TITLE:

Semi-supervised contrastive learning for semantic segmentation of ISH gene expression in the marmoset brain

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ABSTRACT: (character count 2,491)

Gene expression brain atlases such as the Allen Mouse Brain Atlas are widely used in neuroscience research. Such atlases in lower order model organisms have led to great research achievements, but interspecies differences in brain structure and function point at the need for characterizing gene expressions in the primate brain. The Marmoset Gene Atlas, created by the Brain Mapping by Integrated Neurotechnologies for Disease Studies (Brain/MINDS) project in Japan, is an *in situ* hybridization (ISH) database of gene expression in the marmoset brain. The goal of our work is to create a deep learning model to automatically segment gene expression from ISH images of the adult marmoset brain.

Expression patterns of over 2000 different genes can be labelled and visualized using ISH. To characterize gene expression in brain images, ISH signals must be labelled and segmented. Expression intensity and localization can then be analyzed using image processing methods. Deep learning techniques have been widely applied for the segmentation of images on a per-pixel level, known as semantic segmentation. Supervised architectures such as the U-Net have led to impressive segmentation results, but require large labelled training datasets, which are expensive to obtain. Furthermore, in histological images, image variations caused by factors such as tissue preparation and image acquisition methods have been found to profoundly influence outputs from deep learning models, at times more than the signal itself. The ideal model for gene segmentation of the ISH marmoset brain data would require minimal to no labelling and produce consistent segmentations regardless of changes in image hue, brightness, or contrast.

We use a contrastive learning based self-supervised framework in order to create semantic segmentations of gene expressions in the adult marmoset brain. In contrastive learning, the model is trained in latent space, such as by maximizing agreement between the features of different augmented views of the same unlabeled image, or between the features of a labelled image and the model's encoded representations of the unlabeled equivalent. We first create a small labelled 'champion' dataset of easily segmented gene expression brain images, which is then used to train a model to segment more difficult images, such as ones in which the background signal intensity is nonuniform. We propose using a wide range of augmentations to generate strongly perturbed images to account for a range of differences in image profiles. We show an example of a gene that has been fully segmented and mapped to a common 3D template of the marmoset brain. We hope that this work can be used for the segmentation of fine-detailed structures in biomedical images and assist in advancing primate brain research.

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