Lecture 7: Receptive Field

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Introduction

From the Raw Signal to Clusters of Spikes

The experimentally measured signal forming the basis of the data analyzed throughout this report and the previous two tasks has been recorded using a tetrode, i.e. a combination of four active electrodes. The voltage measured by each electrode has been sampled at [30]kHz and covers a total recording time of [640]s. This resulted in a 19.200.000 by 4 matrix of voltages, with each row representing a point in time or sample and each column representing an electrode or channel.

To remove high and low frequency noise, a band-pass filter has been applied to each channel. In the filtered signal, spikes have then be detected using a threshold and for each detected spike, the waveforms recorded by the four electrodes have been extracted. Each waveform consists of a certain number of samples before and after the detected spike time, 32 samples in total covering roughly the usual spike duration of . To reduce the dimensionality, only the first three principal components of the 32 features of each of the four channels have been considered, resulting in a total of 12 features characterizing each spike.

The number of detected spikes is in the order of 20.000, with the concrete spike count varying depending on the threshold and exact method used for spike detection. To cluster these approximately 20.000 points in the 12-dimensional feature space, a Gaussian Mixture Model has been fitted using the expectation-maximization algorithm and limiting the number of mixtures by minimizing the Bayesian information criterion.

Analyzing Clusters of Spikes

Unfortunately, the clusters obtained in the previous steps usually do not correspond one-to-one with the individual neurons. On the one hand, two or more clusters could represent spikes of the same neuron, for example because the neuron's waveform characteristics changed over time. On the other hand, a single cluster could contain spikes from different neurons that were not well separated in the 12-dimensional feature space. Therefore, in the following several methods will be presented to evaluate the clustering

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and detect both types of errors in order to correctly map the spikes to the neurons by which they were generated and thus to be able to reconstruct the spike trains of the individual neurons.

The possibility to correct this mapping from spikes to neurons is however limited by the inherent properties of the errors. While the first type of error, i.e. multiple clusters representing the same neuron, can be easily compensated by assigning the spikes from the respective clusters to the same neuron, the second type of error is more problematic. Even if a so-called multi unit, that is a cluster containing spikes from multiple neurons, has been identified as such, there is no simple way to split the cluster in a way such that the splitted parts correspond to the individual neurons. One approach to address this problem might be to then go back to the higher dimensional feature space before extracting the first three principal components of each channel and trying to distinguish the spikes of the different neurons in the multi unit using the additional features. However, this type of error correction does not fall within the scope of this report. Instead, the following methods will just focus on the detection of multi units and multiple clusters representing the same neuron.

Visual Inspection of Clusters

The most intuitive method to identify candidates for single units is to visualize the clusters. Given that our feature space is 12-dimensional, it is however not possible to just plot the spikes themselves. Instead, only projections of the 12-dimensional vectors onto lower dimensional subspaces, i.e. 1-, 2- or 3-dimensional subspaces, can be plotted. Obviously, the visual separability of clusters depends on the concrete projection. Hence, it's crucial to choose a subspace that is likely to keep the clusters separated.

One set of such 2-dimensional subspaces that can be assumed to provide relatively good separation of clusters compared to other 2-dimensional projections is the set of pairs of the first principal components of the four channels. The resulting plots, which are six scatter plots showing the pairwise comparison of the first principal components of the four channels, should then allow to identify those clusters that are already well separated from the others in these low dimensional subspaces and therefore are good candidates for single units.

Visual Inspection of Spike Waveforms

Another simple method is is based on the actual waveforms of the spikes that have already been extracted in previous steps as explained earlier. By looking at the waveforms of the spikes and comparing different clusters, it is possible to detect potential artifacts such as clusters with atypical waveforms that are due to electrical artifacts and not caused by spikes or clusters consisting of overlapping spikes.

As the clusters might contain quite many spikes, it's not always suitable to overlay the waveforms of all spikes. The plots used in this report just show the mean waveform as well as 100 random samples from the set of waveforms for each cluster. Usually, this should be enough to provide a good sanity check.

Auto- and Cross-Correlograms

Auto- and cross-correlograms are an advanced and very powerful method to detect both multi units, i.e. clusters containing spikes from different neurons, and different clusters representing the same neuron. This analysis is performed pairwise, creating a cross-correlogram for each pair of clusters as well an auto-correlogram for each cluster as a special case of a cross-correlogram of a cluster with itself.

Mathematically, the cross-correlation of two continous functions f and g for the time difference τ is given by

$$(f \star g)(\tau) \stackrel{\mathrm{def}}{=} \int_{-\infty}^{\infty} f(t)\ g(t+\tau)\, dt,$$

with auto-correlation referring to the special case that f and g are identical.

Likewise, for discrete functions, e.g. if the spike times have been binned, the cross-correlation is defined as

$$(f \star g)[n] \stackrel{\mathrm{def}}{=} \sum_{m=-\infty}^{\infty} f[m]\ g[m+n].$$

A cross- or auto-correlogram is a histogram visualizing the cross- or auto-correleation between two functions, in our case between the spike times of two clusters. It can be seen as a histogram of the time difference between all pairs of spikes consisting of one spike from each of the two clusters. In case of auto-correlograms, the bin representing time difference zero needs special treatment, because the auto-correlation always has a huge peak for $\tau = 0$. Thus, auto-correlograms are usually plotted with the that bin set to zero.

To make use of these plots to actually detect multi units and different clusters representing the same neuron, the refractory period of neurons is exploited. Roughly speaking, the refractory period describes the minimal time difference between two spikes produced by the same neuron. Consequently, the auto-correlogram of a single unit is always zero in the region between plus and minus the refractory period. An auto-correlogram that does not show this characteristic property is therefore strong evidence that the corresponding cluster contains spikes from multiple neurons, i.e. it is a multi unit.

In a similar manner, the refractory period can be used to also detect different clusters that contain spikes of the same neuron. In general, spikes of two independent neurons should sometimes occur almost simultaneously. The cross-correlogram of the spike times of these neurons should therefore not contain a region similar to the one just described for auto-correlograms, for which the value of the correlogram is zero. If, however, the cross-correlograms of two different clusters does contain such a region, i.e. the spikes of both clusters seem to be subject to a common refractory period, then it is very likely that both clusters describe the same neuron.

Cluster Separation using Linear Discriminant Analysis

Finally, this last method is somewhat similar to the previously described **??** in the sense that it is also based on the projection of the 12-dimensional feature space to a lower dimensional subspace that can be visualized while still providing good cluster separation. By only considering two clusters at a time, i.e. by also doing a pairwise comparison of clusters as for the correlograms, it is however possible to calculate the optimal projection axis, i.e. the one that provides the best separation of the two clusters, using linear discriminant analysis. Mathemtically speaking, the separation of clusters after projection can be maximized according to Fisher's linear discriminant by projecting on

$$\vec{w} = (\Sigma_1 + \Sigma_2)^{-1}(\vec{\mu}_2 - \vec{\mu}_1),$$

where Σ_1 and Σ_2 are the covariance matrices and μ_1 and μ_2 the means of the clusters.

As a result, a different projection axis is used for each pair of clusters. The plot for each pair then consists of two histograms of projected spikes, one for each cluster, enabling visual evaluation of the separation of the clusters.

Results

The previously described methods to analyze clusters of spikes have been applied to the clusters obtained in the previous steps that were outlined in the section **??**. In the following, the results of this analysis are presented. Throughout all plots, the clusters have been colored in a consistent way such that the same color always represents the same cluster.

Visual Inspection of Clusters

?? shows a scatter plot for each pair of channels where the spikes have been projected to the subspace formed by the first principal components of the respective channels.

Figure 1. Pairwise comparison of the first principal components of all channels

While most of the nine clusters seem to be highly overlapping when being projected to these two-dimensional subspaces, the green cluster is very well separated from the other clusters using the first principal component of the third channel.

Visual Inspection of Waveforms

?? shows the mean waveform as well as 100 random samples from the set of waveforms for each cluster and channel.

Figure 2. Waveforms and mean waveform for the different clusters and channels

The waveforms confirm the previous observation, that the green cluster, that is cluster 4, can be clearly separated using channel 3. Moreover, one can see certain groups of clusters that have somewhat similar waveforms throughout the channels, e.g. clusters 6, 7 and 8, clusters 1 and 9, and clusters 3 and 5, indicating that it might be worth further examining the similarities between these clusters, for example using their cross-correlograms.

Cross- and Auto-Correlograms

The cross- and auto-correlograms shown in **??** have been created by binning the spike times using a bin size of [0.5]ms and consequently applying the discrete cross-correlation formula. The histograms are plotted using the same [0.5]ms bin width. The maximal time lag that has been calculated is [20]ms.

Figure 3. Cross- and auto-correlograms of all channels and pairs of channels

The auto-correlograms strongly suggest that clusters 1, 4 and 9 are single units, because they have clearly visible refractory period. For clusters 2 and 3, the refractory periods are narrower but still clearly visible, so it is likely that they are single units as well. In contrast, the auto-correlograms of clusters 5, 6, 7 and 8 do not show a refractory period and thus are probably multi units containing spikes from different neurons.

Looking at the cross-correlograms, the most prominent finding is the distinct refractory period in the cross-correlogram of cluster 1 and 9, suggesting that these clusters contain spikes from the same neuron. The cross-correlogram of cluster 3 and 5 might show a slight indication of a refractory period as well, but it's not strong enough to draw any conclusion from it.

Cluster Separation using Linear Discriminant Analysis

?? shows subplots comparing each cluster with every other by projecting the spikes of these clusters onto the axis obtained by linear discriminant analysis, or simply LDA, of the two clusters and plotting the corresponding histograms.

Figure 4. Pairwise comparison of clusters after projection on the LDA axis

This again confirms the previous observations, for example that cluster 4 is well separated from the others or that clusters 1 and 9 overlap with each other but are well separated from the rest.

Summary

To briefly recapitulate, the analysis of the clusters using the presented methods provides strong evidence that clusters 1 and 9 together and cluster 4 by itself form single units. Moreover, it indicates that clusters 2 and 3 are both single units as well, whereas the remaining clusters 5 to 8 are probably multi units.

Discussion

The presented methods have proven to be very effective in determining which clusters are single units or multi units and in detecting clusters that represent the same neuron. Especially the correlograms provide a lot of useful information by exploiting the refractory period of neurons. The different methods provided consistent information, hence supporting the interpretations that can be made based on the individual plots.

As already explained earlier, it is however not possible to use these methods to split multi units into single units. If the goal is to improve the clustering such that there are no more multi units, previous steps like feature extraction need to be improved.