Classification of Purkinje Cell Post Synaptic Current Events

Peter Hebden[1,2,*] Lewis D. Griffin[1,2] Guy Moss[3]

[1]Centre for Mathematics and Physics in Life Sciences and Experimental Biology (CoMPLEX), University College London, London, WC1E 6BT, UK
[2]Department of Computer Science, University College London, London, WC1E 6BT, UK
[3]Department of Neuroscience, Physiology and Pharmacology, University College London, London, WC1E 6BT, UK
*Contact: peter.hebden.18@ucl.ac.uk

1. Introduction

The recording and analysis of synaptic currents provides an informative measure of neuronal and circuit behavior, but recordings from the soma of dissociated Purkinje cells contain an overlapping mixture of slow (gabaergic) and fast (glutamatergic) events **with highly variable kinetics**. While traditional template methods are somewhat effective for event detection and classification, neural networks can be more accurate, providing more information about synaptic interactions and presynaptic NMDA receptors.

2. Purkinje cell synapses

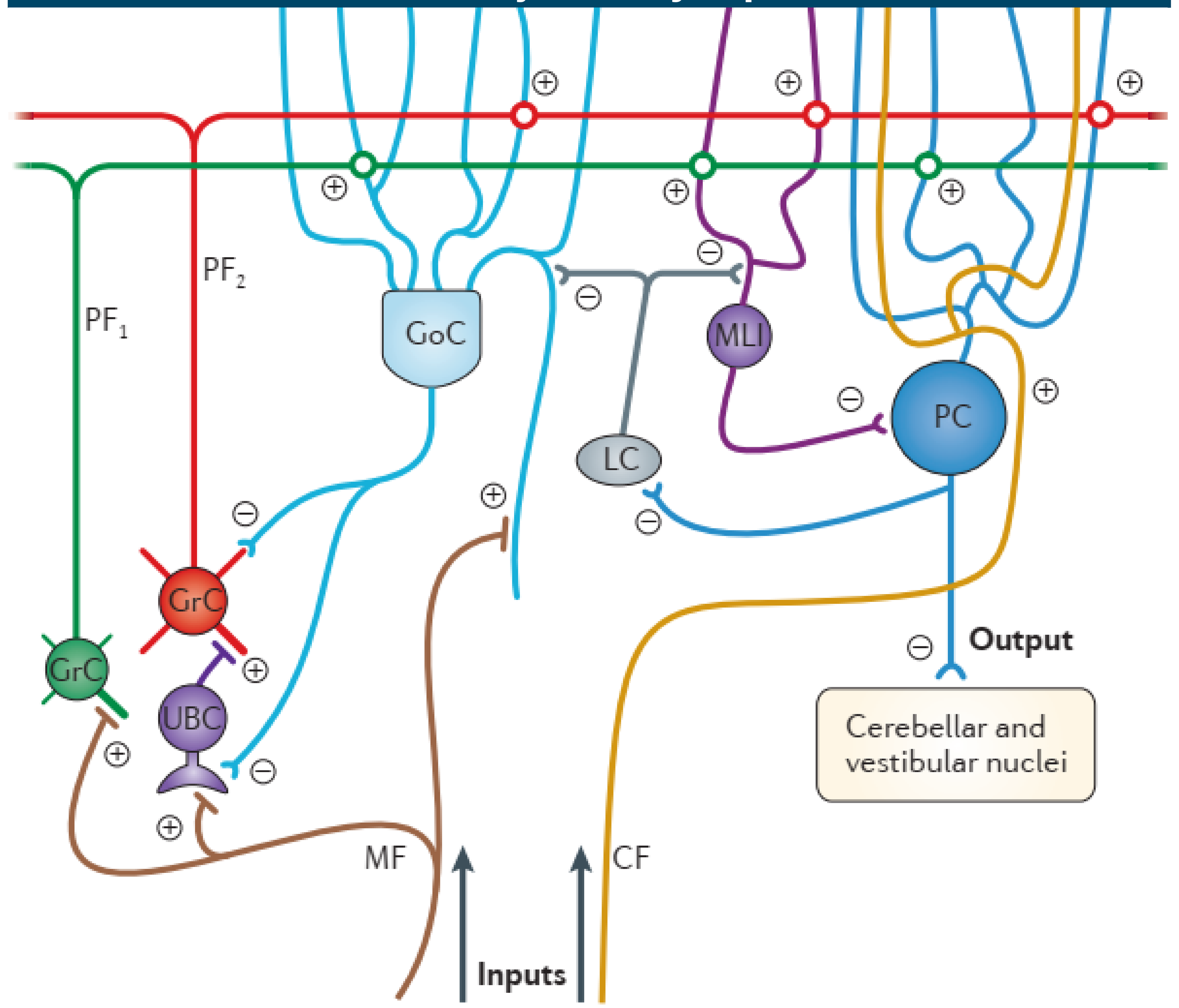
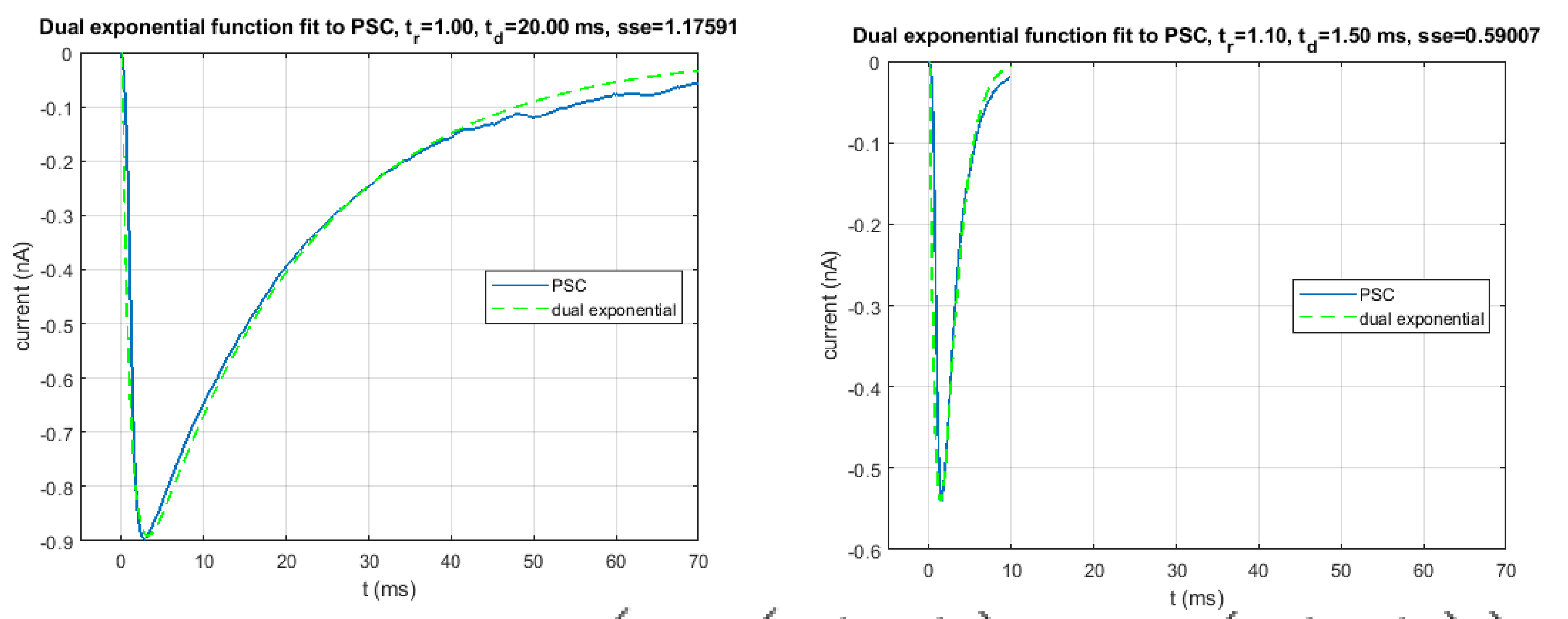


Fig 1. Purkinje cells receive excitatory and inhibitory inputs: Climbing fibres (CF) indirectly make excitatory synapses ⊕ with the Purkinje cell (PC) soma, while molecular layer interneurons (MLI), such as basket cells, make inhibitory synapses with the PC's soma. Parallel fibres (PF) make excitatory synapses ⊕ with the PC's dendritic tree. Other components in this figure include mossy fibres (MF), unipolar brush cells (UBC), granule cells (GrC), golgi cells (GoC), and the Lugaro cells (LC). Image: (Gao et al., 2012).

3. Event Detection and Extraction

Post synaptic event detection was by threshold. **1.** Data was filtered by a bandpass filter built from a 2nd order Butterworth filter, and the MATLAB™ function **filtfilt**, which performs zero-phase digital filtering. **2.** The event detection threshold was set by visual inspection of the filtered data. **3.** Event times were initially detected by threshold, then consolidated at local peak times. **4a.** Template method: mean squared error of template versus unfiltered data at event time. **4b.** Neural network method: extract peak aligned waveform (-10 to +10 or 20 ms) and submit to a neural network classifier already trained on ground truth examples.

4. Template Method



$$I(t) = I_{max}\frac{\tau_d\tau_r}{\tau_d-\tau_r}\left(exp\left(-\frac{t-t_s}{\tau_d}\right)-exp\left(-\frac{t-t_s}{\tau_r}\right)\right)$$

Fig 2: The dual exponential function was used to model the mean waveforms extracted from the PSC data.

5. Neural Network Method

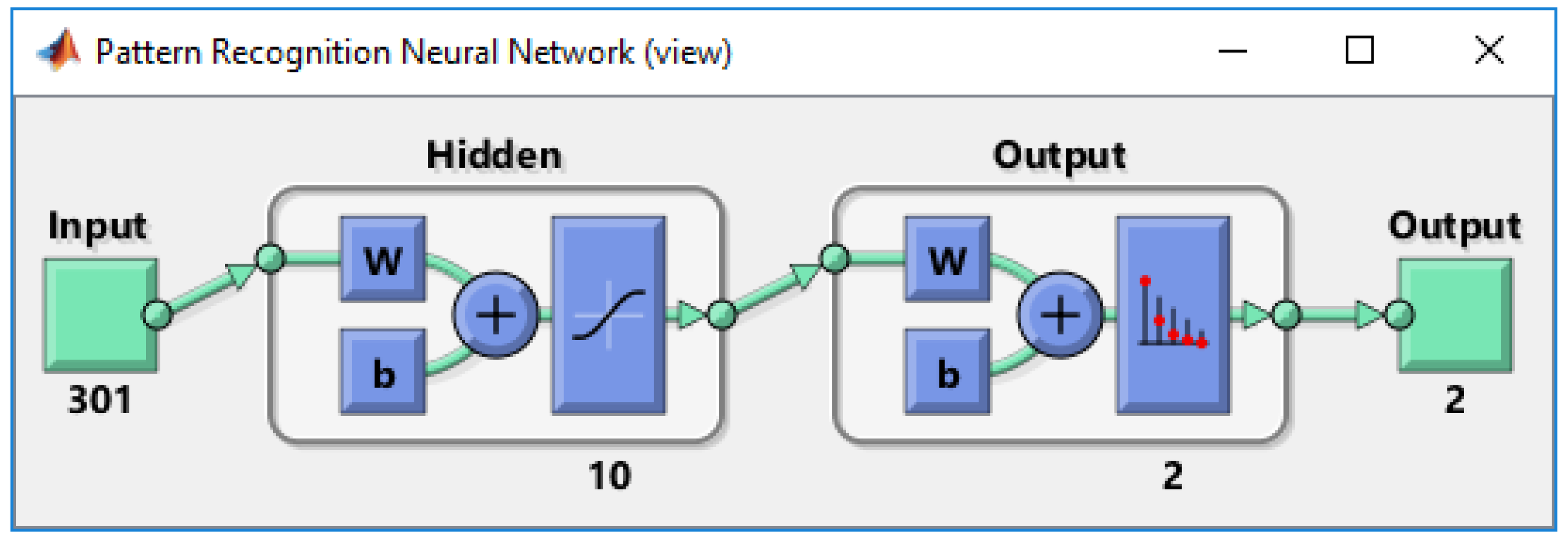


Fig. 3: Neural networks are well suited to problems where the training examples are taken from noisy, complex data.

- This image is from the Deep Learning Toolbox™
- A neural network with a single hidden layer can model any continuous function if the hidden layer contains enough nodes.
  - This network accepts input with 301 features per example.
  - One hidden layer contains 10 neurons with sigmoidal transfer functions.
  - The output layer calculates the posterior probability of the two classes.

6. Synthetic Data

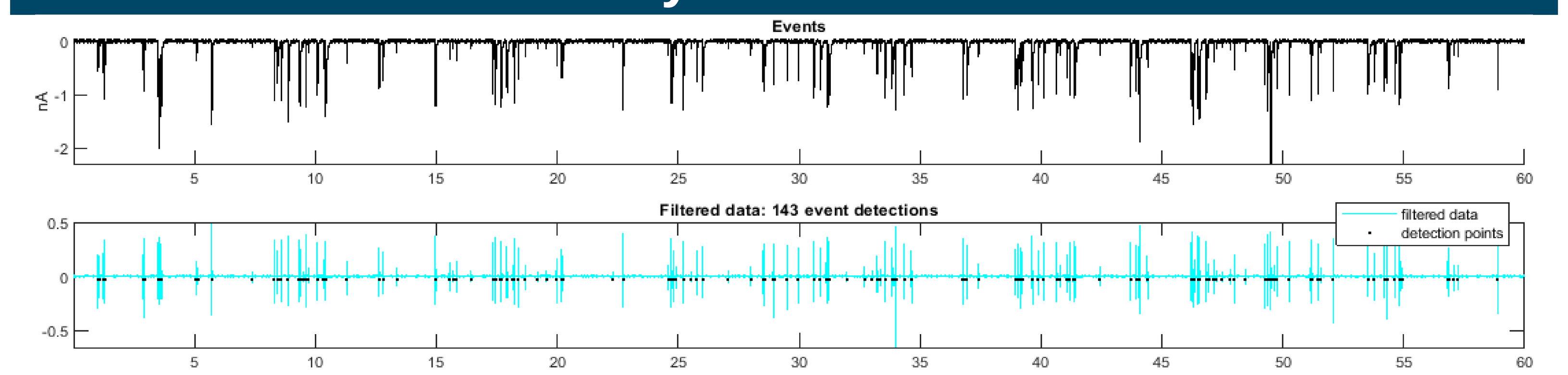


Fig 4: This synthetic data was generated by adding random values to the inter event intervals, event amplitudes, and decay time constants of each slow and fast event. Consequently these events have highly variable kinetics and may overlap in terms of shape and time (s).

7. Classification of Events in Synthetic Data

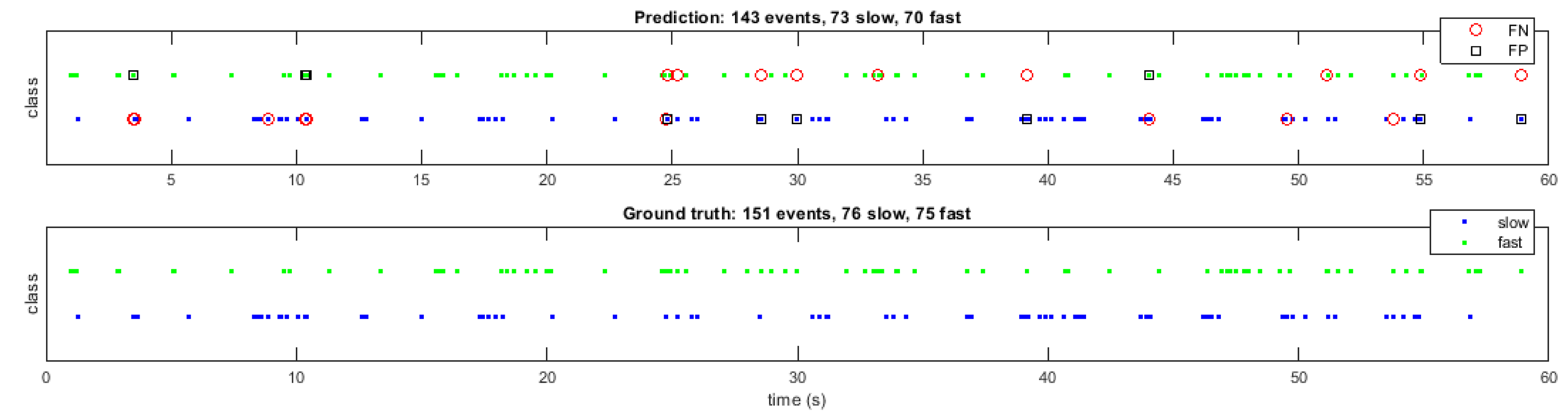


Fig 5: Template method: accuracy = TP/(TP+FN+FP) = 0.83

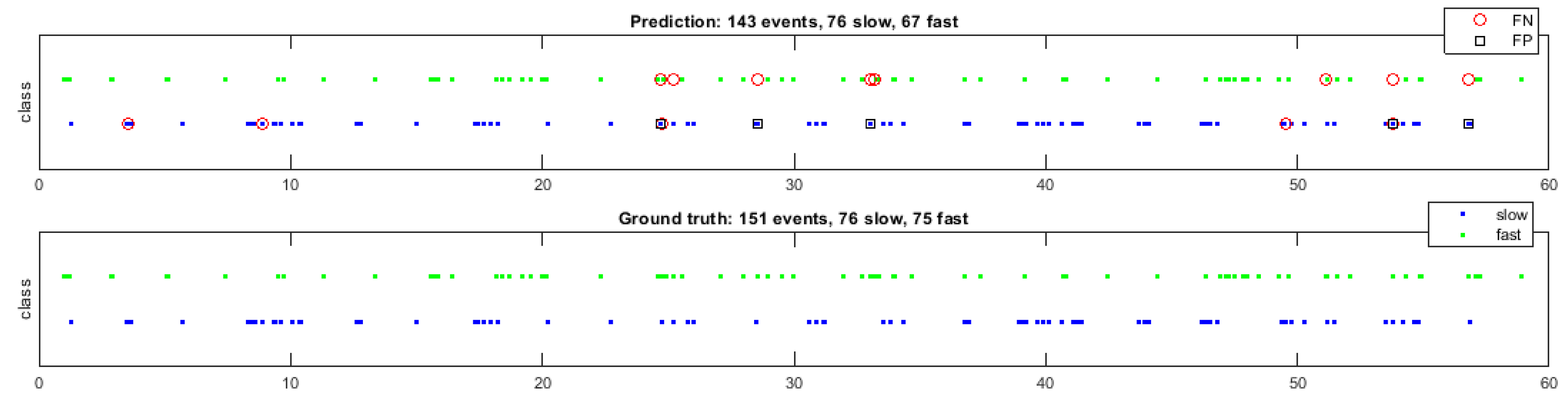
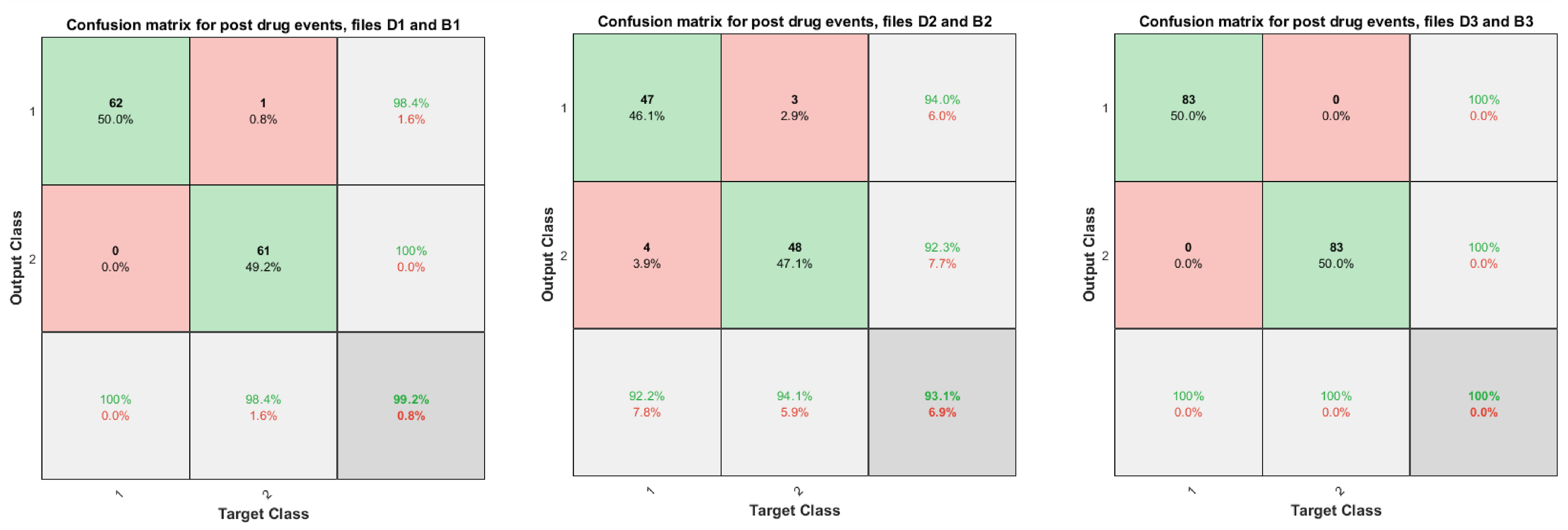


Fig 6: Neural network: accuracy = TP/(TP+FN+FP) = 0.92

8. Classification of Events in Real Data



Neural network accuracy on 6 pairs of real data files using ground truth detection times for event extraction (waveform length 20.1 ms). Recordings were taken after the application of DNQX and bicuculline. Data was partitioned: training (70%), validation (%15), test (15%). Accuracy was about **99%**, **93%**, and **100%** respectively.

9. Discussion

The neural network method was easier to parameterise and had better classification accuracy on synthetic than the template method. The NN also performed well on the real data. However, the real event data was highly variable, with many very small amplitude events, and not amenable to automatic threshold detection. Nonetheless, neural networks are a promising method for this data, and it seems likely that they can deal with event detection as well as event classification.

References

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Zhenyu Gao, Boeke J van Beugen, and Chris I De Zeeuw. Distributed synergistic plasticity and cerebellar learning. Nature reviews. Neuroscience, 13:619–635, September 2012.