Reviewer report on NeuroChaT

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NeuroChaT is a toolbox written in Python that allows a number of measures to be computed based on an animal's neurophysiological data and simultaneously recorded spatial information. Its' application is particularly useful for the analysis of spatially-specific neural activty. The software has been written to use output files generated in Axona and NeuraLynx electrophysiology recording systems, or from other proprietary electrophysiology systems with conversion to the HDF5 file extension format. We agree with the comments made by Poucet and Jacob (2019), especially the suggestion of a short manual that provides formulas to indicate how some of the measures were computed. We have additional comments based on our experience using NeuroChaT.

For this review, we were able to trial the executable GUI version of the NeuroChaT analysis software for Windows 10. Thus, our comments may not apply to the NeuroChaT toolbox if it is generated from the source code. We analysed data acquired using the Axona dacqUSB data acquisition system and analysed using the TINT cluster cutting program. The electrophysiology recording session was conducted in our lab with a rat running around in a square open field arena. To get started with the analysis, the GUI requires the spike times and waveforms information for a tetrode (spike .n file) and a .txt file containing the tracker position data. In order to generate this file, TINT is used to produce a ".txt" file from the ".pos file", which contains a vector of X - Y spatial coordinates of the rat during the recording session. Although the dialogue box indicated that a spike .n file and/or a spatial .txt file could be used, we were unable to get the GUI to work using only a spike .n file, even if the output analyses that we selected did not require any positional information. Nonetheless, the instructions were easy to follow and NeuroChaT created a .pdf file and a numerical output file of our data.

Our comments relate to clarification of the .pdf file and the numerical output file.

Reassuringly, our figures previously generated from custom written code and functions in Matlab matched the equivalent output files of NeuroChaT. In addition, NeuroChaT provided several additional figures that we think are very helpful. For example, the figure showing changes in head direction tuning curves as a function of time and displaying changes in tuning parameters minute by minute. This analysis is useful to visualize preferred firing direction fluctuations around the mean direction, which is not captured by commonly used measures of linear drift. Although there may be sampling bias issues due to the time the rat spends looking toward the preferred firing direction at different time periods, it would be helpful to have some values for these plots, in order to characterise preferred firing direction fluctuations. We suggest a measure of instantaneous drift rate in degrees/minute. This defines the direction and the extent of drift, computed by looking at differences in preferred firing direction between adjacent time periods.

The decomposed clockwise and counter-clockwise tuning functions plot shows the extent of angular separation which enables cells to anticipate the actual head direction. We may suggest to add to this plot a legend showing which of the two clockwise and counter-clockwise curves are represented by the two colours (red and blue). Moreover, a measure of angular separation between the two decomposed functions would be useful, in order to be correlated with the anticipatory time interval analysis.

The program also includes a different way to quantify anticipatory firing of a head direction cell. This is useful, as the standard anticipatory time interval measure commonly used in spatial navigation papers has some drawbacks. First of all, this measure is affected by the smaller number of observations at high angular head velocity values. Secondly, it is difficult to compare this measure across brain regions, as researchers have often used different head direction and angular head velocity bins. The alternative measure implemented by NeuroChaT is based on the optimal time shift value that is required to optimise tuning curve parameters. The relation between optimal time shift and peak firing rate/ Skaggs information content is plotted. It would be useful to generate figures for the relation between tuning width and shift value.

One of the strengths of this program is that it is straightforward and easy to use. It would be a good idea to implement also a GUI version that allows to upload more than one trial at a time, for example to compute a mean spectrogram for the entire session. Similarly, the program conveniently and quickly writes the numerical output associated to each plot in an Excel file. We noticed that these files, at least in our hands, were overwriting each other as we conducted subsequent analyses of different units within the same folder so it might be useful if new file names could be generated for each analysis, possibly with the filename of the spike .n file.

The local field potential (LFP) phase – coherence analysis is very detailed, and provides plots to visualise the extent of phase locking (Rayleigh vector) and preferred phase of each cell. In the polar histogram named “LFP phase distribution plot”, we suggest that the red line detailing the preferred phase of each cell should be proportional to the Rayleigh vector length (the theta modulation depth of that cell). This is because for irregularly firing cells, the mean phase is not a representative measure, as cells do not increase firing on any specific theta phase. Moreover, to avoid binning the phase data, a polar scatter plot could be implemented alongside the polar histograms in which each dot represents the phase of the underlying oscillations at which each spike is emitted. Finally, we think having the option to run the spike-LFP and LFP related functions independent of the spatial data.

For the future, it would be helpful for our lab, to broaden the type of accepted file formats at least to be more compatible with Matlab or Plexon. This would be of great utility to analyse monkey electrophysiology data and quantify spatial firing (e.g. in head direction cells) across different species.

Overall, NeuroChat provides a standardized approach to the analysis of spatial-specific neural data that allows interpretation and comparison across labs, making results more reliable, and reproducible.