

**Title:** Does structure in neural correlations match anatomical structure during spontaneous behaviour?

### 300-word Summary

Information in the brain is carried in correlated network activity. ~~For example, decades of research has established that these correlations play a crucial role in representing sensory information[1].~~ Recent findings show that spontaneous behaviours explain correlations in parts of the brain not usually related to motor control[2]. The question arises, are correlated networks restricted to anatomical brain regions? We found that correlated networks tend to exist *within* anatomical regions at short time-scales, and *across* anatomical regions at longer time-scales. This implies that neural circuits compute locally at short (~50ms) timescales but more globally at longer (~1s) timescales.

Because of limitations in recording technology most research has explored correlations between neurons within a given brain region. Relatively little is known about correlations between neurons in different brain regions. However, the recent development of ‘Neuropixels’ probes[3] has allowed extracellular voltage measurements to be collected from multiple brain regions simultaneously routinely, and in larger numbers than traditional methods. We used a publicly available Neuropixels dataset to analyse correlations between different brain regions.

Using eight probes each in three mice, readings from 2296, 2668, and 1462 cells respectively in nine brain regions were extracted during 1 hour of activity. Each mouse was behaving spontaneously and could use their front paws to turn a wheel[2]. We examined pairwise spike count correlations between neurons within the same region, and between neurons in different regions. We found that cells from the same region tend to be more strongly correlated than cells from different regions. This difference in correlation strength is greater for shorter time-scales, and weakens at longer time-scales.

We used a cutting-edge method[4] to detect communities in the network induced by pairwise correlations. In agreement with our first finding, at shorter time-scales we found many communities dominated by cells from a single region. At longer time-scales communities ~~tended to~~ **spanned** exist across multiple brain regions.

### Additional Detail

The three mice from which the data were collected had some key differences. The first mouse was a female wild type, P73. The second mouse was a male mutant (TetO-GCaMP6s, Camk2a-tTa), P113. The third mouse was a male mutant (Ai32, Pvalb-Cre), P99.

Prior to measuring spike count correlations, we chose suitable time bin widths for binning the spike counts by taking a similar approach to [5]. We evaluated the average correlations from many cell pairs using different values for the time bin width. We found that correlations increased logarithmically with the size of the bin width consistently across mice. We used a bin width of 2s in order to capture the magnitude of the correlations, without completely averaging out short-term dynamics. However, we still performed our analyses at time bin widths ranging from 50ms to 3s in order to assess the effect of the bin width. The same dataset was used in [2]; they used 1.2s time bins for their analyses.

To assess the correlation significance, we measured the shuffled correlation between each pair. We found that the mean correlation was usually an order of magnitude greater than the mean shuffled correlation.

Due to the large number of cells, and the even larger number of cell pairs, in order to make these measurements in a reasonable amount of time, a local supercomputer was used to perform the calculations using parallelisation to speed up the process.

To compare *within-region* mean correlations to *between-region* mean correlations, we created correlation matrices with within-region correlations on the main diagonal and between-region correlations elsewhere. There appeared to be no consistency in correlation patterns across mice.

We compared within-region correlations to between-region correlations at different time-scales by using different values for the time bin width. For a given region, we found that within-region mean correlations tended to exceed most or all of the mean correlations for between-region correlations involving that region. We also found that this tendency was greatest for shorter time bins, and reduced for longer time bins (fig. 1). This dynamic may reflect the dispersion of correlations throughout the brain over time.

The cutting-edge community detection method used involved choosing a null network distribution and testing if this model was valid for the data network. This hypothesis testing applied to network distributions allowed us to determine if the data network contained structure beyond that described by the null networks. It also allowed us to determine a subspace to the data network vector space where this structure exists, and which nodes contribute to this structure. Thus we could remove those nodes not contributing to the extra structure, and perform the community detection algorithm in the subspace. This process is referred to as

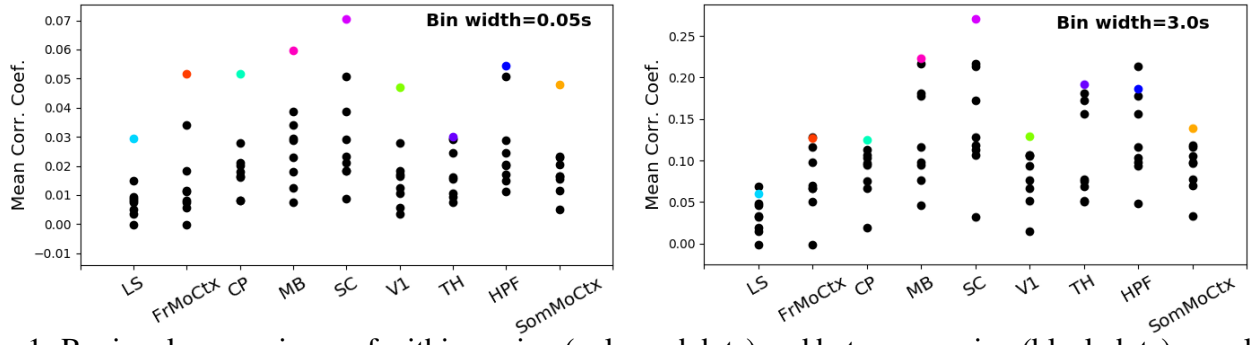


Figure 1: Regional comparisons of within-region (coloured dots) and between-region (black dots) correlations for the same mouse using different time bin widths. The reduction in difference between within-region and between-region mean correlations was also observed at intermediate values for the time bin width.

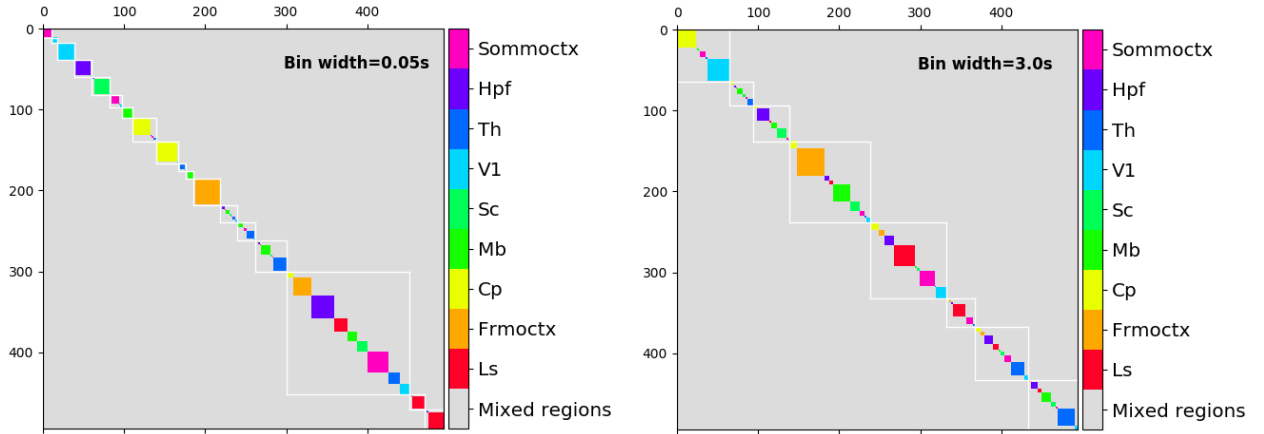


Figure 2: Matrices showing cell regional membership and community membership for the same mouse using different bin widths. Each row and column corresponds to a cell. Within-region pairs are coloured by their regional membership, between-region pairs are left grey. In general, communities include pairs from multiple regions. But, at shorter time-scales communities dominated by a single region are more prevalent. (left panel)

*Network Noise Rejection* [4]. The community detection itself is analogous to ensemble methods for time-series analysis. It uses the output of many different modularity clustering attempts to find one final clustering through *consensus-clustering*.

We performed the network noise rejection and community detection on weighted networks created by spike count correlation measurements. We did this using different values for the time bin width. We found that correlated communities generally included neurons from multiple brain regions. But, we found that communities dominated by neurons from a single region were more likely to be observed when using a smaller time bin width (fig. 2). This result may also reflect dispersion of correlations throughout the brain over time.

## References

- [1] Marlene R Cohen, John H R Maunsell, *Attention improves performance primarily by reducing interneuronal correlations*, Nature Neuroscience 12, 1594–1600, (2009)
- [2] Carsen Stringer, Marius Pachitariu, Nicholas Steinmetz, Charu Bai Reddy, Matteo Carandini, Kenneth D. Harris, *Spontaneous behaviors drive multidimensional, brainwide activity*, Science 364, (2019)
- [3] James J. Jun, Nicholas A. Steinmetz, Timothy D. Harris, *Fully integrated silicon probes for high-density recording of neural activity*, Nature 551, 232–236, (2017)
- [4] Mark D. Humphries, Javier A. Caballero, Mat Evans, Silvia Maggi, Abhinav Singh, *Spectral rejection for testing hypotheses of structure in networks*, arXiv:1901.04747, (2019)
- [5] Marlene R Cohen, Adam Kohn, *Measuring and interpreting neuronal correlations*, Nature Neuroscience 14, 811–819, (2011)