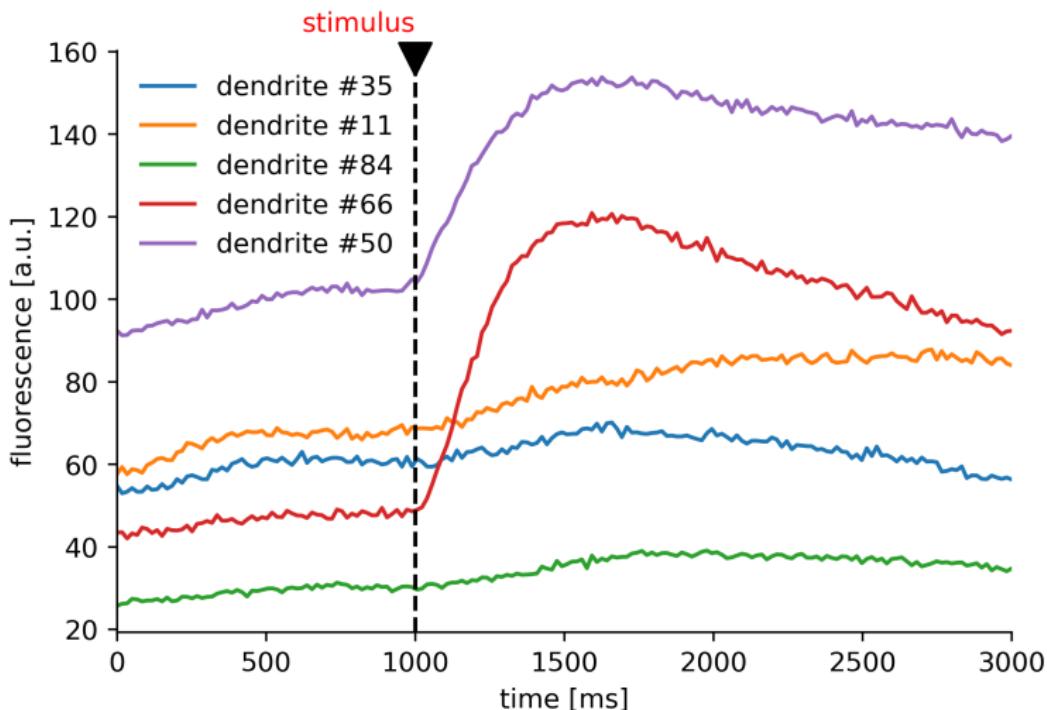
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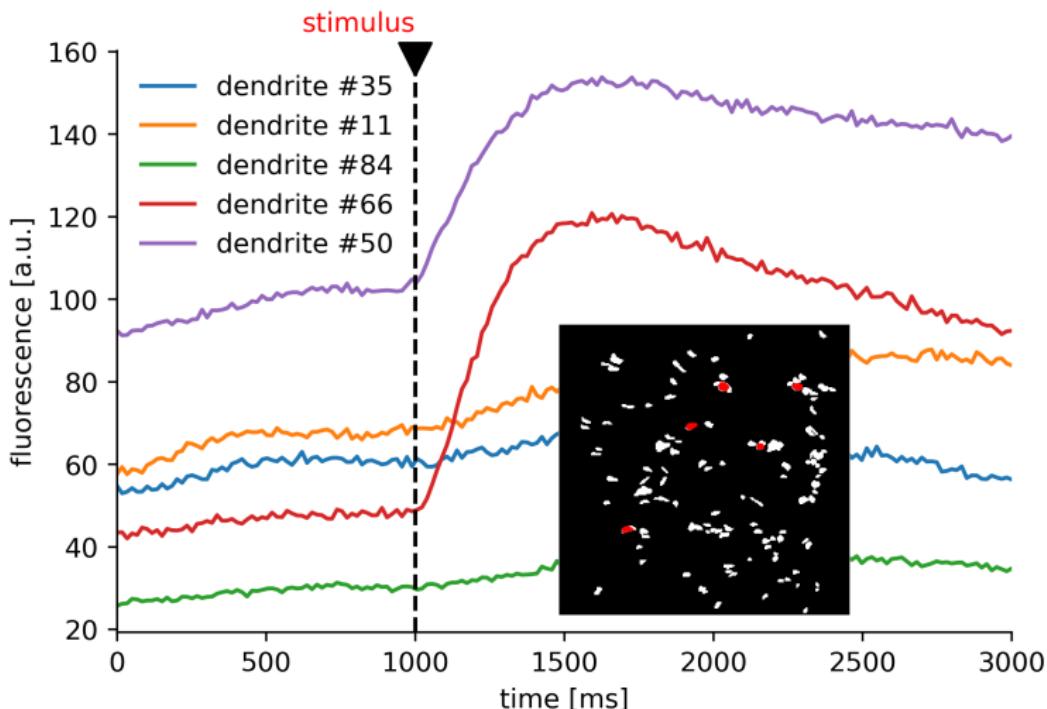
The Data - Neuronal

Trial-averaged Ca^{2+} fluorescence traces of random dendrites

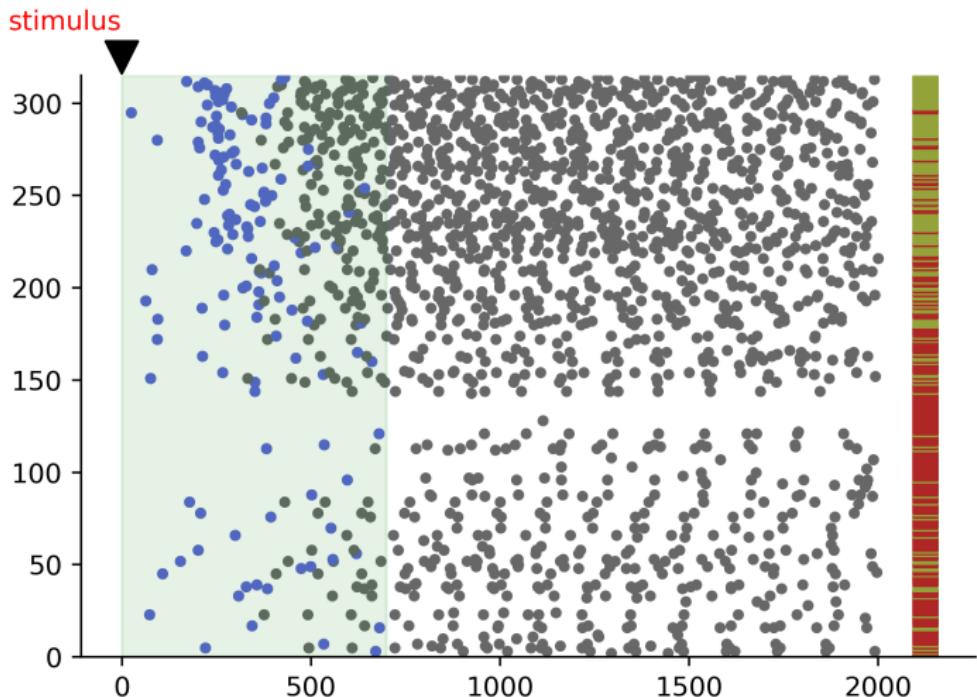


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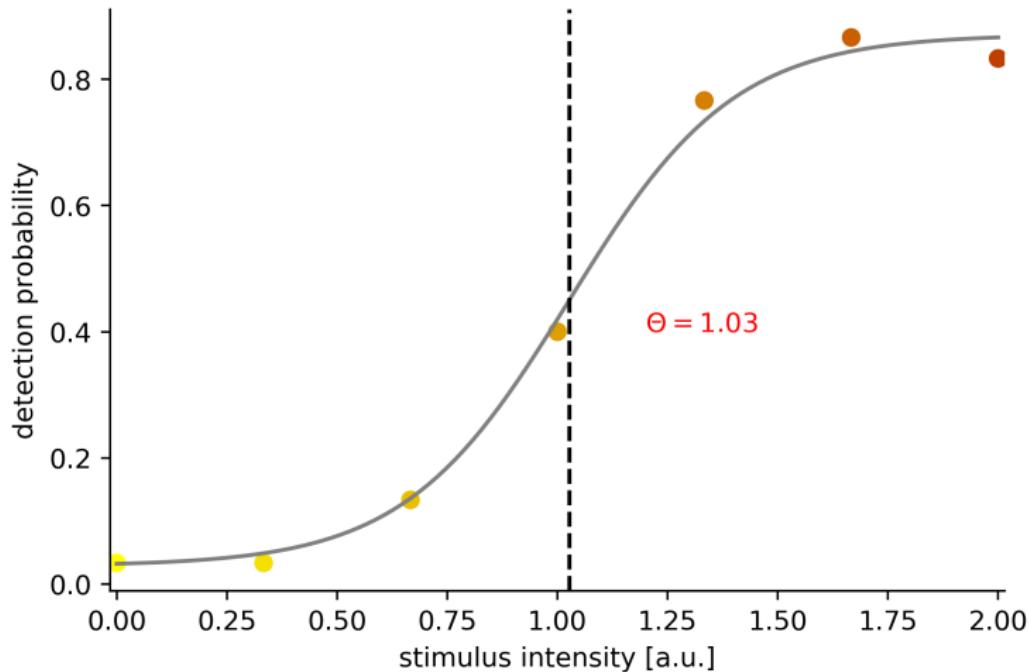
Trial-averaged Ca^{2+} fluorescence traces of random dendrites



The Data - Behavioral



The Data - Psychometric Curve



Goal

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The goal of this project is to investigate the following:

- What is the relationship between Ca^{2+} activity and stimulus intensity/behavior

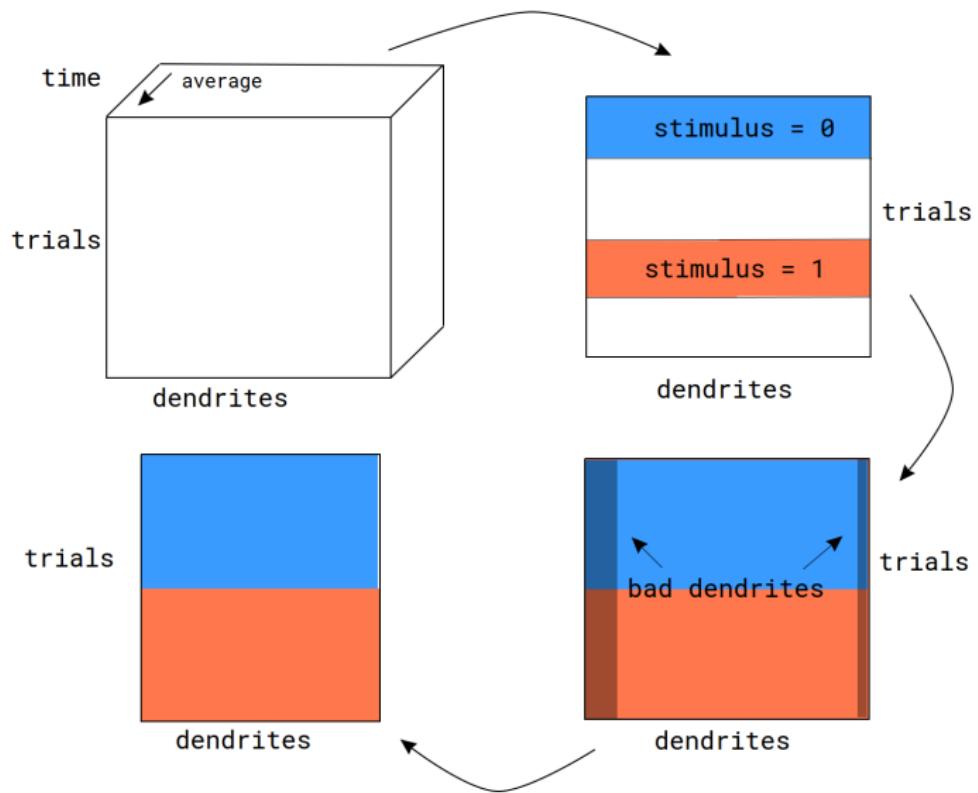
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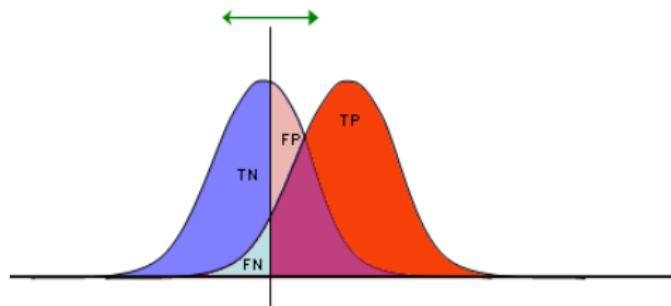
- What is the relationship between Ca^{2+} activity and stimulus intensity/behavior
- Does a multivariate approach give us any significant advantage over a univariate one?

Univariate Analysis

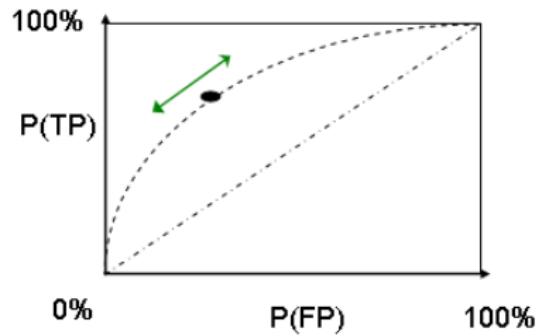
Stimulus Presence Detection



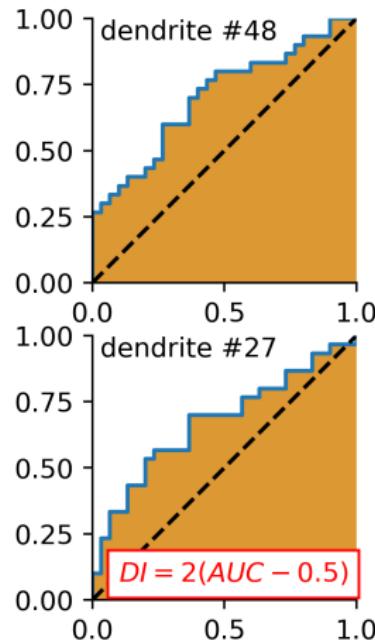
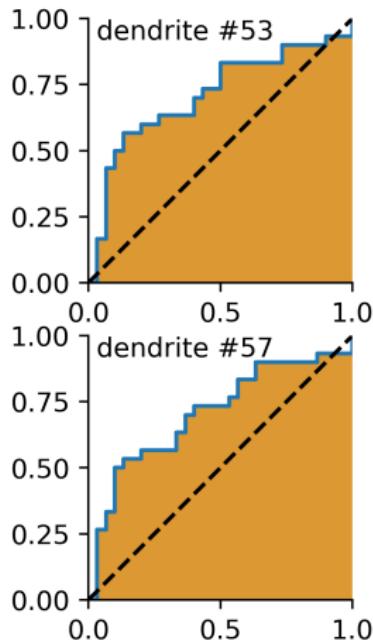
ROC



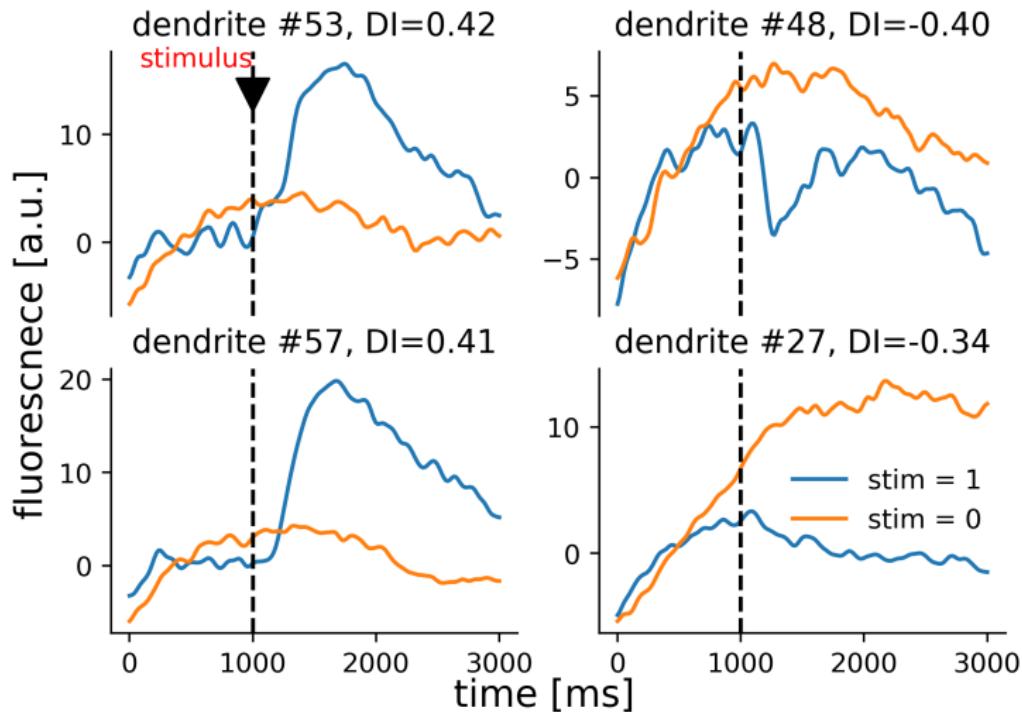
TP	FP
FN	TN
1	1



ROC - Best ROC Curves

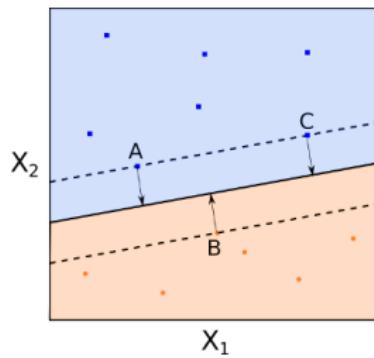


Ca^{2+} -Trace of Largest $|\text{DI}|$ -Dendrites

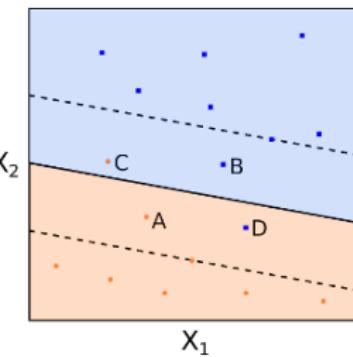
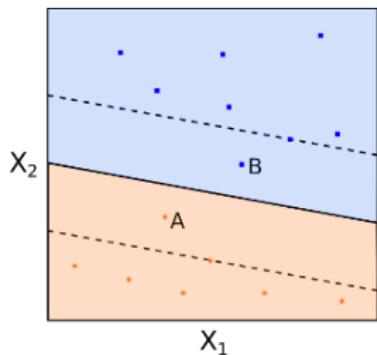
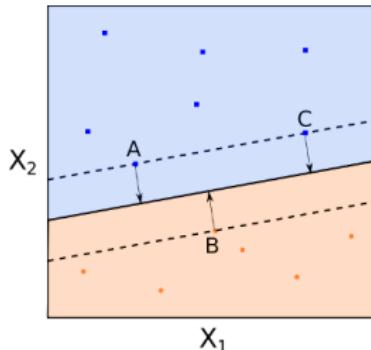


Near threshold-stimulus (≈ 1)

SVM - What is an SMV?



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Why SVM?

- staple of machine learning
- regularization parameter limits overfitting
- good for small samples with many features (in theory)

SVM - Most Accurate Dendrites

Stimulus strength 1 (near threshold)

Dendrite #	μ_{acc}	σ_{acc}
57	0.70	0.12
53	0.68	0.14
48	0.63	0.13
27	0.62	0.08

Rank Order Correlation

We want to quantify the similarity between two rank orders of dendrites R and Q , which both have length n .

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Weighted Rank Order Correlation Coefficient

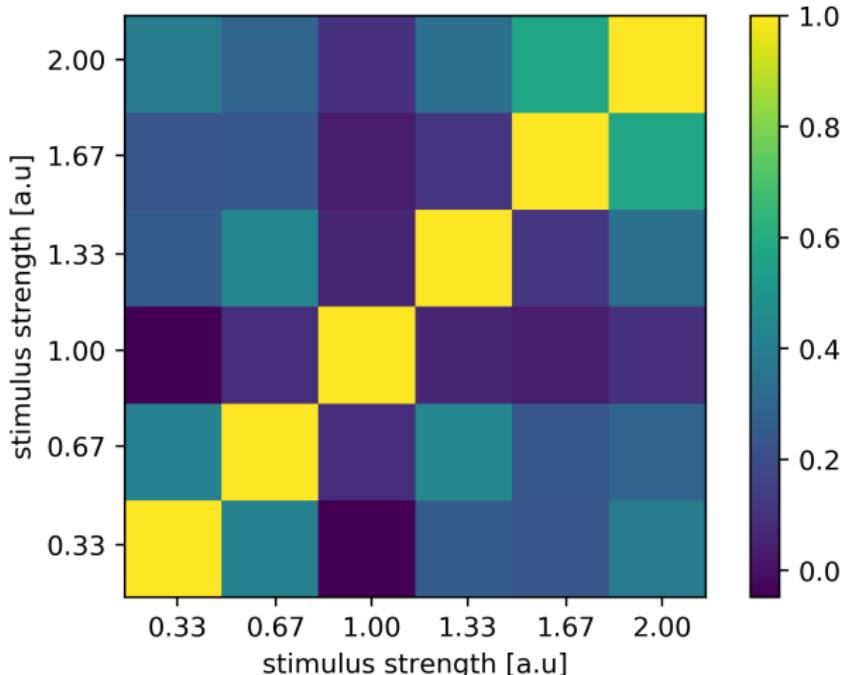
One possible solution:

$$\rho_W(R, Q) = 1 - \frac{-2 \sum_i^n w_i D_i^2}{\sum_i^n w_i (n - 2i + 1)^2}$$

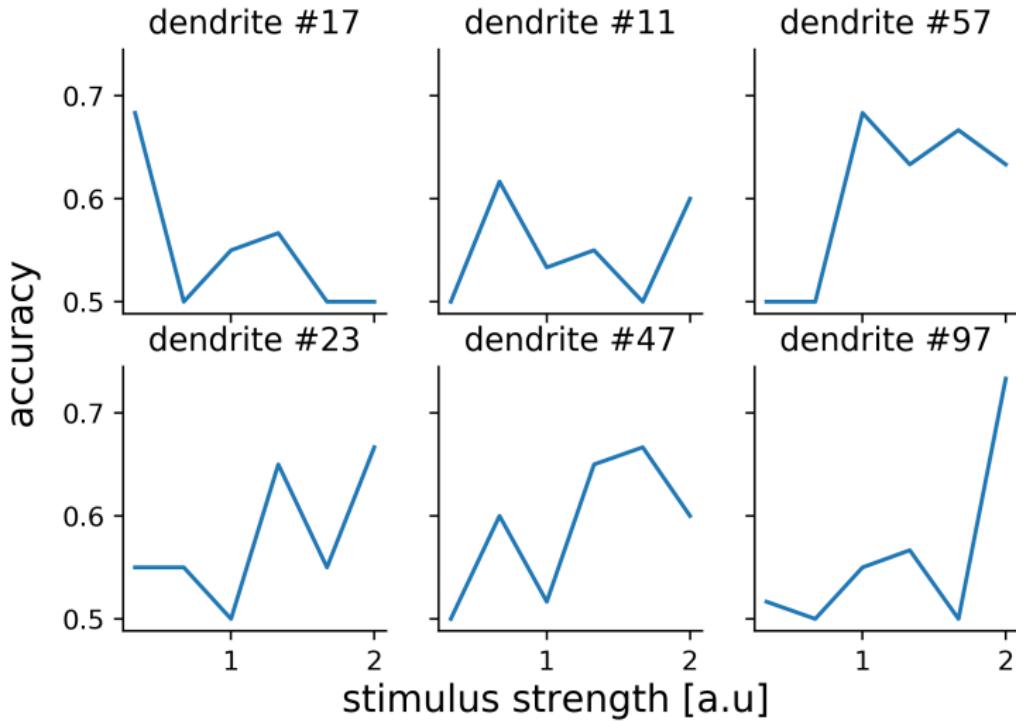
With a monotonicity constraint on W .

Rank Order Correlations of Dendrites Over Stimuli

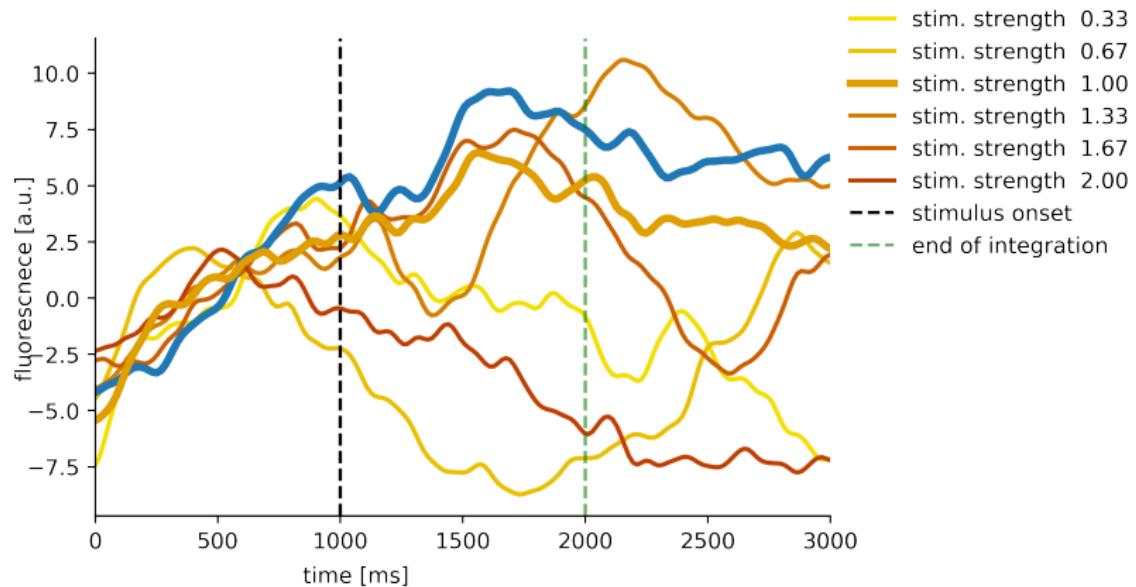
Weighted rank coefficient ρ_ω (todo: find more optimal weights)



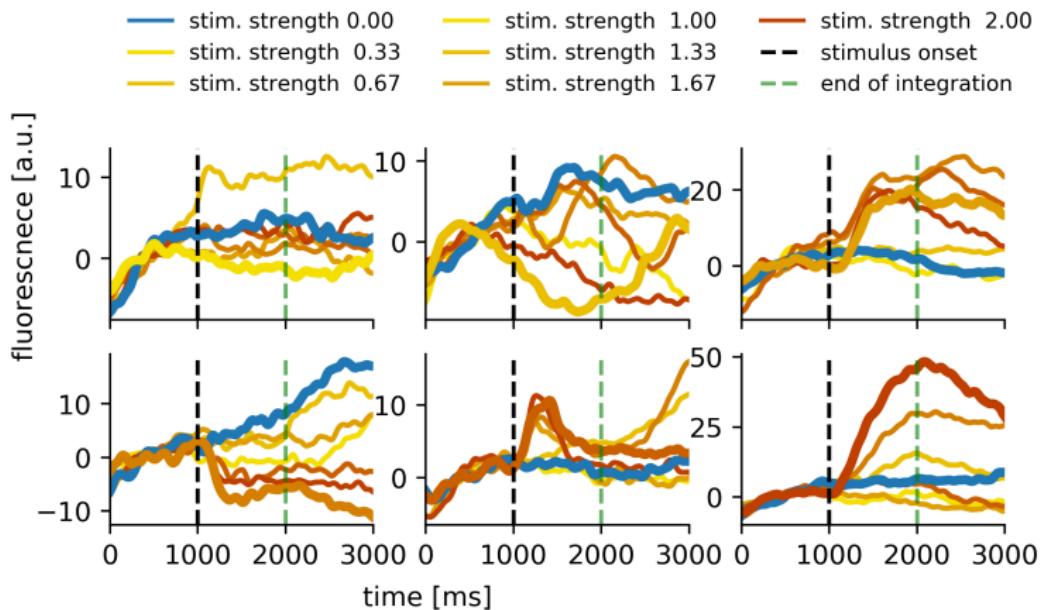
Tuning Curves



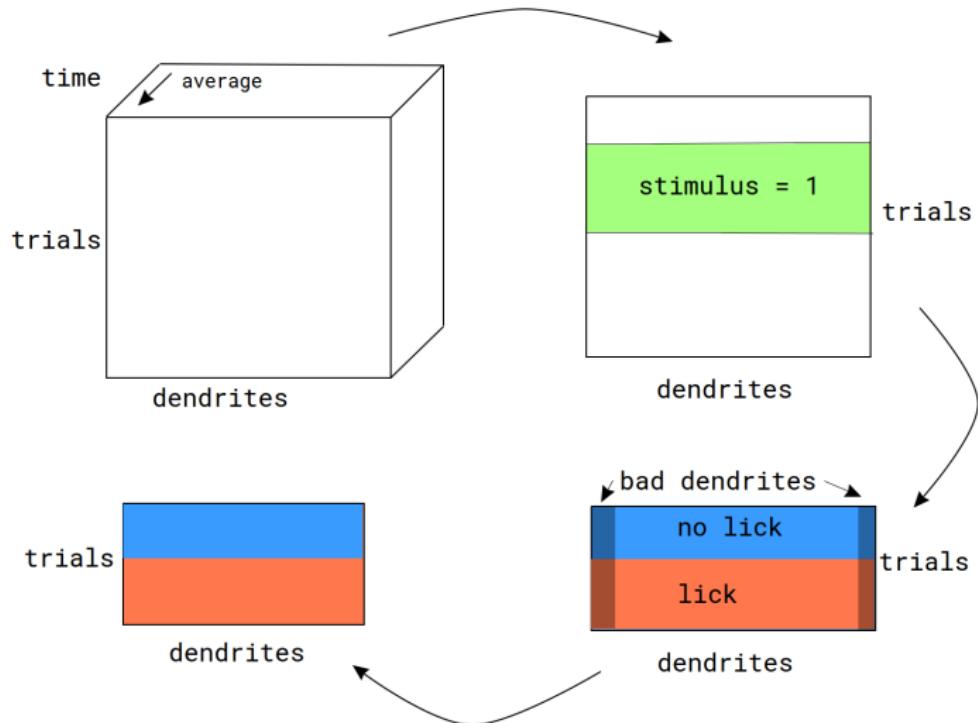
Tuning Curves



Tuning Curves



Bevahior Detection



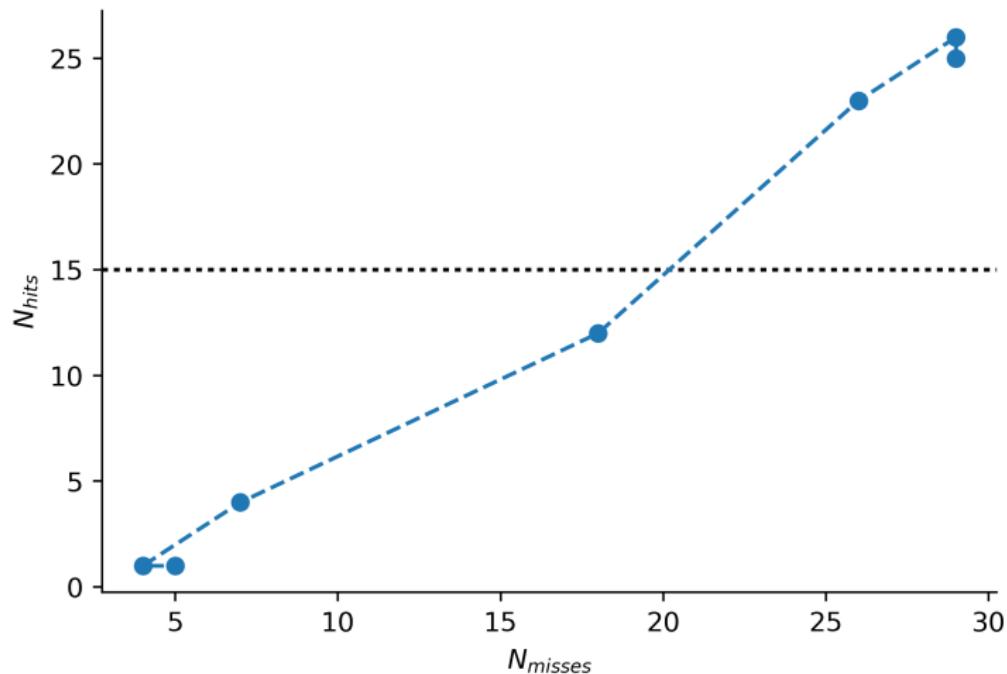
Behavioral Prediction - Most Accurate Dendrites

Different dataset - Stimulus strength 1 (near threshold)

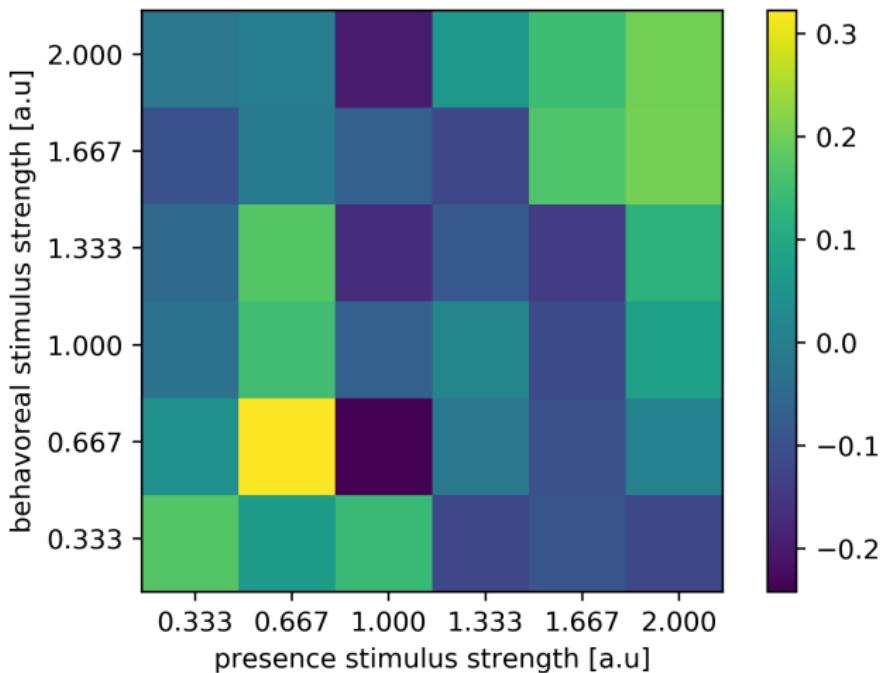
Dendrite #	μ_{acc}	σ_{acc}
88	0.80	0.08
57	0.80	0.08
92	0.78	0.06
56	0.76	0.10

Behavioral Prediction - Imbalance

$N_{no-lick}$ vs. N_{lick} for all stimuli



Rank Correlations of Behavoreal and Presence Dendrites



Multivariate SMV Analysis

Presence Detection - Feature Selection

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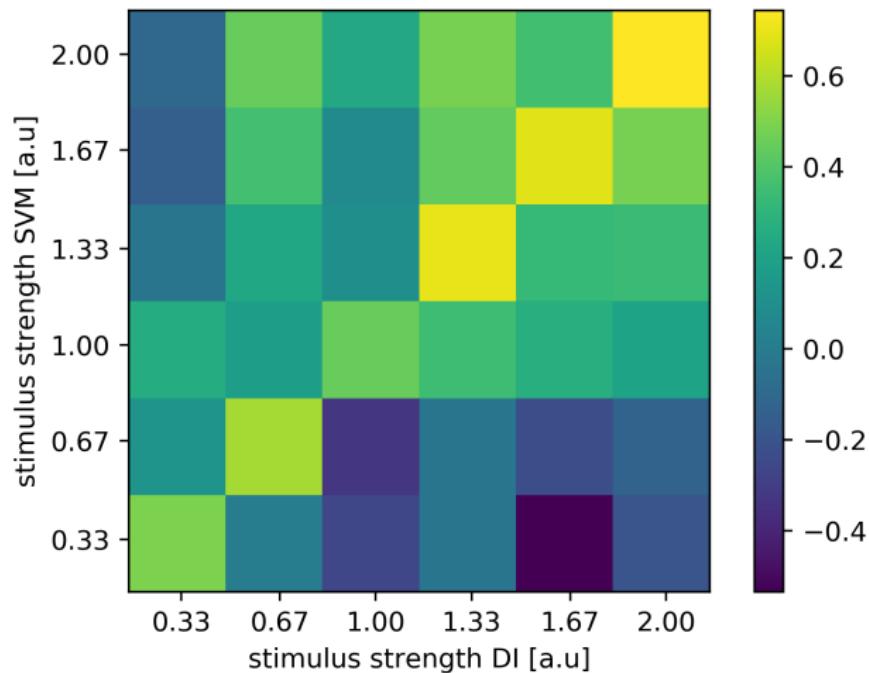
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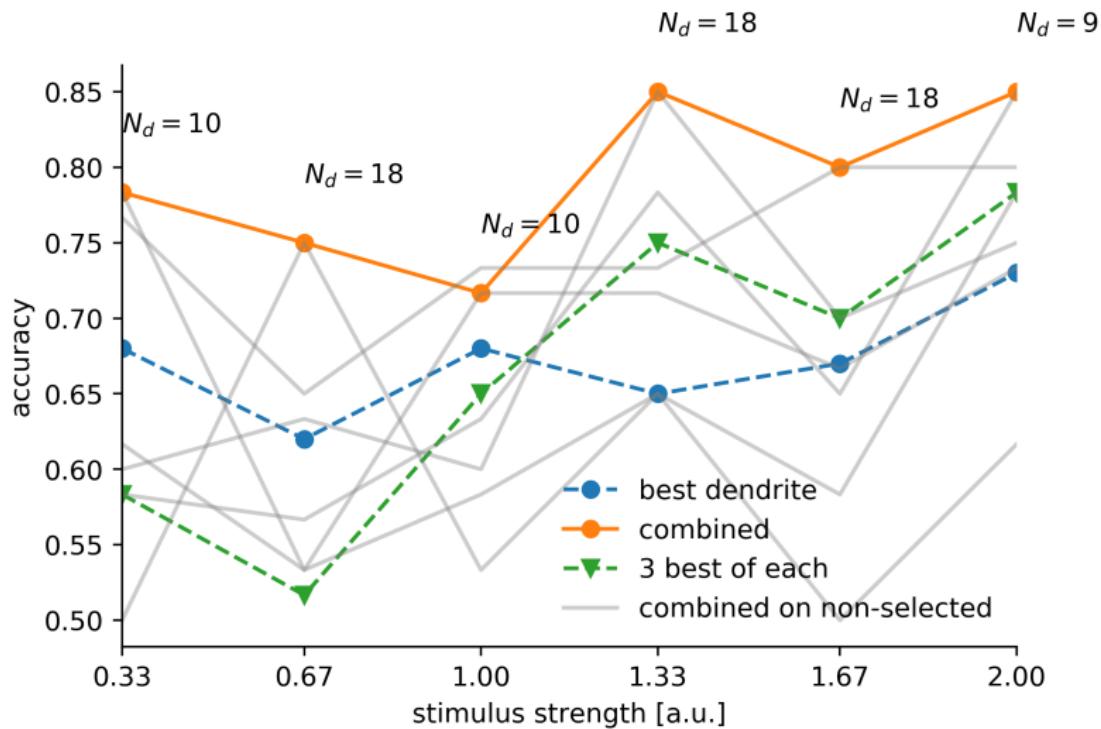
⇒ we have to do **feature selection**.

We can use the previously best discriminating dendrites (SVM/DI).

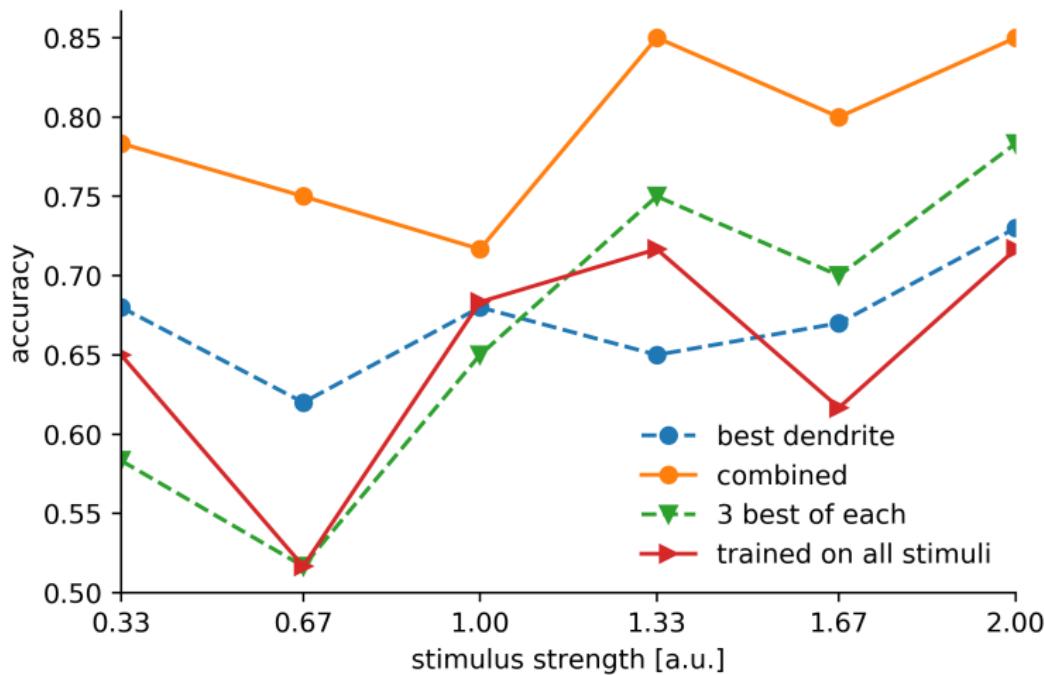
DI and SVM Dendrite Rank Order Correlation



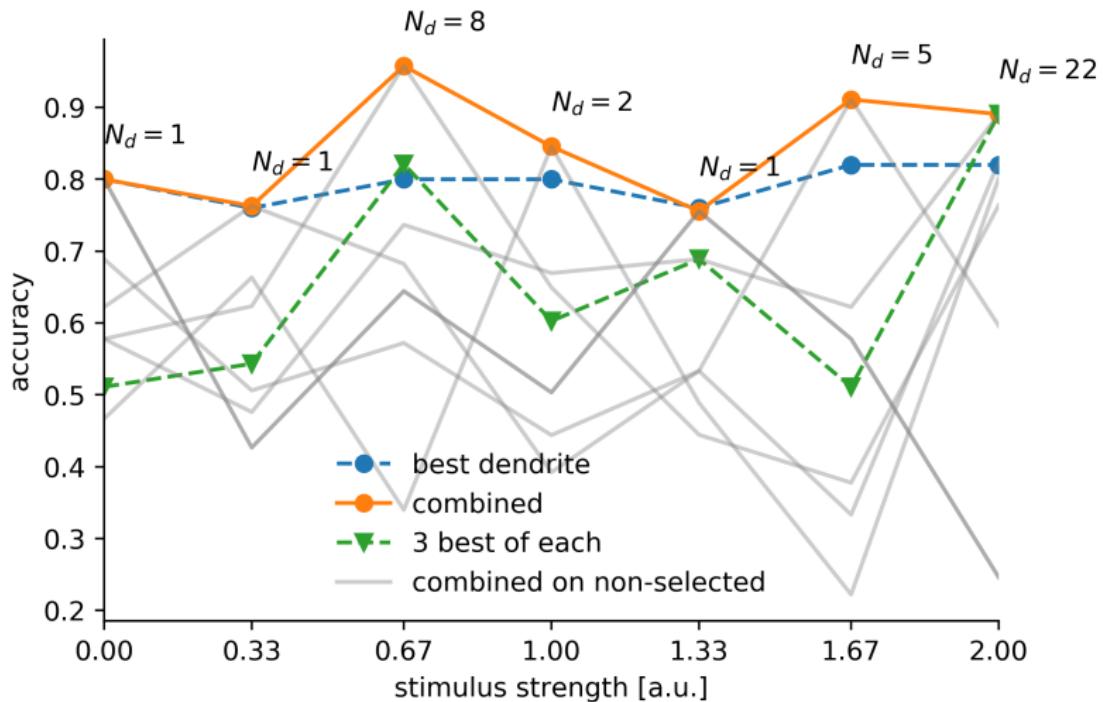
SVM Performance on Combined Dendrites - Presence Detection



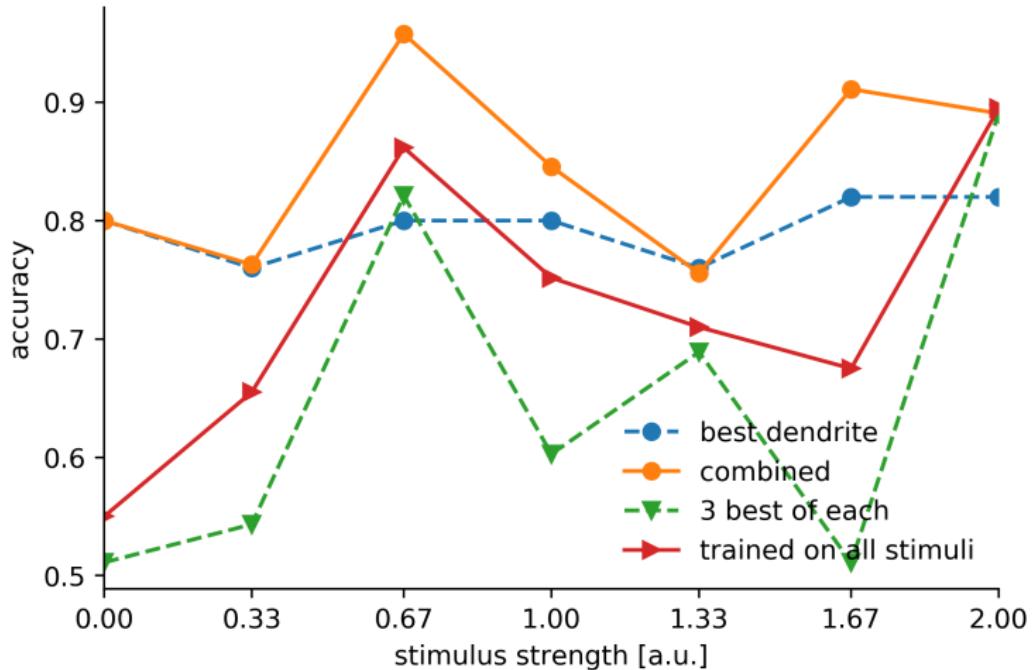
SVM Performance on Combined Dendrites - Presence Detection



SVM Performance on Combined Dendrites - Behavioral

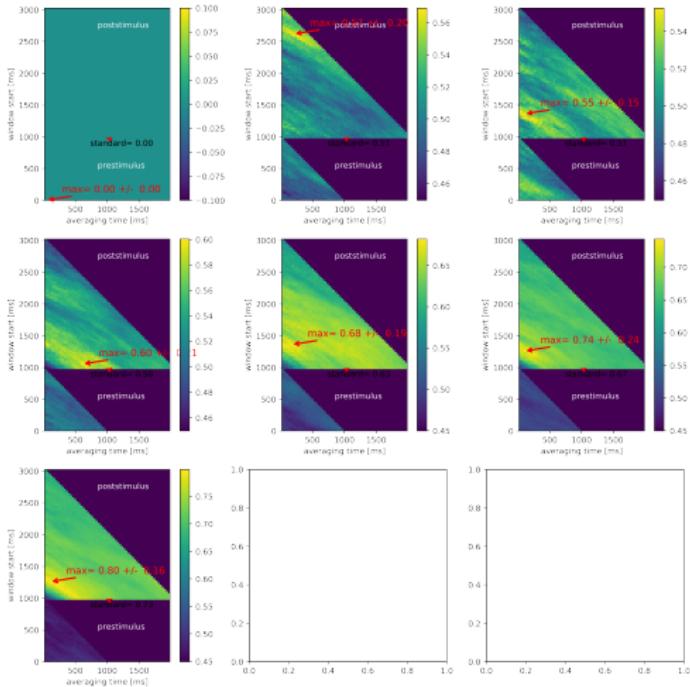


SVM Performance on Combined Dendrites - Behavioral



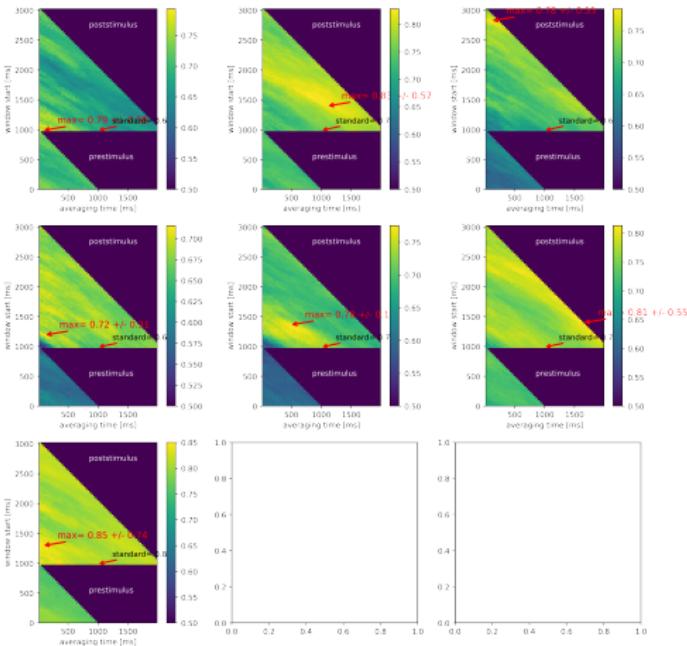
Optimal Averaging Times

Dummy



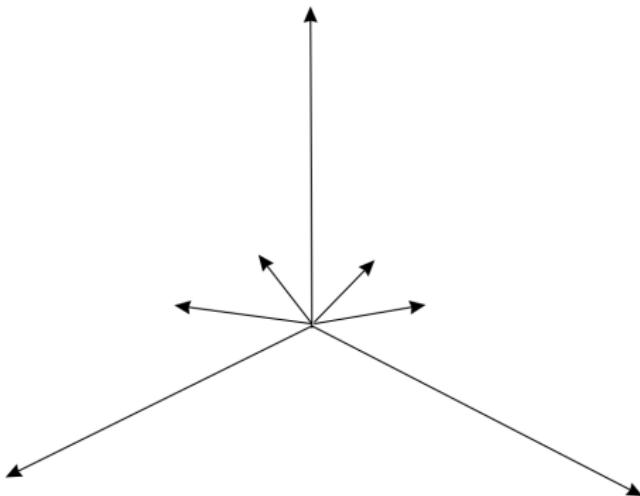
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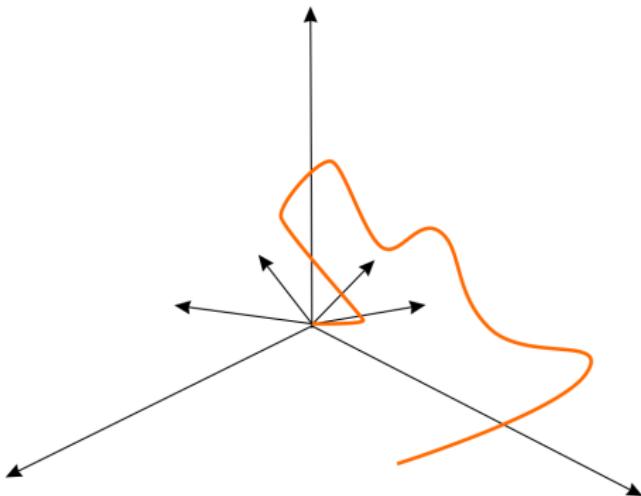


Population Coding

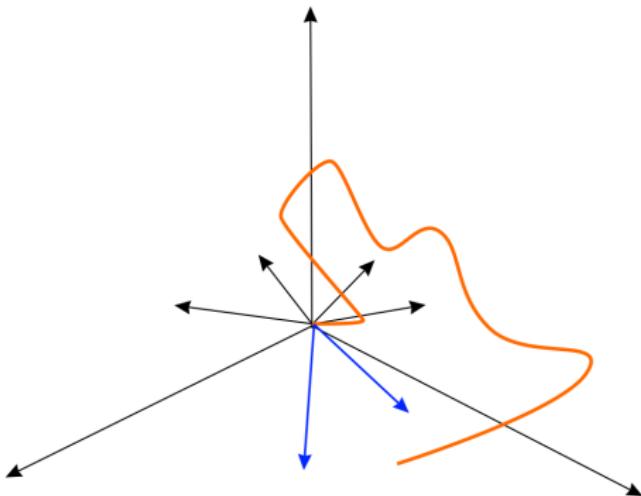
Population Coding - Idea (Mante, Sussillo 2013)



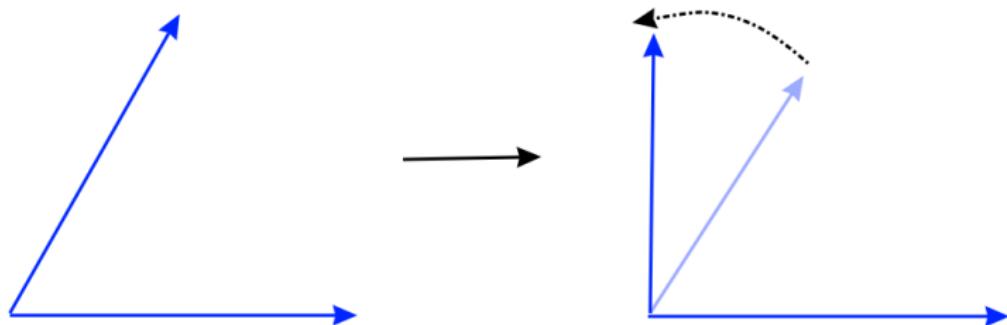
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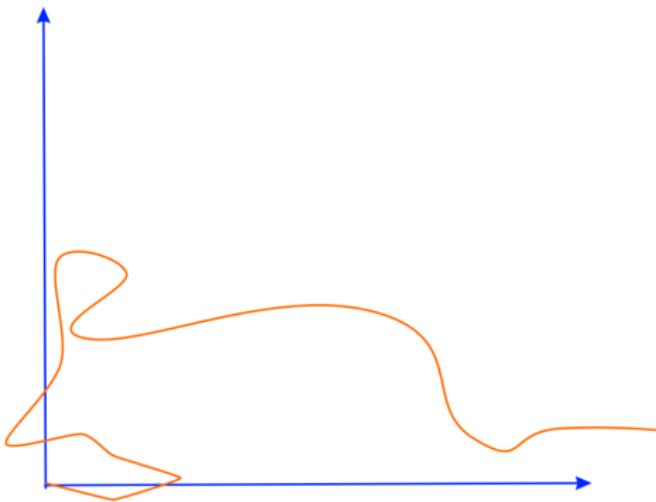
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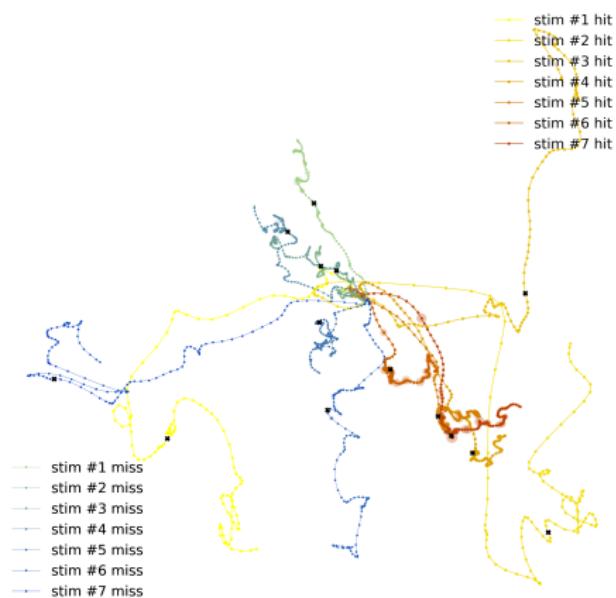


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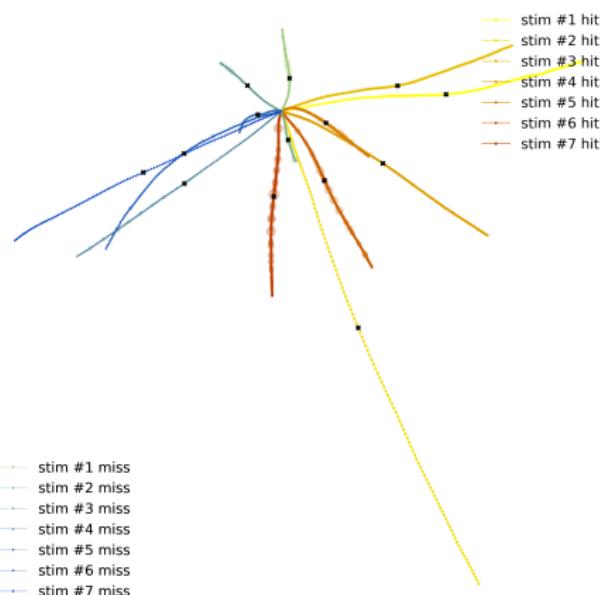
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Solve Problem with combined SVM first



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-  Takahashi, N., Oertner, G. T., Hegemann, P. & Larkum, E. M. Active cortical dendrites modulate perception. *Science* 335, 1587-1590 (2016)
-  Mante V., Sussillo D., Shenoy KV., Newsome WT. Context-dependent computation by recurrent dynamics in prefrontal cortex. *Nature* 503, 78-84 (2013)
-  Pinto da Costa, J. New Results in Weighted Correlation and Weighted Principal Component Analysis with Applications, Chapter 2 (2015)

Extra Slides

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Thus:

$$\boxed{\rho_W(R, Q) = 1 - \frac{-2 \sum_i^n w_i D_i^2}{\sum_i^n w_i (n - 2i + 1)^2}}$$

Population Response in Task Variable Space

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To that end we use linear regression to write the normalized response of dendrite i at time t in trial k as a linear combination of these task variables:

$$r_k^{i,t} = \beta_1^{i,t} choice_k + \beta_2^{i,t} stimulus_k + \beta_3^{i,t}$$

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The regression coefficients $\beta_\nu^{i,t}$ describe how much the activity of dendrite i at time t in trial k corresponds with variable ν .

Population Response in Task Variable Space

We define

$$\mathbf{F} = \begin{bmatrix} choice_1 & \dots & choice_n \\ stimulus_1 & \dots & stimulus_n \\ 1 & \dots & 1 \end{bmatrix}$$

and estimate for each dendrite i and timepoint t

$$\beta^{i,t} = (\mathbf{F}\mathbf{F}^T)^{-1}\mathbf{F}\mathbf{r}^{i,t}$$

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The goal is to use β to find a two-dimensional subspace of the dendrite space into which we can transform $\mathbf{x}^{c,t}$.

Population Response in Task Variable Space

We then use PCA to denoise the data matrix

$$\mathbf{X} = \begin{bmatrix} \mathbf{x}_{c_1, t_1} & \dots & \mathbf{x}_{c_1, t_n} & \dots & \mathbf{x}_{c_m, t_n} \end{bmatrix}$$

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and we apply the denoising matrix to all $\beta^{\nu, t}$ as well, which yields the denoised regression vectors

$$\beta_{pca}^{\nu, t}$$

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$$\beta_{max}^{\nu} = \beta_{pca}^{\nu, t_{max}}$$

$$t_{max}^{\nu} = argmax_t ||\beta_{pca}^{\nu, t}||$$

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We would like these β_{\max}^ν to be the basis vectors of our new coordinate system, however, they are not yet orthogonal. We fix this by applying QR-decomposition to

$$\mathbf{B}^{\max} = \begin{bmatrix} \beta_{\max}^1 & \beta_{\max}^2 \end{bmatrix} = \mathbf{Q}\mathbf{R}$$

where \mathbf{Q} is an orthogonal matrix whose columns β_\perp^ν are the **basis vectors** of our new coordinate system. We can now transform our data into it.