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January 29, 2016

Dear

Please find enclosed the manuscript "A comparison of computational methods for detecting bursts in neuronal spike trains and their application to human stem cell-derived neuronal networks".

Accurate identification of patterns of bursting activity is an essential aspect in the analysis of experimental recordings of neuronal activity in a variety of contexts. Despite this, no one widely used method for identifying periods of bursting activity in neuronal spike trains has been adopted in the field. Instead, many methods have been proposed for detecting bursts. However, assessment of these methods has generally only been performed by their original authors, using very specific sets of conditions. In this manuscript we present an unbiased assessment of eight previously published burst detection methods, comparing the performance of recently developed innovative methods for burst detection with well-established techniques such as the Poisson surprise method.

We develop a list of desirable properties that a method should ideally possess to accurately detect bursts in a variety of spike trains. We assess each method in regards to these properties using both simulated and experimental data, and show that a number of existing techniques perform poorly at detecting bursts in a range of contexts. Based on this, we provide recommendations for the robust analysis of bursting in neuronal spike trains using existing methods. We also employ a number of the high performing burst detection methods to analyse novel recordings of networks of human induced pluripotent stem cell-derived neurons, and describe the ontogeny of bursting activity in these networks over several months of development.

Several articles that have been previously published in J. Neurophysiology employ burst detection techniques that were assessed in our study. Since the choice of burst detection technique used to analyse experimental recordings of neuronal activity can have implications for the con-

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clusions about the nature of the bursting activity in these networks, we consider an awareness of the limitations of burst detection techniques and the conditions under which they are most suitable to be important. We thus believe that our study would be of relevance to the audience of J. Neurophysiology, and your journal would allow the recommendations from our analysis to be accessible to a wide range of both computational and experimental neuroscientists working in this area.

This manuscript has not been published before and all authors have approved the final manuscript.

Thank you in advance for your consideration.

Yours sincerely,

Ellese Cotterill