TOWARDS PREDICTING DISTRIBUTIONS OF NEUROTRANSMITTER RECEPTORS BASED ON CYTOARCHITECTURE AND ANATOMICAL LOCATION

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MOTIVATION

High-resolution multilevel brain atlases are crucial for capturing the multi-scale organisation of the brain. Recent atlases combine cytoarchitecture, receptor architecture, and fibre architecture to reflect brain organisation at the micrometer level [1]. However, while whole-brain measurements of cytoarchitecture are in reach [2, 3], other modalities are, so far, only available for some regions of interest. In this recently launched project we started to investigate the following questions: (i) How far can a generative model predict realistic and representative receptor distributions [4] using cytoarchitectonic features and anatomical location as conditional inputs? (ii) What is an appropriate model of anatomical location for this purpose? (iii) Are additional priors required to solve the problem?

METHOD

We propose a generative adversarial network (GAN) [5] aiming to predict cortical distributions of neurotransmitter densities given high-resolution image patches of cell-body stained tissue sections as an input. As shown in the figure below, we use the recently proposed pix2pix loss [6].

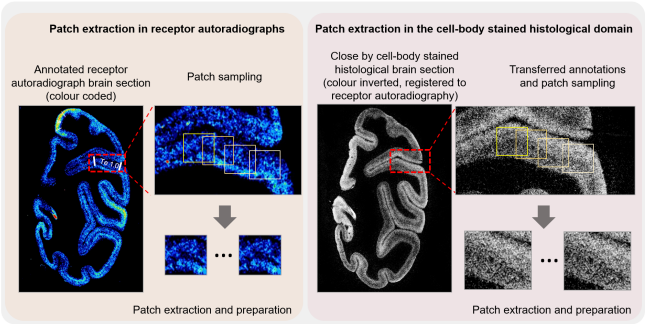

Figure: Patch extraction from receptor autoradiography and cell-stained histological brain sections. First, we use expert annotations provided on the autoradiographs to sample rectangular image patches in a well-defined brain area. Then, using spatial correspondence established by multi-modal image registration of close-by sections, we can sample approximately corresponding patches of cell body-stained tissue. Finally, given the fact that the cortical thickness varies along the cortex, we proceed by resizing the patches extracted from both modalities to the same size (per modality).

Here, we perform a feasibility study in two stages: (i) We train separate "specialist" models for selected cytoarchitectonic areas, thus encoding anatomical location implicitly into different models. (ii) We implement a conditional GAN on input patches from multiple regions, which is additionally informed by the area label.

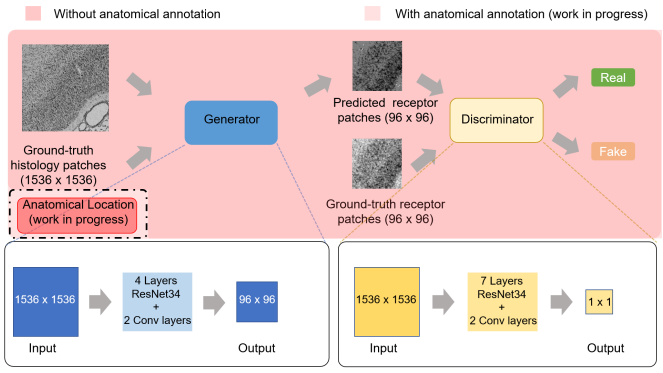

Figure: We train two different versions of our proposed GAN: (i) Predicting the receptor patches given only the histology patches, and (ii) predicting receptor patches given histology patches and anatomical location. Both generator and discriminator are built on top of a ResNet34 encoder architecture.

Here, we propose to use the loss function similar to pix2pix framework [6]. Our generative loss is defined as follows:

$$L_{adv} = \mathbb{E}_{(x)\sim p_{(\mathbb{X}_{tr})}}[\log D(\hat{x}|y)] + \mathbb{E}_{(x)\sim p_{(\mathbb{X}_{tr})}}[\log(1 - D(G(x|y)))]$$

where x denotes the histological patches, x_{tr} denotes the training set of histological patches, $\hat{x}$ denotes the predicted receptor patch, and y denotes the given brain area (i.e., anatomical location (see the prior figure)). Finally, the final loss is a combination of $\mathcal{L}_{adv}$ and an $L1$ loss between the ground-truth and the predicted receptor patches.

RESULTS

We assess the performance of the models using established metrics such as the inception score, and analyze differences in cortical profiles between the predicted and ground-truth neurotransmitter patches. We evaluate our model visually by projecting predicted patches of receptor densities back into the original image sections. So far, the feasibility study has been conducted on two distinct cytoarchitectonic areas in the macaque monkey brain.

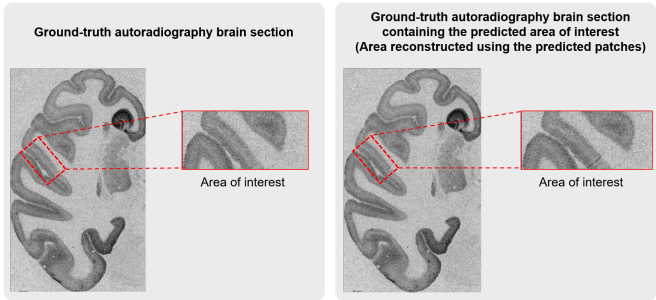

Figure: Back-projection of cortical patches of autoradiography predicted by the generative model into the original scan. Predictions are solely based on cell-stained patches from a nearby and previously unseen tissue section.

CONCLUSION

- We see initial evidence that cytoarchitectonic patches can be used to generate receptor distributions with realistic laminar patterns when training region-specific GANs.
- **Ongoing work:** in the future we aim to investigates how to efficiently condition the generative models by anatomical location to generalize across different regions.
- Important applications are missing data imputation for brain atlases and cross-modality studies of brain structure.

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