Distinguishing firing patterns of SNr neurons with quantitative features of neuronal discharge

Chris Ki[2], Amanda Willard[2,3], and Aryn Gittis[2,3]

[2]Center for the Neural Basis of Cognition (CNBC), [3]Department of Biological Sciences, Carnegie Mellon University

Introduction

The firing patterns of SNr neurons can be split into three categories: regular, irregular, and burst firing. A prominent method by which investigators conduct this classification is through the visual inspection of a spike train's interspike interval histogram (ISIH) and its associated autocorrelogram.

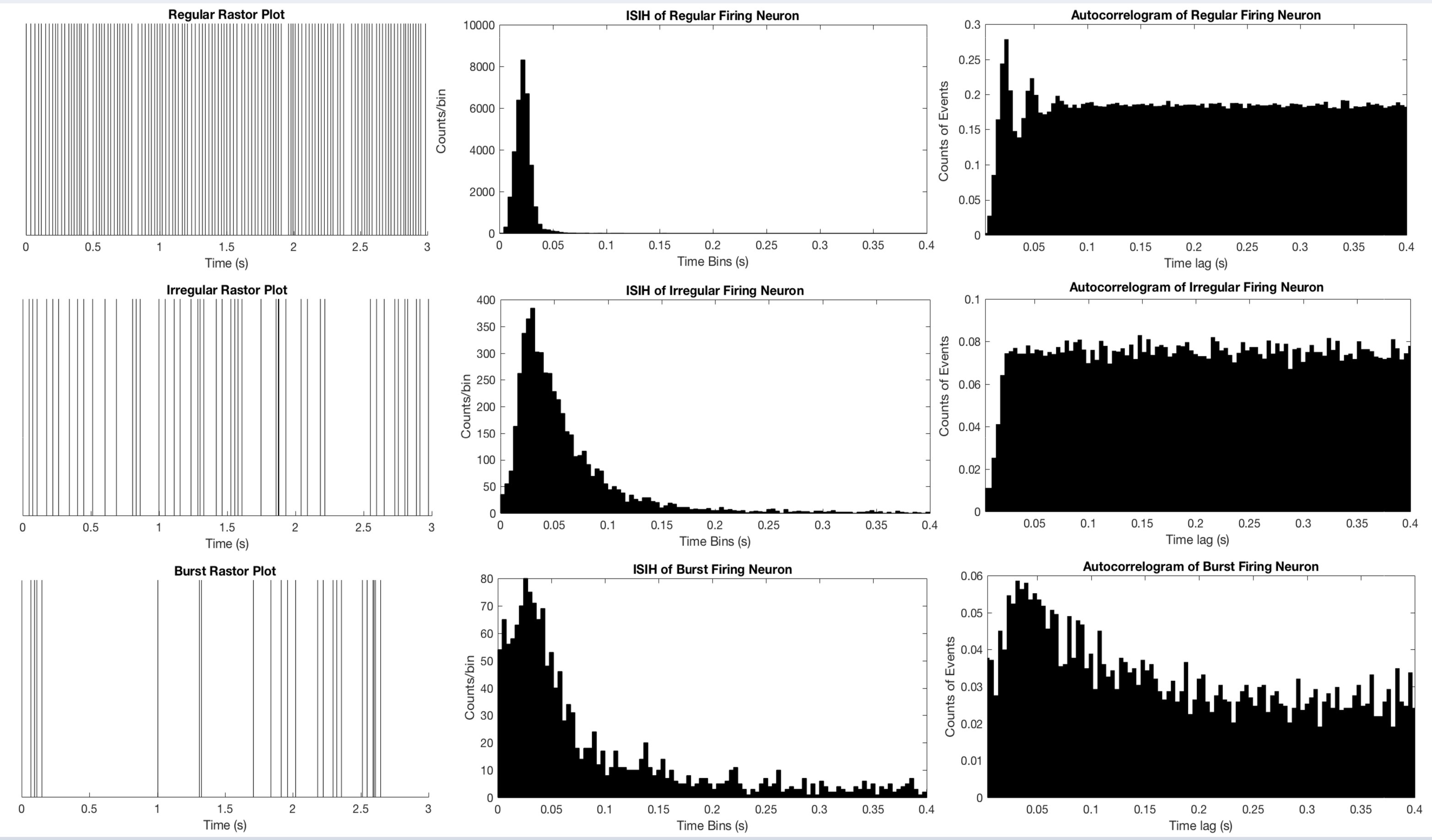


Fig. 1: Regular Firing Neuron (First Row): Symmetric ISIH distribution and Autocorrelogram with 1+ peak. Irregular firing neuron (Second Row): Asymmetric ISIH distribution and Autocorrelogram with an initial trough that rises to steady state. Burst firing neuron (Third Row): Positively skewed ISIH along with initial peak followed by a decay to steady state in Autocorrelogram.

However, one can imagine that this technique is a painstakingly slow process that is also vulnerable to an examiner's biases. Furthermore, these obvious features are not always present in the ISIHs and autocorrelograms of all neural spike trains. The findings in this project suggest an alternative approach that uses three quantitative measures (Fano Factor, Pearson's moment coefficient of skewness, and Double exponential fit) to expedite and provide consistent and accurate classifications.

Methods

- Statistical analyses were conducted on in-vivo neural spike train data collected from mice with varying levels of dopamine depletion. These recordings were pre-processed and sorted through Plexon Offline Sorter.
- Features of each firing class were consistent throughout all the conditions.
- Time-domain and nonlinear analyses were only carried out on the first 3000 ISIs of data segments that contained at least 3000 ISIs.
- Outliers were found through the use of the interquartile range rule and replaced if additional ISIs were available.

Fano Factor

- A nonlinear statistical value that measures self-similarity of a data stream.
- The Fano factor for a Poisson process is 1.
- Bursting activity contains spike patterns that are more irregular than Poisson processes, burst neurons should have Fano factors > 1.

$$FF = \frac{\sigma_w^2}{\mu_w}$$

Eq. 1: Equation for calculating the Fano Factor where , μ_w is the mean and σ_w is the standard deviation of the windows

- Each data series was split into non-overlapping time windows (50ms). The FF was then calculated by the ratio of the variance of spike counts in each window divided by the mean of the spike counts in each window.

Pearson's moment coefficient of skewness

- Pearson's moment coefficient of skewness measures asymmetry of a probability distribution of a real-valued random variable about its mean.
- A value close to zero indicates symmetry while a value greater than or equal to one indicates positive skewness.

$$\gamma = E[(\frac{X-\mu}{\sigma})^3] = \frac{E[(X-\mu)^3]}{(E[(X-\mu)^2])^{\frac{3}{2}}} = \frac{\mu_3}{\sigma^3}$$

Eq. 2: Equation for calculating the moment coefficient of skewness where E is the expectation operator, μ is the mean, σ is the standard deviation and μ_3 is the third central moment.

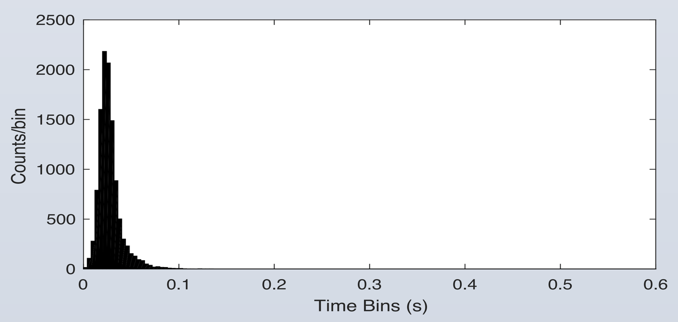


Fig. 2: Nearly symmetric distribution with a skewness close to zero.

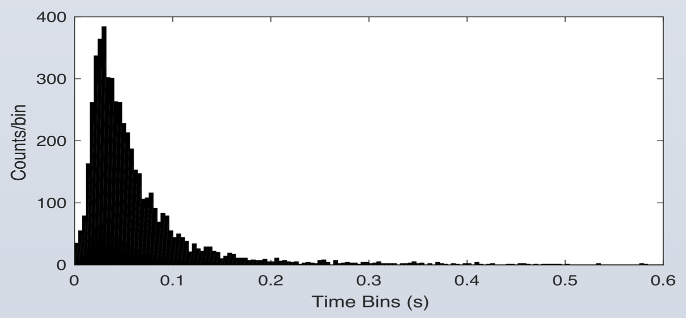


Fig. 3: Asymmetric distribution with skewness greater than zero but less than 1.

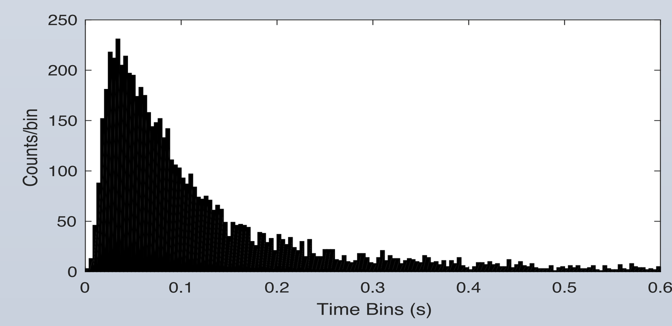


Fig. 4: A positively skewed distribution with skewness greater than 1.

Double Exponential Fit

In an effort to capture the presence of peaks in the autocorrelograms, for a given spike train, we fit a double exponential curve from the initial crest of its autocorrelogram to its first minimum value found after the initial peak. The double exponential curve was chosen as it differentiated the three firing patterns best.

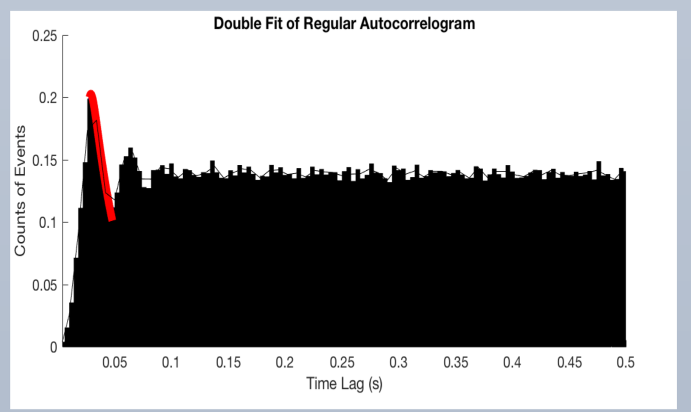


Fig. 5: The double exponential fit of the regularly firing neuron has a very steep line-like curve.

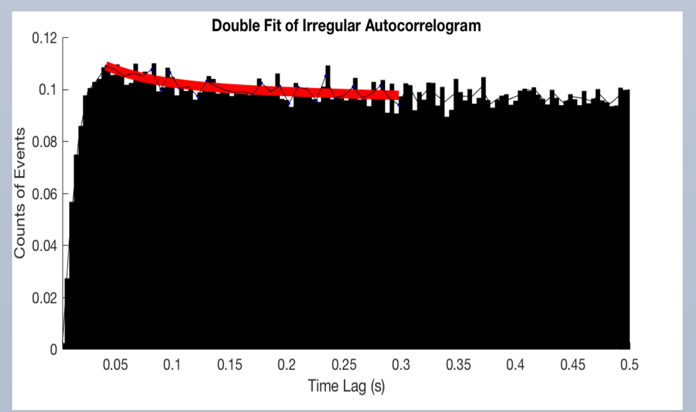


Fig. 6: The double exponential fit of the irregularly firing neuron has a very flat line-like curve.

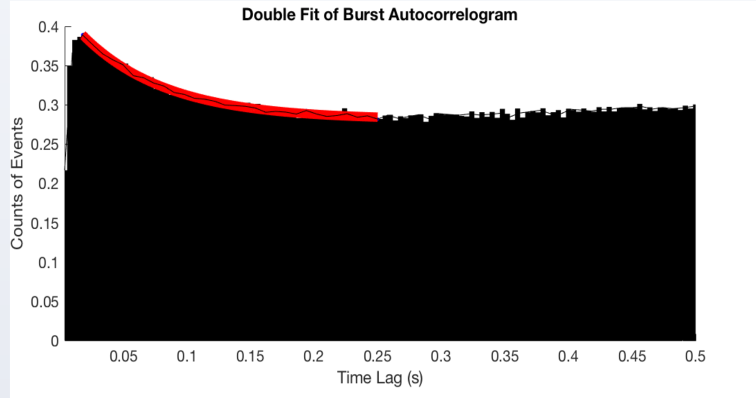


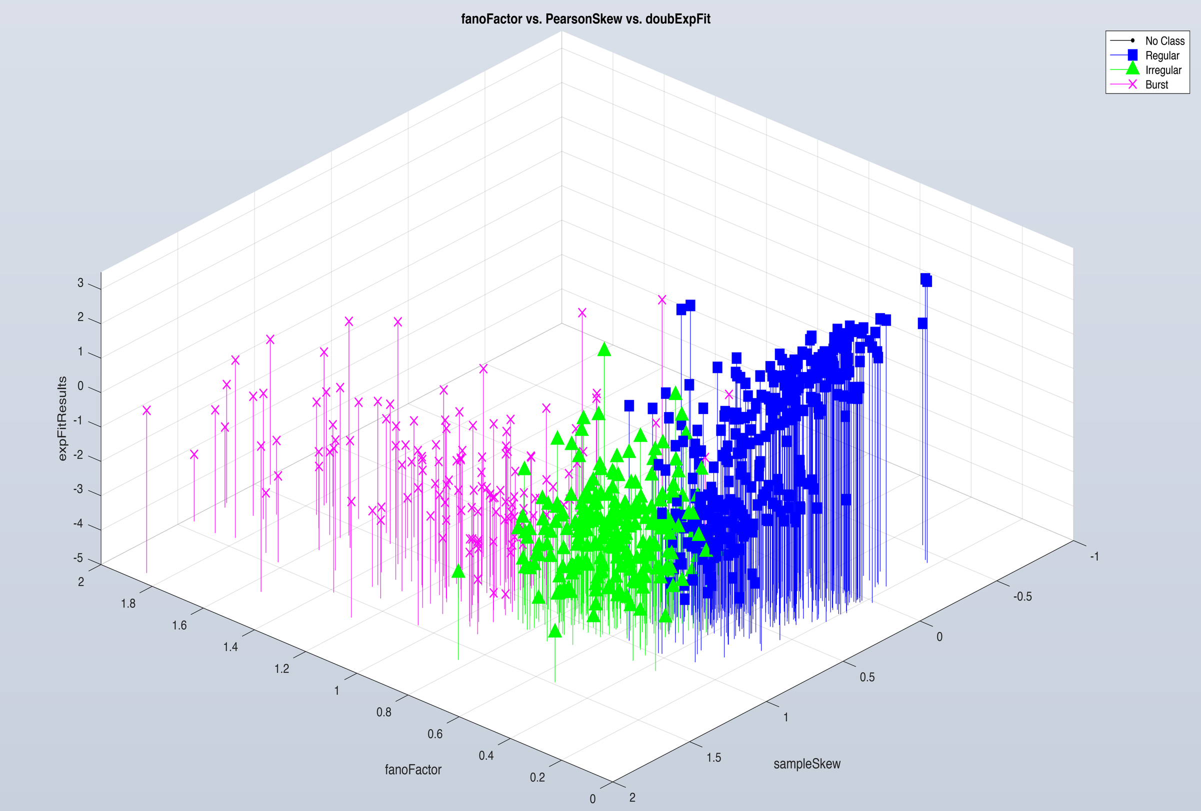
Fig. 7: The double exponential fit of the burst firing neuron has a curve that displays a decay to steady state.

- To quantify this difference, the average of the instantaneous slopes at a 100 points in the double exponential fit was calculated.

$$\text{dExpFit} = log(|\frac{1}{100}(\sum_{x=1}^{n=100}\frac{d(Ae^{Bx}+Ce^{Dx})}{dx})|)$$

Eq. 3: Equation for calculating double exponential fit value where A, B, C, and D are the coefficients of the double exponential equation returned by the fit function.

Conclusion



With these three features, we determined threshold parameters that successfully recreated the clusters formed by visual ISIH/Autocorrelogram classification of these data points. Burst neurons had FFs(Fano Factors) greater than 0.9. Irregular neurons had skewness values greater than 0.5, FFs above 0.6, and dEFs(doubExpFit) below 0. Lastly, regular neurons had FFs below 0.6, skewness values below 1, and dEFs above 0.

Future Directions

The accuracy and consistency of this classification paradigm can be improved through the addition of additional parameters such as Approximate Entropy, Hurst Exponent, StatAv, etc., yielding a high-dimensional parameter space. Dimensionality reduction and clustering algorithms could then be used to better classify these neuron subtypes. The effects of movement modulation on neural spike train variability can also be examined.

Acknowledgements

Thank you to Amanda Willard, Aryn Gittis, and Tim Whalen for your mentorship and direction this summer. Funding was provided by the NIH-sponsored uPNC (Undergraduate Program in Neural Computation) of the CNBC(Center for Neural Basis of Cognition).