NEURAL NETWORKS IN THE AUTOMATED CLASSIFICATION OF NEURAL CELL MORPHOLOGY – RAPID, UNBIASED MORPHOMETRY.

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Background – Accurate three-dimensional images of neurons labelled using multiple markers can be readily generated. Such images, obtained using fluorescent markers specific to the cell type(s) of interest, were used in a heterogeneous population of cells for the accurate analysis of cell numbers [1]. Importantly, neural cells are highly plastic, mirroring their functional state in their morphology. Therefore, data from further classification of the three dimensional images from individual cells would enable the functional state of the cell to be established, including the morphological change associated with cellular dysfunction, degeneration and disease. The detection of morphological changes may be performed manually, but is open to bias and is time consuming. The availability of accurate three dimensional data in a digital medium has allowed the use of *neural networks* to rapidly process large data sets by *'learning' or adapting*. In this paper we demonstrate using a neural network to *classify* 3 subpopulations of dopaminergic neurons based on their three dimensional *morphological features*.

Methods - High resolution 3D image data from three populations of fluorescently labelled dopaminergic neurons were captured on a Zeiss axioimager with ApoTome and the resultant images processed using Imaris software by Bitplane. A number of features were extracted from each cell and the data was fed into a neural network which automatically classified each feature set as a specific cell type. The cell types were defined during the training process which involved exposing the neural network to features generated from cells of known phenotype as initially defined by their neurochemical code. Thus, the neural network identified each 'typical' cell type based on its morphological features.

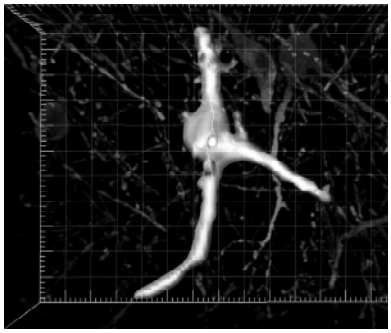

Figure 1: An example of a 3D images after processing, showing a single dopaminergic neuron amongst other neurons.

Results – On completion of training, the neural network was able to distinguish the three cell types to within 91% accuracy. It outperformed a human expert in accuracy (72%) and speed on the same set of data.

Conclusion – With the ever increasing dimensionality and quantity of image data, information analysis is challenging to a human, thus automated methods of analysis are required. Neural networks are one possible solution that enable not only high throughput analysis, but also the adaptability inherent in the networks themselves. The *unbiased automation of cell classification* has multiple applications including *disease diagnosis and biomedical research* where the plasticity of neural morphology allows the *morphometric analysis of cellular state*.

[1]Cavanagh, B. , Meedeniya, A.C.B. , Muller, D. , Blumenstein, M. , Mackay-Sim, A. (2007) Introducing "Fluorescence Neurosteriology": Novel methods for mapping the brain. *Focus on Microscopy* 2007.