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# Practical tools for analysing rhythmic neural activity

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ABSTRACT

This report describes an integrated software package, DataView, which contains a number of tools for analysing rhythmic neural activity. These include simple autocorrelation, a merge-and-drop filter, an enhanced version of the Poisson surprise method and a flexible hill-and-valley analysis tool. The package contains facilities for identifying, examining, and if appropriate, correcting, outliers arising from misidentification or rhythm abnormalities. The package has a full graphical user interface which provides flexible and rapid feedback on the progress of analysis, and the consequences of choices regarding parameters for the various tools. The user can thus easily experiment with different methodologies and tool settings, and tune the analysis to the most appropriate form for the data in question.



## 1. Introduction

A common task in electrophysiology is analysing rhythmic activity such as that driving locomotion, respiration, mastication or copulation. The simple presence of a rhythm and its fundamental frequency characteristics can be detected by autocorrelation (Perkel et al., 1967), but for more detailed analysis a key requirement is correct identification of the bursts of activity. If the onset and offset times of bursts are known, information about the episode duration, burst frequency, burst duration, phase of the activity, and sequential changes therein can be extracted. Most methods for detecting bursts fall into three broad categories: manual analysis, rectify-and-smooth, and interval-based statistical analysis.

In manual analysis the experimenter determines the onset and offset times through visual examination of the data. This has the advantage that an experienced analyst can use an overview of the general characteristics of the activity combined with a lot of background knowledge to make particular decisions. It is very difficult to encapsulate such experienced-based pattern recognition within a computer program. However, it has two major disadvantages: first, it is difficult to remove the possibility of experimenter bias, and second, it is prohibitively expensive in time to analyse a large amount of data. Double-blind analysis may alleviate the former problem, but it exacerbates the latter. It is also extremely tedious to perform such analysis.

A common method which attempts to automate the process is to rectify (or square) the data and then to smooth them with a filter or leaky integrator (e.g. Mulloney et al., 1987; Kjaerulff and Kiehn, 1997). This produces a series of “hills and valleys” whose regularity reflects the regularity of the rhythm. It is usual then to set a threshold level, and the time at which the hill climbs over this threshold defines burst onset, and the time at which it drops below it defines burst offset. An advantage of this method is that it includes amplitude as well as time information within the analysis (e.g. Mulloney, 2005), since bigger hills reflect more intense activity. Problems with the method include the choice of filter, and the level of the threshold. These choices affect the relationship between the time of the threshold crossing, and the time of the actual burst activity. Furthermore, higher order metarhythms (e.g. alternating periods of weak and strong rhythmic activity) can cause baseline shifts so that no single absolute threshold is adequate.

Interval-based statistical analysis methods start by converting the continuous (albeit digitized) recorded signal into a series of “events”—objects with unit amplitude, and an on-time and off-time (possibly of unit duration). The analyses are usually grounded on the notion that intervals between events within bursts are likely to be shorter than intervals between events not within bursts, or those delimiting adjacent bursts (Cocatre-Zilgien and Delcomyn, 1992; Chen et al., 2009). Various statistical measures have been proposed to identify contiguous events whose intervals are less than would be “expected” from non-burst activity, including parametric Poisson surprise maximisation (Legéndy and Salcman, 1985) and non-parametric rank surprise maximisation (Gourévitch and Eggermont, 2007). However, neither of these methods takes account of any underlying rhythm. Therefore, when

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applied to bursts that are known to be rhythmic, information regarding the probability of occurrence of bursts at particular times is not used. Furthermore, brief (single event) "bursts" are obviously undetectable since there is no within-burst interval by which to be surprised.

This report describes an integrated analysis package, DataView (http://www.st-andrews.ac.uk/~wjh/dataview), which provides practical tools for carrying out these procedures. It introduces a new "merge-and-drop" (merge/drop) filter method which makes use of the regularity of rhythmic activity to enhance interval-based burst detection, and provides extended versions of the Poisson surprise and hill–valley analysis methods. DataView has a full graphical interface that provides immediate visualization of the emergent burst frequency and duration characteristics as analysis progresses (Fig. 1). The user can therefore readily compare the outcomes of different procedures and parameter sets, and choose which is best for a particular problem.

## 2. Materials and methods

The end-point of primary rhythm analysis in Dataview is to identify the bursts within a rhythm as a list of events with unit amplitude and appropriate on-times and off-times. The timing characteristics of the rhythm can be fully extracted from these events. The amplitude characteristics (peak voltage, RMS voltage, power, area, etc.) can be extracted by analysing the data within the time windows defined by these events, and DataView has facilities for this. DataView can hold up to 26 separate lists of events (identified by the characters a–z), each with an arbitrary number of events within it.

### 2.1. Manual analysis

In manual analysis, the user simply drags the mouse over a burst of activity identified visually within the chart-recorder display of the data. Each such operation enters an event into a selected list, until the user exits the analysis mode. The chart view can be scrolled during analysis, and the selected list can be changed by key press, so different channels of data can be entered into different lists for, e.g., phase analysis.

### 2.2. Interval-based analysis

DataView has three main interval-based analysis tools: an autocorrelation histogram, a merge/drop filter (see below) and Poisson surprise burst detection. Rank surprise burst detection is also supported, but this did not prove appropriate for rhythm analysis and is not discussed in this report.

The first task in interval-based rhythm analysis is to convert the raw signal into a series of digital events that indicate periods of activity. This is done by simple threshold crossing. The user places vertical cursors to delimit a silent or inter-burst period (e.g. bar in Fig. 2A) and the program calculates the mean and standard deviation of the signal within the cursors. The recording is then scanned for data which exceed the mean plus or minus some user-set multiple of the standard deviation. The result is a series of source events, many of which come from activity within bursts, but some of which come from between-burst activity. The task is to identify the rhythm from the timing information of these source events.

### 2.3. Merge/drop filter

The source events arising from bursts will generally be characterized by brief inter-event intervals, while the source events arising from between-burst activity will generally be shorter in duration than the bursts themselves and more widely separated than source events within bursts. This means that a process of merging source events which are separated by only a short interval, followed by dropping brief events, is likely to lead to many of the resulting "rhythm" events encompassing the times of the bursts (Fig. 2A). The problem lies in determining the appropriate minimum off-time for the merge filter, and minimum on-time for the drop filter. These are derived by an iterative process which attempts to optimize the regularity of the frequency and duration of the rhythm events that emerge from the filtering process. The process is as follows. A minimum off-time and minimum on-time are selected for trial, and the source events are processed through the two filters sequentially. Two graphs are constructed from the rhythm events, showing the instantaneous cycle period (start-time to next start-time) plotted against time, and the burst duration (start-time to end-time) plotted against time. A robust polynomial or smoothed trendline is fitted to each of these graphs using the LOWESS technique (Cleveland, 1979; the algorithm is well described by Hen et al., 2004). It is essential that these trendlines should be robust, because at many stages in the analysis there are multiple outliers with respect to the main trend, and these would skew a non-robust method. The optimal choice of filter parameters is the one that minimizes the deviations in both graphs relative to their respective trendlines (Fig. 2B, frequency but not duration plots shown).

In practice the filter settings can either be adjusted by hand to produce a good visual fit to the trendlines, or the optimal settings can be detected automatically. The latter requires a cost function to define what constitutes a good fit. A function which seems to yield good results (i.e. ones that are largely consistent with bursts defined "by eye" by experienced investigators) is the product of the average absolute normalized deviation of the instantaneous cycle periods and burst durations from their respective robust trendlines. Thus

$$\mathrm{cost}_{\mathrm{freq,duration}} = \frac{1}{n}\sum_{i=1}^{i=n}\left|\frac{y_i-\bar{y}_i}{\bar{y}_i}\right| \quad (1)$$

and

$$\mathrm{cost}_{\mathrm{total}} = \mathrm{cost}_{\mathrm{freq}} \times \mathrm{cost}_{\mathrm{duration}} \quad (2)$$

where $y_i$ is the value of the $i$th data point out of a total $n$, and $\bar{y}_i$ is the value of that point as predicted by the robust trendline. Note that it is extremely unlikely that either cost will be zero, so neither factor will completely dominate the other.

This cost function has a very jagged distribution across the range of possible filter parameters, so a brute force search is employed. This is not as bad as it sounds, because the discrete distributions of times due to digital sampling means that only a limited sub-set of the potential range of filter parameters needs to be tested. The sub-set is further limited by the user, who seeds the search by entering a "best guess" for the average cycle period after visual inspection of the data or preliminary autocorrelation analysis. This value does not have to be very accurate. The programme rejects solutions in which the average period of the emergent rhythm is less than half or more than double this value. This is necessary to prevent spurious solutions in which, for instance, all the source events are combined into a small number of "megabursts". It also substantially speeds the search process since the major computational expense is in calculating the robust polynomial fit, and this can be skipped for filter parameters that yield rhythms outside the acceptable frequency range.

#### 2.3.1. Trimming bursts

Since source events are detected as deviations from the mean voltage, it is inevitable that some will arise from non-burst activity, either as noise or between-burst spikes. If these occur close to genuine bursts, the merge filter may incorporate them into the