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Autoencoders for cluster analysis of rat brain histology

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Introduction. Extracting quantitative information from the whole brain in histology is one big challenge in neuroscience [1]. Software programs [2] helped in histological quantification, although being time-consuming and relying on individual expertise. Further, machine learning allowed the automation of processes such as segmentation [3] and classification [4], but being, at best, semi-supervised. Here, we propose a novel method to automatically cluster rat brain histology using autoencoders.

Methods and materials. The method consists of first, using autoencoders (AE) to extract local tissue features from photomicrographs of myelin-stained rat brain sections; and second, to cluster the AE-derived features from patches of the sections using Gaussian mixture models (GMM). AE acquire a compressed representation of the tissue patterns from the myelinated axons. The compressed representation (latent space) can be used to create unsupervised maps using GMM, thus automatically separating tissue properties.

We used photomicrographs of myelin-stained sections from brains of three rats sham-operated and three rats after mild traumatic brain injury (mTBI). RGB images were converted into grayscale and differences in the staining intensity among brain sections were corrected by histogram matching, both between and within animals. After that, an AE was trained with 3 random million square patches of 64x64 pixels from the image sections, and the dimensionality of the latent space was set to 128. After training, all brain sections were passed through the AE, thus converting every 64x64 pixel patch into 128 values that are clustered using GMM. The optimal number of clusters was decided based on Bayesian Information Criterion (BIC) score.

Results. The resulting maps separate regions that vary in density and organization of myelinated axons. The figure shows two coronal sections from a sham (panel A) and mTBI brain (panel B), and their corresponding 10-cluster-maps (panels C and D). Clusters 7:9 represent highly myelinated areas, i.e., white matter areas such as the corpus callosum and optic tract. The cluster maps show the lamination in the sham cortex, whereas in the mTBI cortex the lamination changed at the lesion site. The sham external capsule is represented by clusters 8 and 9, and mTBI external capsule denotes less myelin content, with clusters 5:7. The granule cell layer of the sham is represented by cluster 2, while in the mTBI animal is represented by clusters 0 and 1. The overall presence of cluster 5 is higher in the mTBI animal compared to the sham-operated animal.

Discussion. The proposed method allows to classify and quantify tissue properties, thus allowing to identify local features of histological sections. Notably, the method is suitable for extracting information from massive histological samples in an automatic manner. Currently, we are working on training an AE with myelin-stained sections from more animals. Next steps will be to add Nissl-stained sections from the same animals, as well as to combine the information of both stainings. By co-registering and clustering consecutive sections stained for myelin and Nissl, we expect to distinguish histopathological changes in the whole brain after mTBI.

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