Unsupervised Spike Sorting

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***Abstract*—In this paper, we outline our approach to automatic spike sorting in the context of electrical response from neurons. Using compression techniques such as PCA and polynomial approximations, we were able to find a tractable subspace in which to analyze our features. On our reduced dimension samples, we then applied two algorithms wrapping k-means which help find k: g-means clustering and using the Davies-Bouldin index. We were able to get some very good clusters while other clusters were not as well separated, indicating that there was a combination of a large degree of noise in our features and high variability in terms of the response of each sensor when a single cell spikes.**

I. Introduction

Lab equipment gathers extracellular neurophysicological voltage samples at a rate of 10 kHz. These readings are a mixture of the responses from the many surrounding cells. The responses are then clustered into similar shaped groups which represent different cells. Our project aims to take this analysis step which is usually done manually and automate it using machine learning. The data is 100 seconds of recorded retinal ganglion cell responses. The data is extracellular recordings from 60 different channels. Each channel represents a data stream of voltage potentials at a specific microelectrode.

Example microelectrode recording.

The aim of the project is to cluster each spike into clusters which each share a similar shape.

Example single channel cluster center shapes

II. Algorithmic Exploration

A. Model

Model Parameters

N = # of datapoints per channel
CH = # of channels
S = # of points to smooth raw data over
T = Threshold for spikes
L = # points to take from left of spike location
R = # points to take from right of spike location

Definitions We begin with the raw waveform:

$$R = \{R \in \mathbb{R}^{N \times CH}; i = 1, ..., CH\}$$

Smoothing over S points we define a new waveform where R^i_j is the jth datapoint in the ith channel:

$$W^i_j = \frac{1}{s} \sum_{s=-S/2}^{S/2} R^{(i)}_{j+s}$$

We then define W' as the zero mean normalized to the standard deviation on each channel of W. The next step is to separate out the possible spikes to cluster. We define the spike locations of interest as:

$$P = \{i; \frac{\partial}{\partial t} W = 0 \cap (W'_1(P_i) > T \cup ... \cup W'_{CH}(P_i) > T) \cap i \in 1, ..., N\}$$

This represents any point that is a local maximum and is above the threshold T on any channel. Peaks are then cut to ensure that they are a minimum of $\alpha = 15$ from each other. To form a single feature vector $X^{(i)}$ we take the surrounding points on each channel and concatentate them.

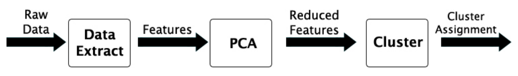
$$X^{(i)}_j = W'^{floor(i/(L+R+1))+1}_{mod(j,L+R+1)+P(i)}; i = 1, ..., |P|, j = 1, ..., (L+R+1) * CH$$

$$X^{(i)} \in \mathbb{R}^{CH(L+R+1)}$$

X is the feature vector we use to then cluster on.

B. Process Overview

For reference, the high level overview of our process pipeline is shown below:



We paramaterize our feature vectors from the raw data with the following representations:

$$X = M(R; S, T, L, R)$$

We then use different methods to reduce the dimensionality of the feature vectors to improve performance and to emphasize more discrimanent features.

$$Red(X, N, M; X^{(i)} \in \mathbb{R}^N) = Y; Y^{(i)} \in \mathbb{R}^M$$

Clustering then takes the dimension reduced feature vectors and assigns them to clusters which represent possible cells.

$$Clus(X; X^{(i)} \in \mathbb{R}^M) = (Y^{(i)} \in \mathbb{R}^M, I^{(i)} \in \mathbb{R})$$

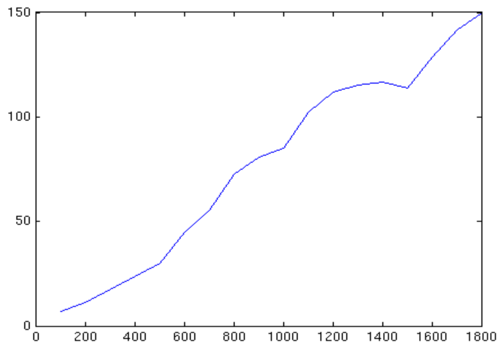


Fig. 1. This plot of the time clustering took (using g-means) vs the dimension we reduced to using PCA shows the roughly linear relationship between dimensionality of our feature vector and running time.

C. Dimensionality reduction and compression

1) PCA: At this point, we have our features and are ready to run unsupervised learning algorithms on the data set. However, as we began experimenting with our data set, we realized that the time needed to learn on our data set was simply too great. We needed a way to reduce the dimensionality of our features. Since a feature vector consists of 30 measurements for 60 channels each, we have features in $\mathbb{R}^{1800}$.

The first approach we took was to apply PCA. Figure 2 shows the error versus target dimensions reduced to. Factoring in compression and percentage of error, 300 principal components optimizes both. We then take the components and project our features into that space, $\mathbb{R}^{300}$.

Performing this optimization allowed us to run k-means clustering in 13% of the time needed without compression. This significantly reduces the time needed without sacrificing too much in terms of underfitting. Figure 1 shows the relationship between the dimensionality of our feature vectors and the time it takes to run our clustering code. As we iterated on our project, reducing the running time of our algorithm was critical to being able to try many different ideas quickly.

2) Fitting Polynomials: Another approach to reducing the dimensionality was to take into account the dependencies of the features within each channel. Since these values are continuous we can fit a polynomial model to them with fewer parameters. Here we let n be the number of coefficients we want to fit per channel. Since we have 60 channels the end result is $\mathbb{R}^{60(n+1)}$ since the intercept parameter must be included per channel as well.

Our results with polynomial fitting were not as strong as PCA. While they do a good job of making sure each channel is fit well, the condensed features must encode all the information unlike PCA where the principle components hold the information. As a result, it takes many more features to get the same amount of information back.

While polynomial fitting does take temporal information into account per channel in the condensation, it fails to encode the meaningful information as well.

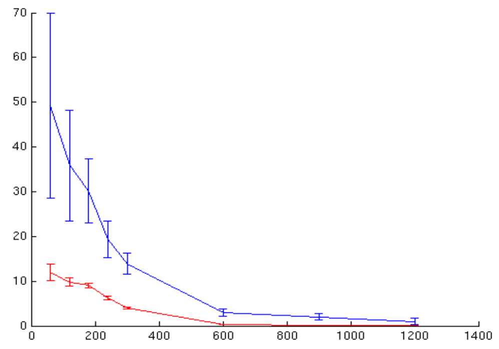


Fig. 2. This plot compares the error of the compression techniques we used. In blue is polynomial fitting and in red is PCA. The plot is of the percentage error vs dimension we reduce to.

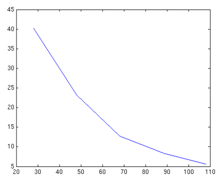


Fig. 3. The Anderson-Darling statistic is computed per cluster, so to show how it improves, we take the average value across all clusters and for each k plot the mean here.

D. Clustering Algorithms

As the engine for both of the clustering algorithms, we used k-means clustering. However, the real work at this stage is to determine which k should be used in k-means. We tried two approaches to solving this problem.

1) G-Means algorithm: One way to choose k in the k-means algorithm is to use an algorithm developed in 2003 by Greg Hamerly and Charles Elka, presented in the NIPS 2003 conference. In this method, a small value for k is chosen and k-means is run. Then, for each cluster produced, we use a heuristic function to decide whether to split that cluster. The heuristic used is the Anderson-Darling statistic. If that statistic is greater than some threshold critical value, then we decide that the cluster should be split. The Anderson-Darling statistic is computed as follows:

$$A^2(Z) = -n - \frac{1}{n}\sum_{i=1}^{n}(2i-1)[\log(z_i) + \log(1 - z_{n+1-i})]$$

$$A^2_*(Z) = A^2(Z)(1 + 4/n - 25/n^2)$$

If the $A^2_*(Z)$ is greater than the threshold, we split. For this project we experimented with many thresholds and found that with $t = 12$ we got good separation between clusters.

2) Davies-Bouldin Index: The DB Index is another way to determine k by favoring sets of clusters with high intra-cluster similarity and low inter-cluster similarity. The formula is as follows:

A^j = Center of cluster j

$T^j = \{X^{(i)}; X^{(i)}\text{is in cluster}j\}$

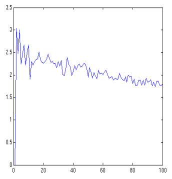


Fig. 4. The graph above shows k vs the Davies-Bouldin Index

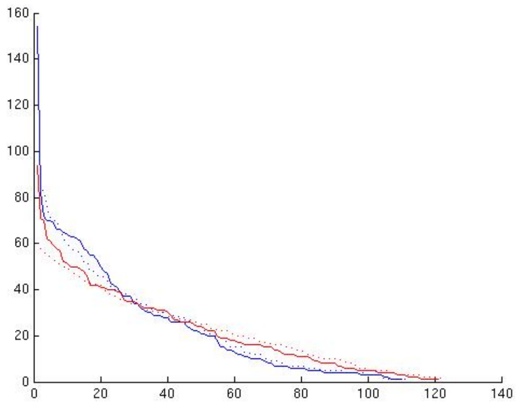


Fig. 5. Shows the number of samples in each cluster sorter. Red is PCA and blue is polyfit. Dashed is L=8, R= 21; Solid is L = 21, R = 8.

S^i = the intra cluster similarity of cluster i
M^{ij} = inter cluster similarity of clusters i, j

$$S^i = (\frac{1}{|T^i|}\sum_{j=1}^{|T^i|}(T^i_j - A^i)^q)^{\frac{1}{q}}$$

$$M^{ij} = (\sum_{k=1}^{N}|a^i_k - a^j_k|^p)^{\frac{1}{p}}$$

$$DB = \frac{1}{N}\sum_{i=1}^{N}\max_{j:i\neq j} R_{ij}$$

III. Results

The results are clusters that each represent a unique waveform shape. However, while these clusters are unique, there is no guarantee if they are correct cells are not. Since this is unsupervised learning further analysis with the stimulus would be needed to see how clean these cells are.

Looking at how the clusters lay out we see that many clusters have few points within them. These could be far away cells that can be separated out but it is hard to tell over the noise of the system. We compare the different methods of obtaining features and see that on the mostpart they result in a similar distribution of cluster sizes(Fig. 5.).

Next we look at how the clusters compare with each other. To view the results, the top 3 clusters were chosen. Taking the top two principle components of the combined data from the clusters and then plot each $X^{(i)}$ within this space gives these plots. Each point is colored for its cluster. First we compare how different parameters for forming the features compare by adjusting R and L. We see that having features more based on what is after the spike leads to more separable datapoints (Fig. 7 and 9 versus Fig 6 and 8). We also see that PCA does better than polyfit not only in that the clusters are more separable but also PCA gets more datapoints in the top clusters (Fig. 10 and 11). Furthermore, taking the top five clusters within a three dimensional space using the top three priciples componenets, we see they also mostly separate (Figure. 12).

IV. Conclusions

We found PCA to be very useful to compress the data so we could work in a high dimension more efficiently. However, understanding the meaning of the data and how to format it correctly is important when forming features. We also found clustering to be challenging since the number of clusters and the confidence of them is very dependent on the heuristic used. Lastly, this highlights the challenge in performing unsupervised learning with real world data.

A. Future Work

Future work within this space could be to try using scale and translation independent encoding of the waveforms. This could make the algorithm less sensitive to variations. We also believe there could be better clustering algorithms to take specific physiological aspects into account.

Acknowledgment

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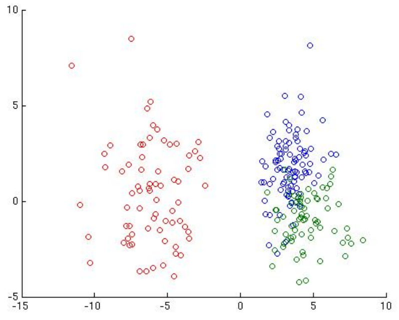

Fig. 6. Top three clusters using polynomial features. L = 21, R = 8.

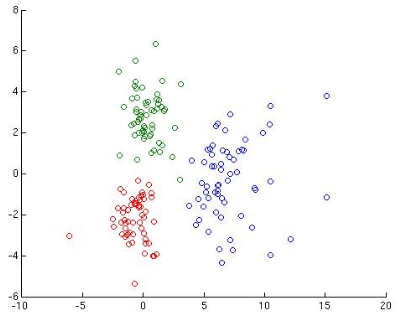

Fig. 7. Top three clusters using polynomial features. L = 8, R = 21.

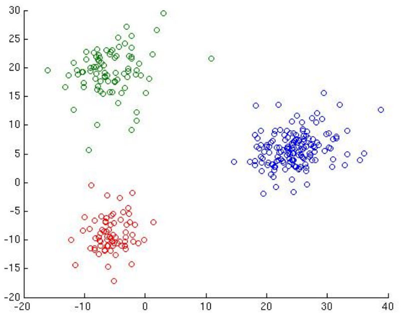

Fig. 8. Top three clusters using PCA features. L = 21, R = 8.

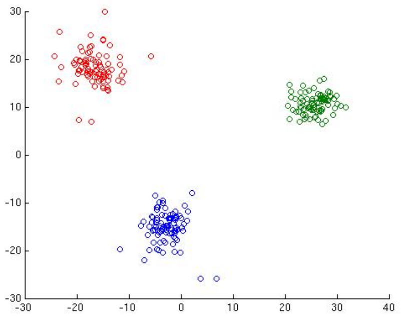

Fig. 9. Top three clusters using PCA features. L = 8, R = 21.

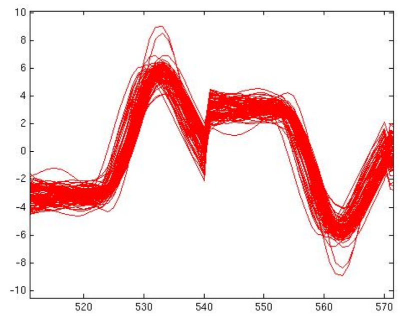

Fig. 10. Traces of top cluster using PCA. Top two channels.

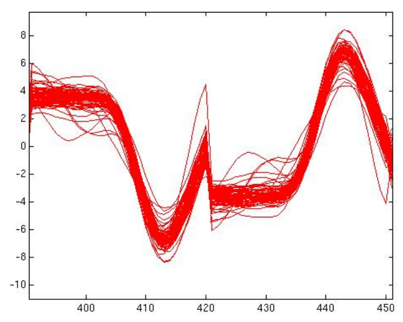

Fig. 11. Traces of top cluster using Polynomial fitting. Top two channels.

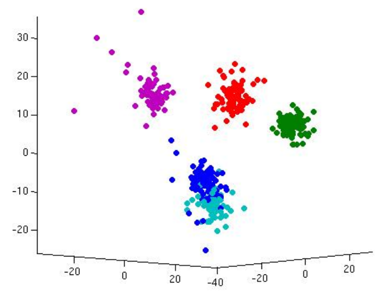

Fig. 12. Top 5 clusters using PCA transformed into three dimensional space using top three principle components.