3D Distribution of Synapses in Cortex

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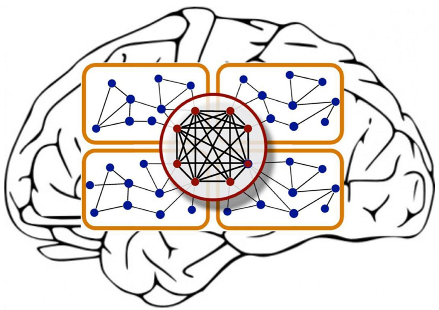
Significance

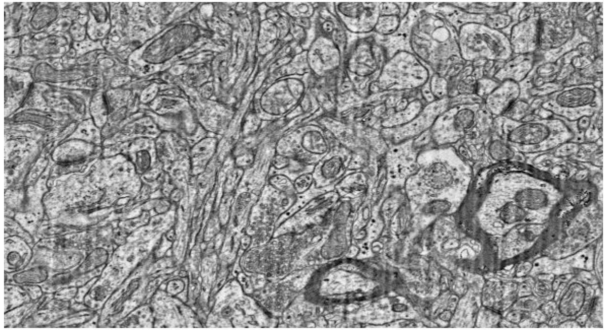
- The ultimate goal of systems neuroscience is to fully map the human connectome



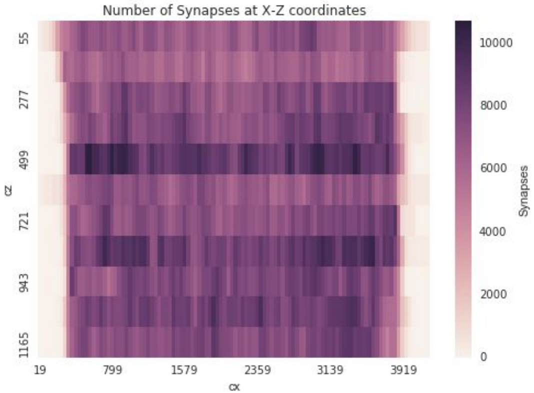
- Traditional neuroscience techniques involve studying individual neurons in isolation. This cannot capture:
  - ***Spatial Distribution***
  - Connectivity
  - Information processing

Need/Gap

- Electron microscopy now affords the ability to map entire sections of cortex in detail
- It is now possible to assess the distribution of synapses in cortex
  - Also possible to assess Connectivity

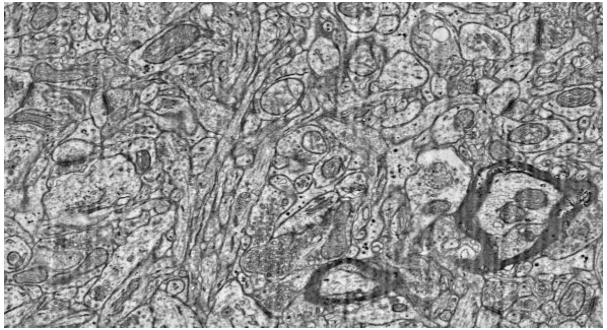


- This project will focus on synaptic density across “layers” of cortex



Challenges

- Annotation of neural markers
  - Labeling of synapses
  - Labeling of neurons / cell types
  - Separating cortical layers



- Stratifying synapses
  - This project is focused on synaptic density across “layers”
  - Resolving different cortical layers from the EM data is non-trivial.
  - We considered different Z-layers instead of cortical

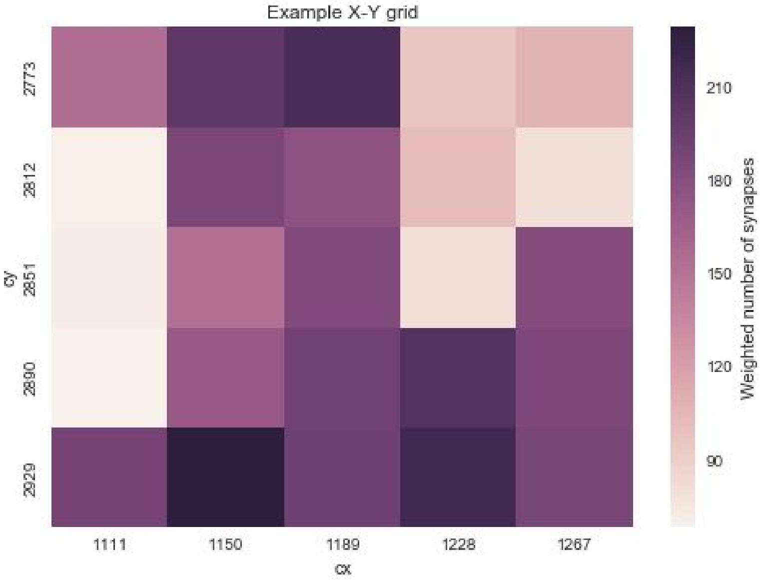
Formal Statement of Problem

$$N = \# \{\text{Synapses}\}$$

$$X_i = \text{X position} \qquad Y_i = \text{Y position}$$

$$X_i,\ Y_i,\ N \sim F := \{F_{X,Y,N}\ (.;\theta):\ \theta \in \Theta\}$$

$$W_i = \{High\ Density,\ Low\ Density\}$$



$$L = \sum_{-\infty}^{\infty} I(\hat{W} \neq W)$$

$$E[L] = \sum_{-\infty}^{\infty} I(\hat{W} \neq W)/N$$

- Z layers labeled (8 low, 3 high density)
- Classify grids by mean synapses per bin
- Get the expectation of loss function

Model Assumptions

- Grid means are independent of X, Y dimensions

$$X_i,\ Y_i \ \| \ U_i$$

- Grid means are i.i.d

$$(u_1, u_2, \ldots, u_i) \sim F = \prod F_i,\ F_i = F_j,\ \forall\ i \neq j$$

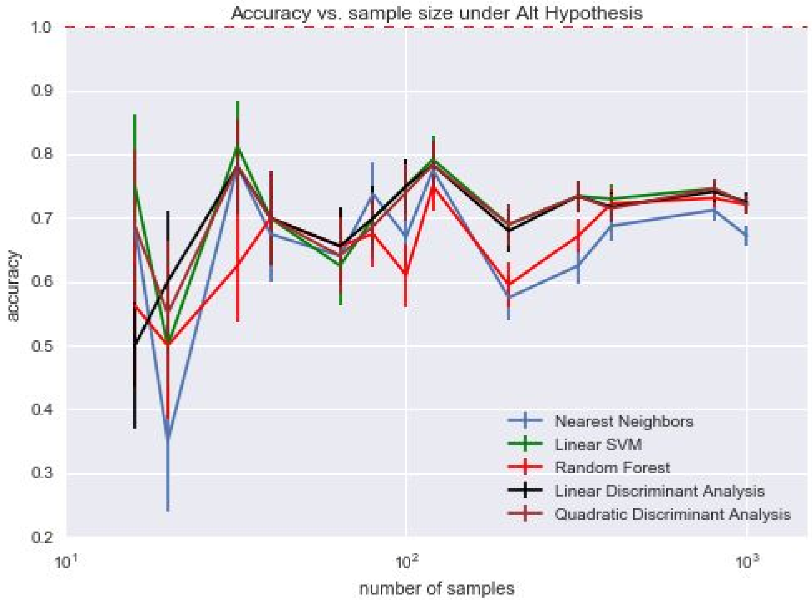
- Class conditional difference exist

$$f(x) = y + \varepsilon,\ \varepsilon \sim Normal\ (\mu, \sigma^2)$$

Formal Statement of Algorithm

- Linear Discriminant Analysis (LDA)
- Quadratic Discriminant Analysis (QDA)
- K-Nearest Neighbors (kNN)
- Support Vector Machines (SVM)
- Random Forest (RF)

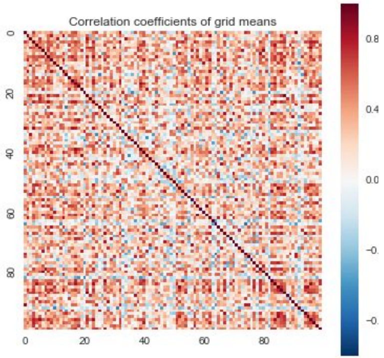
Results

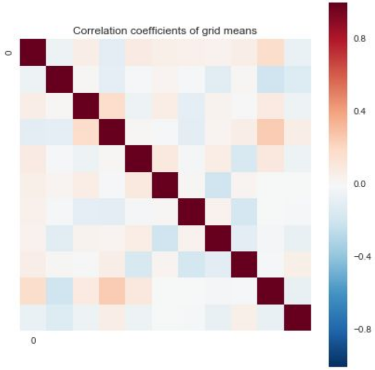


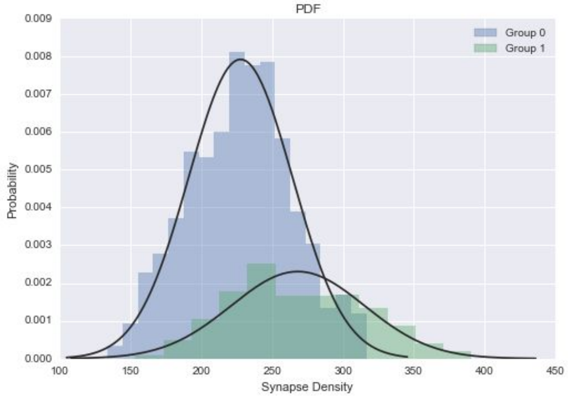
Algorithm	**Accuracy**
Nearest Neighbors	0.74 ± 0.01
Linear SVM	0.78 ± 0.01
Random Forest	0.77 ± 0.01
LDA	0.78 ± 0.01
QDA	0.78 ± 0.01

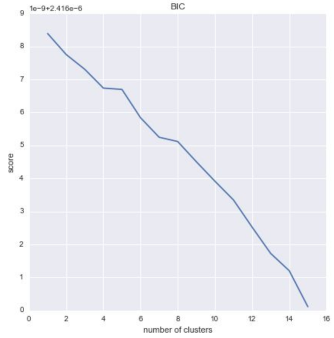
- All classifiers performed similarly, with accuracy slightly above 73% (prior probability of low-density layer).
- Grid means don’t seem to provide enough additional information.

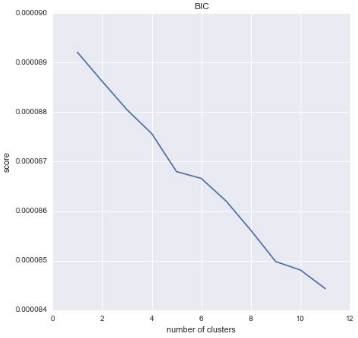
Model Checking











- Grid means not independent across (X,Y)
- Grid means independent across Z
- Grid means identically distributed in both (X,Y) and Z
- Grid means aren’t sufficient to distinguish between layers

Discussion / Future Work

- Framework for testing classifiers and identifying strengths/weaknesses
- Preliminary results indicate that more information is needed for successful classification of Z layers
    - Larger grids
    - Alternative metric (instead of means)
    - Quantify spatial organization
        - Clustering
- Functional information
    - Cortical layers vs. Z layers