NoLITiV: an implementation of nonlinear methods of signal processing: application to pharmacological data

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There has been substantial growth in the technological sophistication used in measurement of cellular activity and its associated pharmacology by in vitro methods. In particular, the use of multi-electrode array (MEA) electrophysiological recording has allowed researchers to collect large volumes of multivariate, real-time data (Egert et al., 2002) from a number of neuronal preparations (e.g. acute brain slices). However, analysis of such datasets necessitates consideration of nonlinear interdependencies which may provide a more detailed understanding of underlying pharmacological effects and physiological functions than more traditional approaches.

A MATLAB-based software tool (NoLITiV; Non-Linear Interdependencies Time Varying toolbox), based upon principles previously applied to EEG data (Quiroga et al., 2002), was developed, implemented and tested to allow the application of a range of synchronisation measures to bivariate electrophysiological datasets (x & y). In addition to including data preprocessing steps, the toolbox allows estimation of three related synchronisation measures, S(x|y), H(x|y) and N(x|y) (Quiroga et al., 2002). NoLITiV’s capabilities were validated using synthetic bivariate, coupled datasets. The robustness of the measures to noise and varying levels of interdependence in the data was tested by varying coupling parameters or amount of empirically realistic noise. The latter was obtained from planar MEAs perfused with Krebs’ solution, under normal laboratory conditions with no biological preparation present.

Results from these tests demonstrated that the synchronisation measures implemented in NoLITiV provide appropriate characterisation of interrelationships for synthetic data. Moreover, application of NoLITiV to data collected from two electrodes located in the same Purkinje cell (PC) layer of acute cerebellar brain slices from adult (>3 weeks; male) C57BL/6 mice, both showing consistent levels of spiking over the recording period suggests a level of nonlinear coupling between adjacent PC populations (S(x|y)=0.0743; H(x|y)=0.0785; N(x|y)=0.0579). When these results are compared with a conventional linear cross-correlation value obtained from the same datasets (0.2421), it is clear that the subtleties of interactions between the PC populations have not been captured by linear methods. It is further suggested that, since both linear and nonlinear methods show differing coupling levels, their comparison will be of interest. However, further application of complex statistical methods is required to fully examine these differences including statistical and physiological significance. This work forms a valuable basis from which to develop analyses of the pharmacological blockade of receptors or ion channels in acute brain slices and so assess the contribution of individual proteins to PC synchronicity and cerebellar output.
