7th BigBrain Workshop: Challenges of big data integration



Contribution ID: 33

Type: Talk

Morphology-based correction of batch effects in histology and autoradiography

Thursday 5 October 2023 11:15 (12 minutes)

Introduction

Imaging of 2D post-mortem tissue sections presents challenges due to potential differences in digitized pixel intensities across batches of acquired tissue. This issue is particularly pronounced in human in vitro autoradiography, where chemical fixation is not possible and the brain's size prohibits uniform shock freezing. Instead, the donor brain must be sectioned into discrete slabs for independent processing under different experimental conditions. We propose a novel approach to correct batch effects across adjacent 2D sections derived from contiguous tissue slabs based on the cortical morphology of the donor brain.

Methods

Our method uses 2D sections that have been aligned to a 3D structural reference volume, i.e., the donor's T1w MRI, using a reconstruction pipeline [1].

- 1. Corresponding pairs of points between adjacent caudal and rostral tissue slabs are identified on a cortical surface mesh extracted from the structural reference volume [2]. These points minimize the geodesic distance along the cortical manifold between the adjacent tissue slabs (Fig.1)
- 2. The difference in ligand binding densities between the paired points is calculated and the mean of the differences is used to calculate a correction factor for the rostral tissue slab: $V_i^{caudal_s} V_i^{costral_{s+1}}$ where $V_i^{caudal_s} V_i^{costral_{s+1}}$ where $V_i^{caudal_s} V_i^{costral_{s+1}}$ where $V_i^{caudal_s} V_i^{caudal_s} V_i^{caudal_s} V_i^{caudal_s} + 1$ and $V_i^{caudal_s} V_i^{caudal_s} V_i^{caudal_s} + 1$ and $V_i^{caudal_s} V_i^{caudal_s} V_i^{caudal_s} V_i^{caudal_s} + 1$ and $V_i^{caudal_s} V_i^{caudal_s} V_i^{caudal_s}$

To assess the efficacy of the morphology-based batch correction, we employed simulated data generated on a cortical surface mesh. Synthetic ground truth vertex values were assigned corresponding to each vertex's caudal-rostral position along the mesh. Synthetic data were then perturbed by introducing random batch effects. The performance of the batch correction algorithm was evaluated based on the r^2 correlation of the true and corrected vertex values. We also applied the batch correction algorithm to reconstructed autoradiographs that measure GABA_B receptor density.

Results The r^2 between the synthetic ground truth vertex values and the corrected values was 0.99 (p < 0.1). Visual inspection of the corrected GABA_B receptor density volume revealed that the batch correction was able to remove the obvious batch effects seen in the uncorrected volume (Fig.2&3).

Discussion

We developed a batch correction method that successfully removes batch effects by minimizing the differences between nearby vertices in adjacent tissue slabs on the cortical surface. Future work will apply this method to real autoradiography data and compare corrected ligand binding densities to those observed using positron emission tomography.

[1] Funck, T, et al. "3D reconstruction of ultra-high resolution neurotransmitter receptor atlases in human and non-human primate brains." bioRxiv (2022): 2022-11.

[2] Lepage, C. et al. 2017. "Human MR Evaluation of Cortical Thickness Using CIVET v2.1", OHBM (poster 4166), Vancouver.

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Session Classification: Contributed Talks 1