Uni- and Multivariate Analysis of Dendritic Ca2+ Data

In a Stimulus Detection Task

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July 18, 2017

BCCN Berlin

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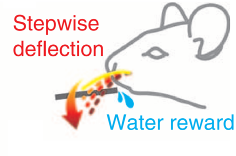
Introduction

The Experiment

Takahashi et al. 2016



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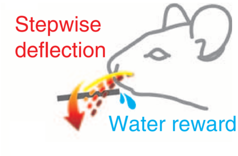
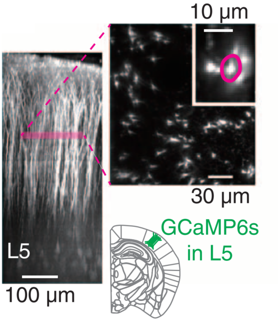
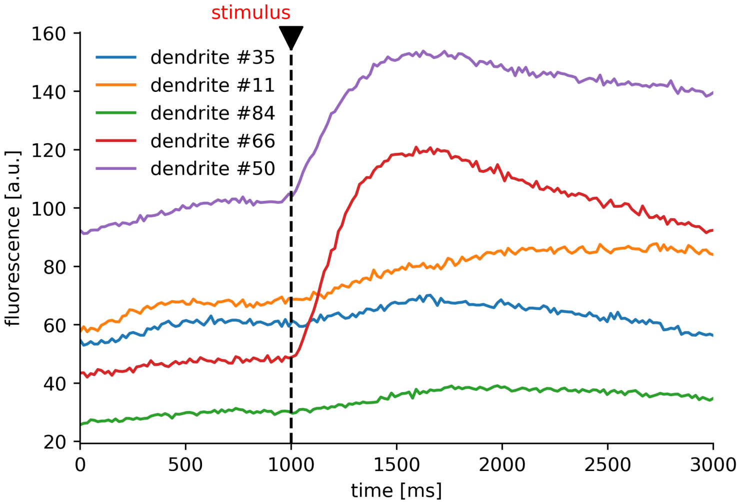




The Data - Neuronal

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



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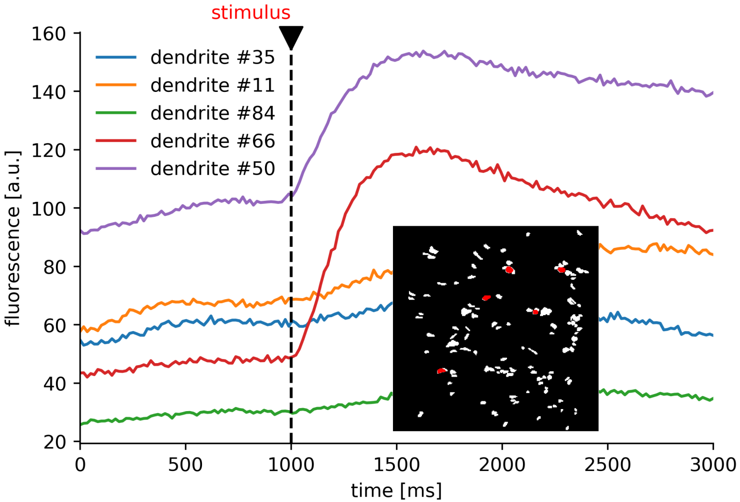
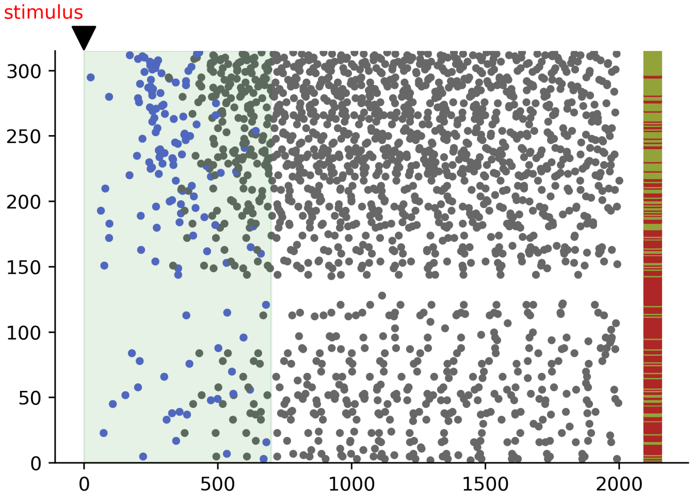
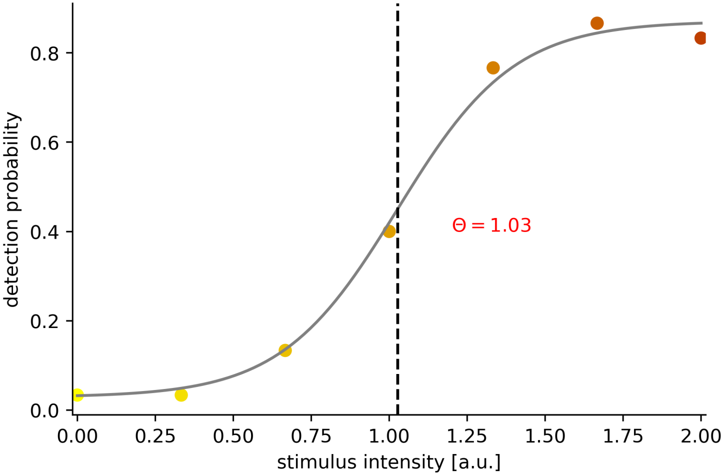


The Data - Behavioral



The Data - Psychometric Curve



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The goal of this project is to investigate the following:

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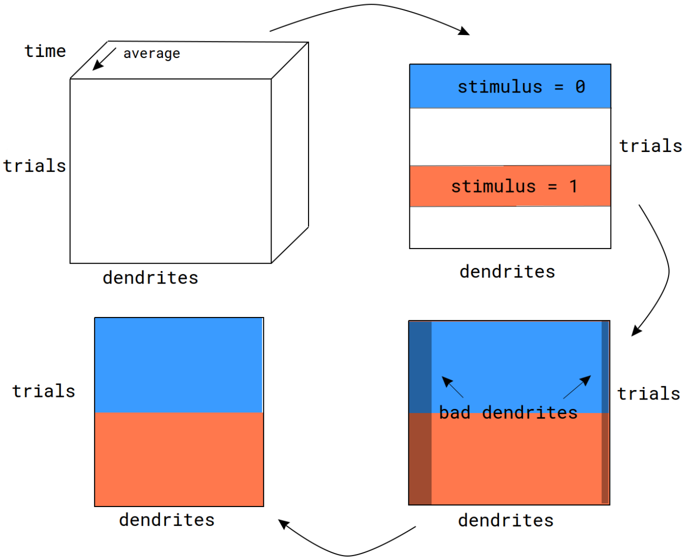
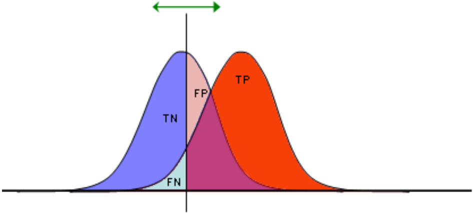
- What is the relationship between Ca2+ activity and stimulus intensity/behavior
- Does a multivariate approach give us any significant advantage over a univariate one?

Univariate Analysis

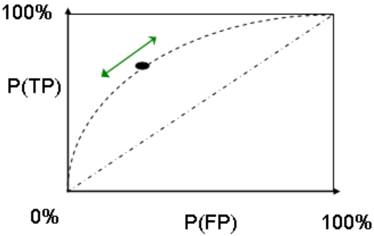
Stimulus Presence Detection

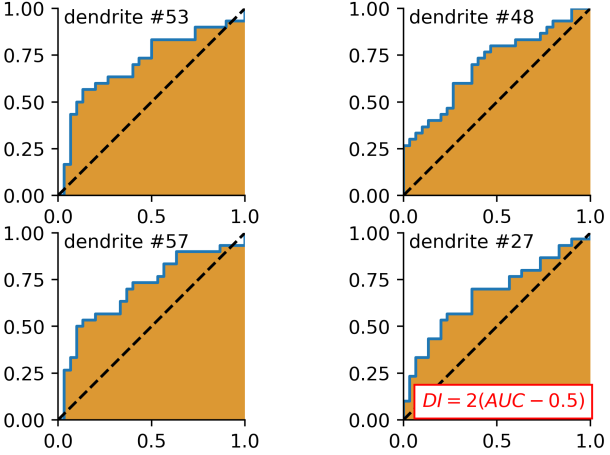


ROC

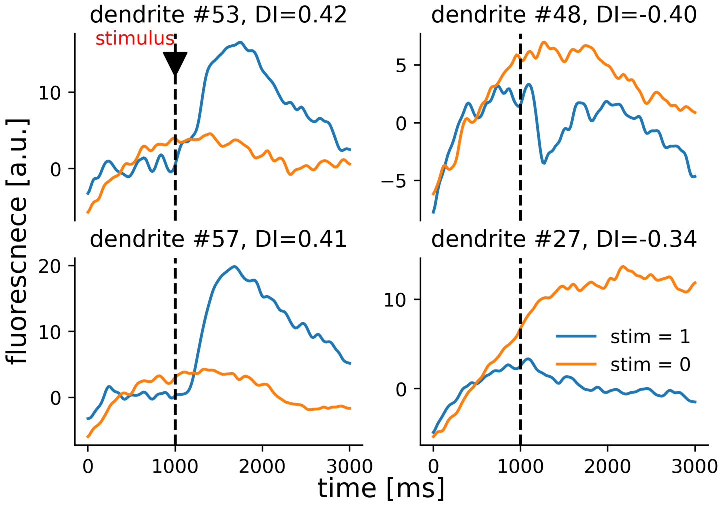


TP	FP
FN	TN
1	1



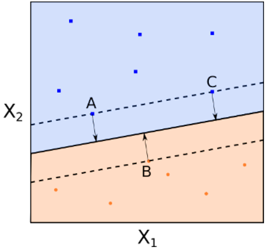

dendrite #53
dendrite #48
dendrite #57
dendrite #27
$DI = 2(AUC - 0.5)$
1.00
0.75
0.50
0.25
0.00
0.0
0.5
1.0

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



Near threshold-stimulus (≈ 1)

SVM - What is an SMV?



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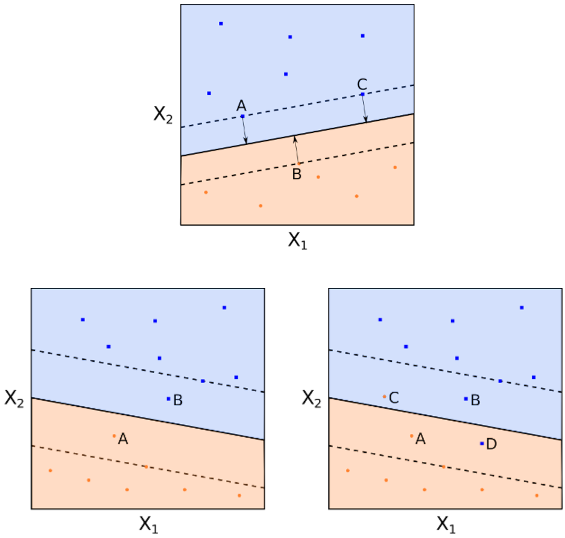

Why SVM?

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

SVM Specifics

- All data are normalized to zero mean and unit variance
- Crossvalidation is performed to conrol for overfitting

SVM - Most Accurate Dendrites

Stimulus strength 1 (near thereshold)

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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Problem: Many of the dendrites are not significant for classification but affect ρ greatly. We would like to be able to **weight our $\mathbf{D_i}$**'s.

Weighted Rank Order Correlation Coefficient

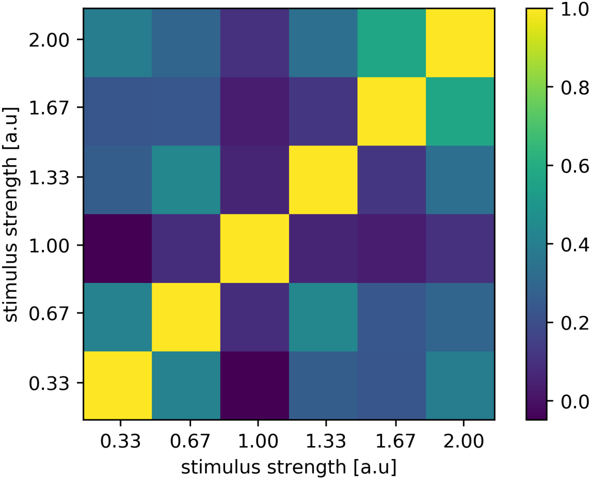
One possible soulution:

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

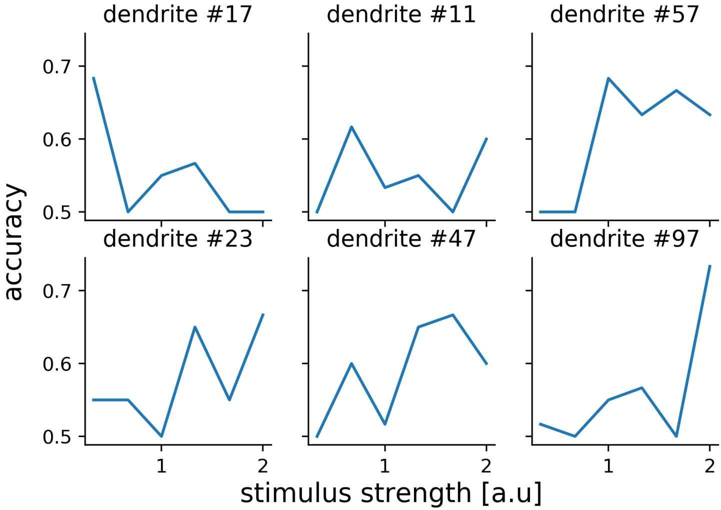
With a monotonicity constraint on W.

Rank Order Correlations of Dendrites Over Stimuli

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



Tuning Curves



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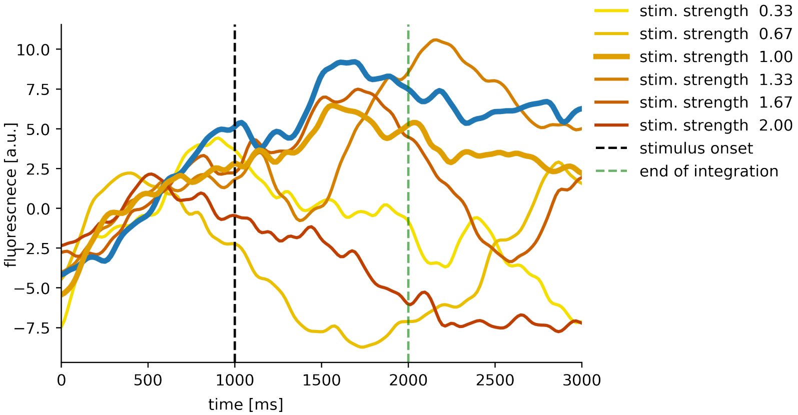

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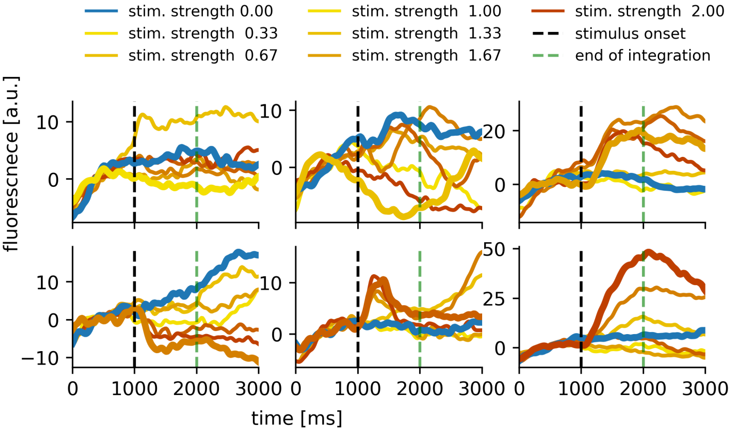
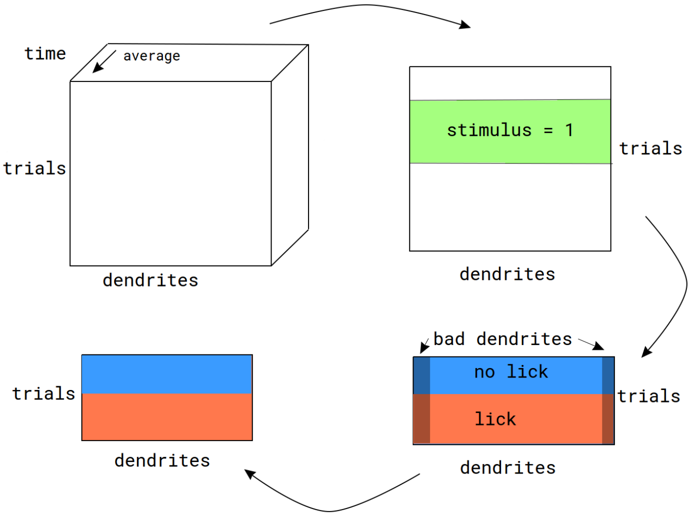


Bevahior Detection

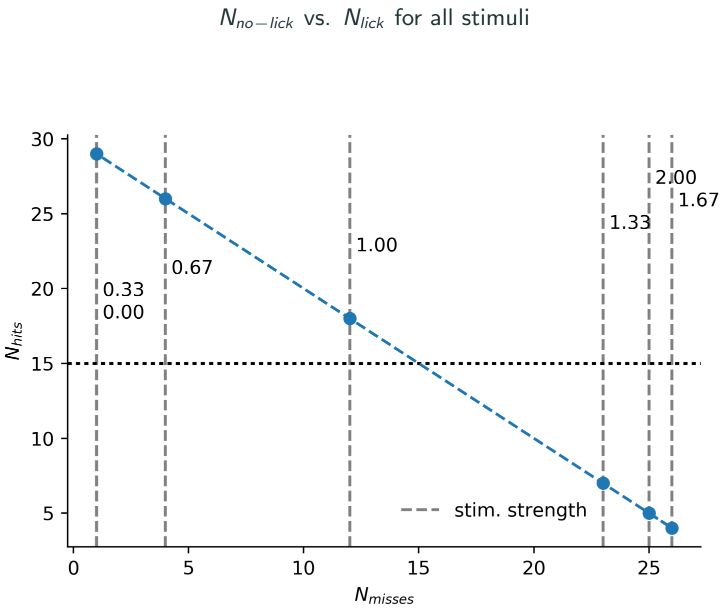


Behavioral Prediction - Most Accurate Dendrites

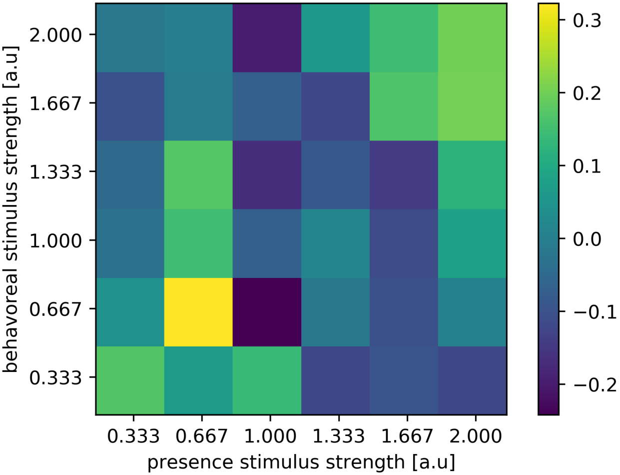
Different dataset - Stimulus strength 1 (near thereshold)

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

Behavorial Predition - Imbalance



Rank Correlations of Behavoreal and Presence Dendrites



Multivariate SMV Analysis

Presence Detection - Feature Selection

Since we have only few datapoints per condition (30-50 per class) in comparison to the number of features (100-150), we are prone to overfit to noise.

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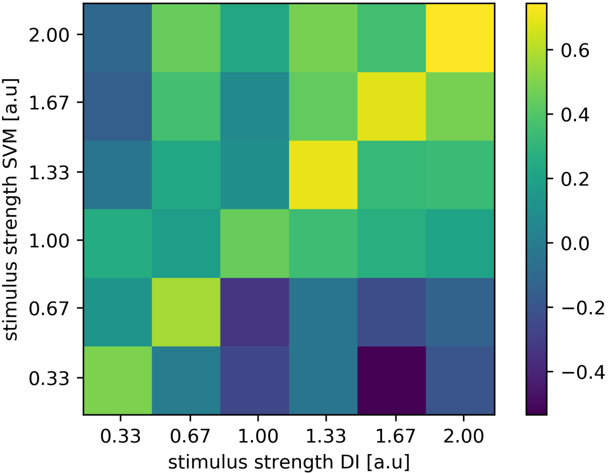
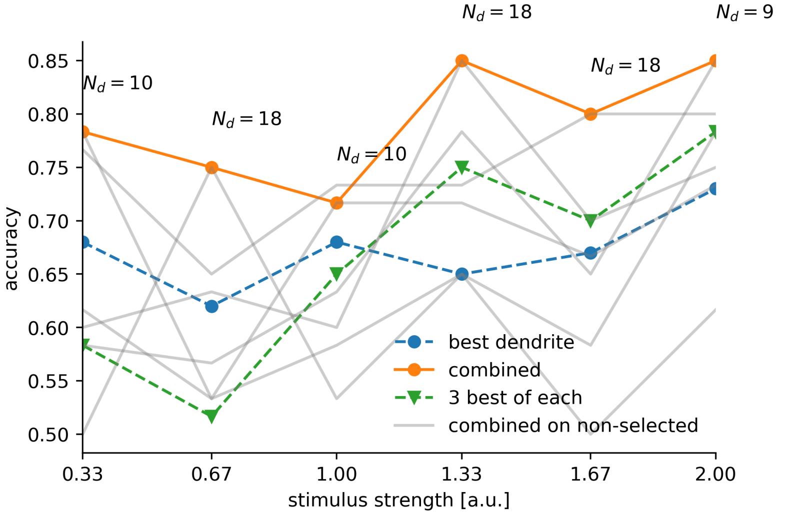
$\Rightarrow$ we have to do **feature selection**.

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

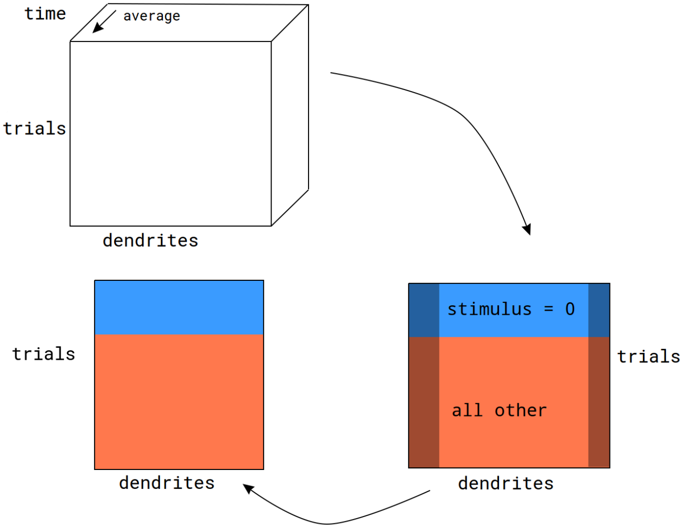
DI and SVM Dendrite Rank Order Correlation



SVM Performance on Combined Dendrites - Presence Detection



SVM Performance on Combined Dendrites - Global Presence



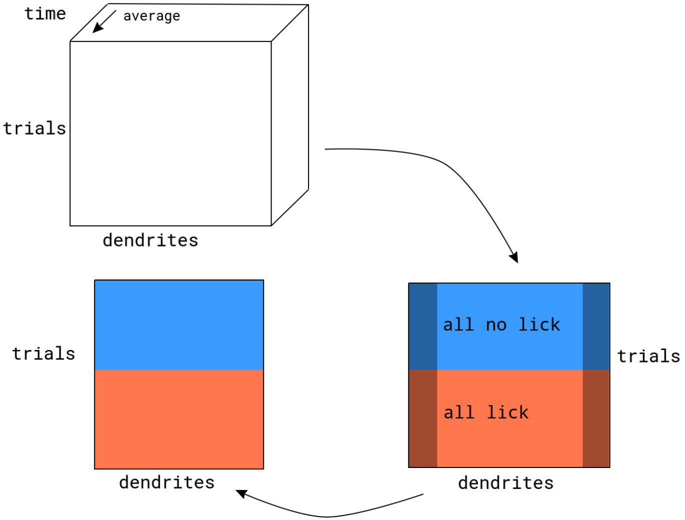
SVM Performance on Combined Dendrites - Global Presence

Performance on global presence detection:

Mean: 0.68

Standard deviation: 0.08

SVM Performance on Combined Dendrites - Global Behavior



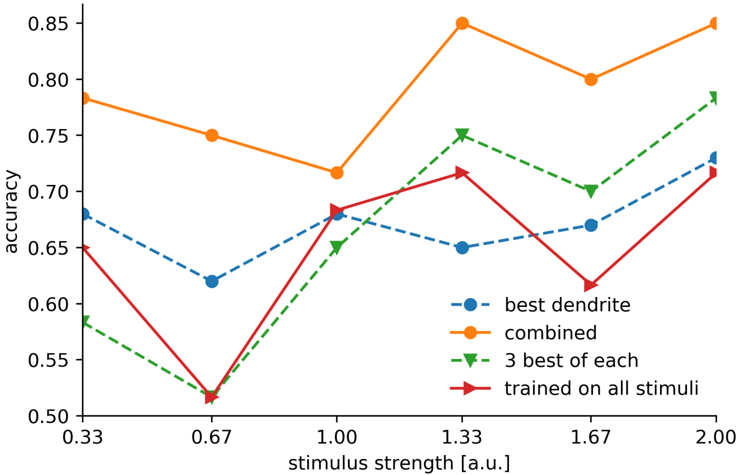
SVM Performance on Combined Dendrites - Global Behavior

Performance on global presence detection:

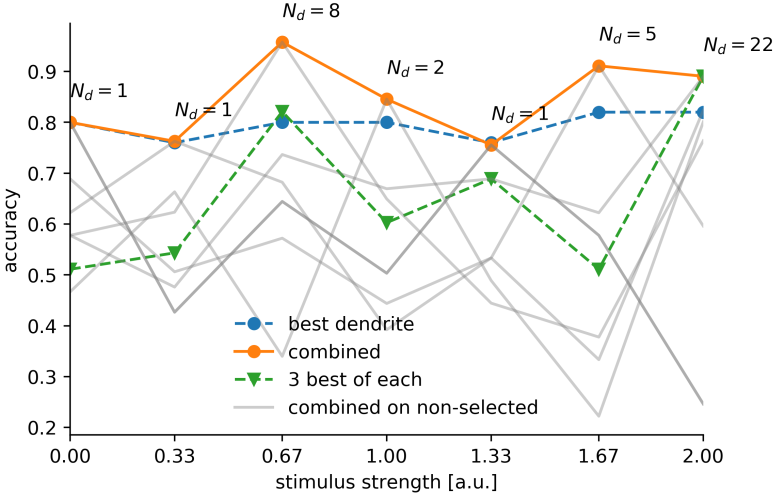
Mean: 0.71

Standard deviation: 0.1

SVM Performance on Combined Dendrites - Presence Detection



SVM Performance on Combined Dendrites - Behavioral



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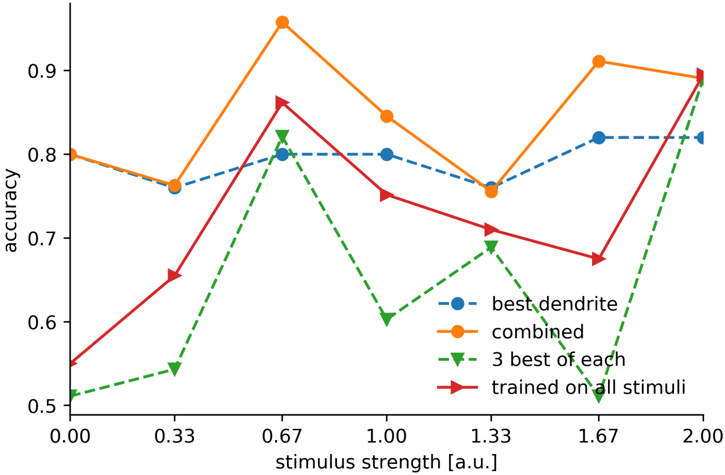
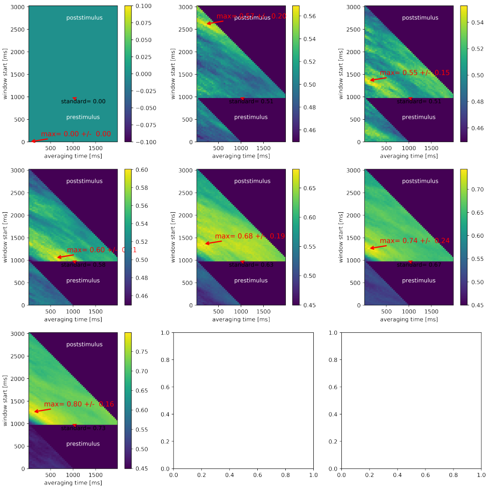


Optimal Averaging Times

Dummy



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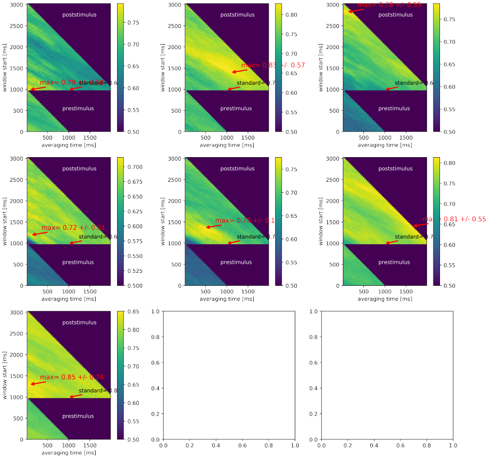
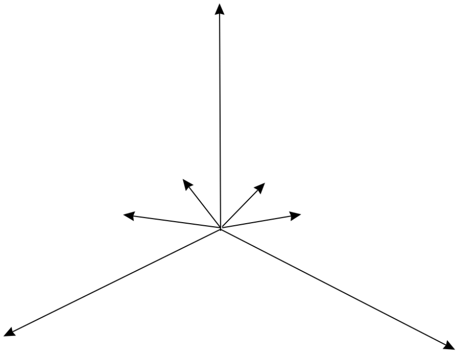


Population Coding

Population Coding - Idea (Mante, Sussillo 2013)



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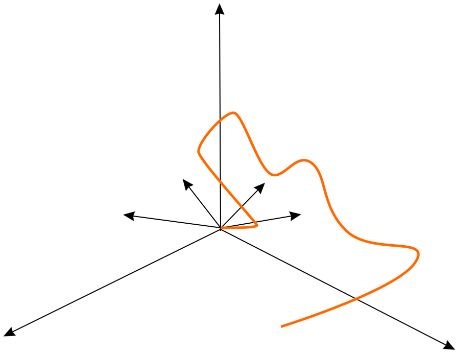

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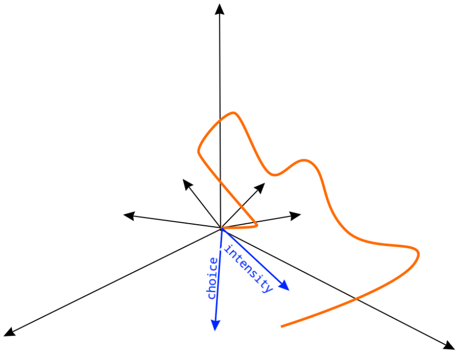

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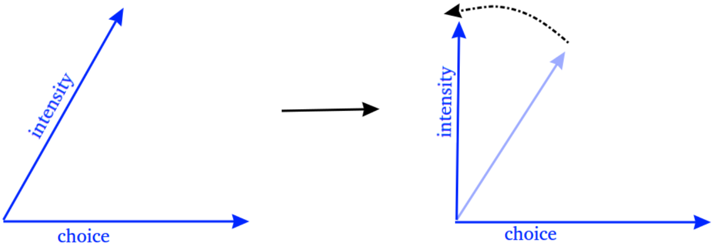

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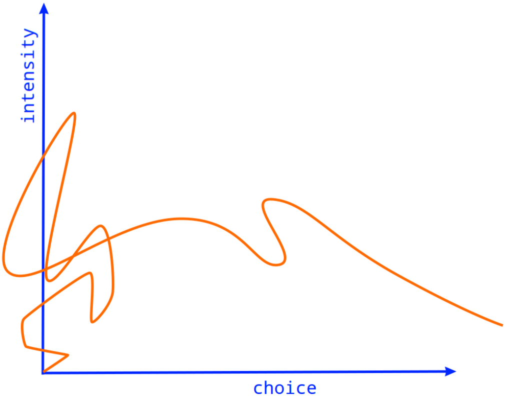
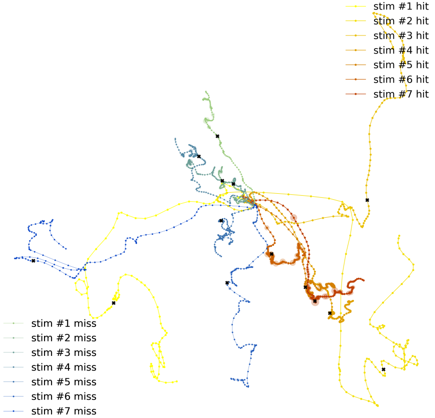


Population Response in Task Variable Space

Solve Problem with combined SVM first



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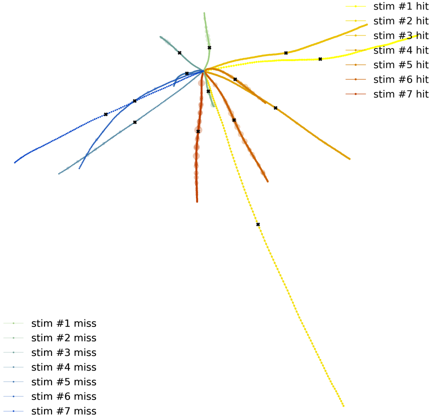

- Takahashi, N., Oertner, G. T., Hegemann, P. & Larkum, E. M. Active cortical dendrites modulate perception. Science 335, 1587-1590 (2016)
- Mante V., Sussillo D., Shenoy KV., Newsome WT. Context-dependent computation by recurrent dynamics in prefrontal cortex. Nature 503, 78-84 (2013)
- Pinto da Costa,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

Extra Slides

Weighted Rank Order Correlation Coefficient

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The first condition gives us $A = 1$, and the second one

$$B = \frac{-2}{\sum_i^n w_i (n - 2i + 1)^2}$$

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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

We would like to visualize the time evolution of the population response in a coordinate system in which the axes represent stimulus strength and choice.

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To that end we use linear regression to write the normaized 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

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

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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 $\mathbf{x}^{\mathbf{c},\mathbf{t}}$.

Population Response in Task Variable Space

We then use PCA to denoise the data matrix

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

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

$$\beta^{\boldsymbol{\nu},\boldsymbol{t}}_{\boldsymbol{pca}}$$

Population Response in Task Variable Space

Since the $\beta_{\boldsymbol{pca}}^{\boldsymbol{\nu},\boldsymbol{t}}$ are time variing but we would like a coordinate system that is fixed in time, we "freeze" them at the point in time at which there is maximum correlation:

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$$\boldsymbol{\beta}_{\boldsymbol{max}}^{\boldsymbol{\nu}} = \boldsymbol{\beta}_{\boldsymbol{pca}}^{\boldsymbol{\nu},\boldsymbol{t}_{max}^{\nu}}$$

$$t_{max}^{\nu} = argmax_t ||\boldsymbol{\beta}_{\boldsymbol{pca}}^{\boldsymbol{\nu},\boldsymbol{t}}||$$

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$$\mathbf{B}^{\mathbf{max}} = \begin{bmatrix} \beta^{\mathbf{1}}_{\mathbf{max}} & \beta^{\mathbf{2}}_{\mathbf{max}} \end{bmatrix} = \mathbf{QR}$$

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