Deep learning-based virtual histology staining

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Abstract and Introduction

Histological analysis of tissue samples is an important method used for the diagnosis of many diseases, but the process of staining the sample to allow for visual inspection can be long and labor intensive. We demonstrate a label free method to virtually-stain microscope images of a tissue sample using a single auto-fluorescence image. A convolutional neural network (CNN), trained by a generative adversarial network (GAN) is used to perform the virtual staining. We demonstrate the success of this method by applying our technique to a variety of human tissue samples which were then blindly evaluated by a panel of board certified pathologists.

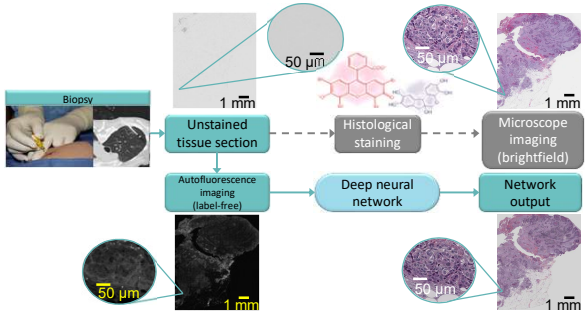
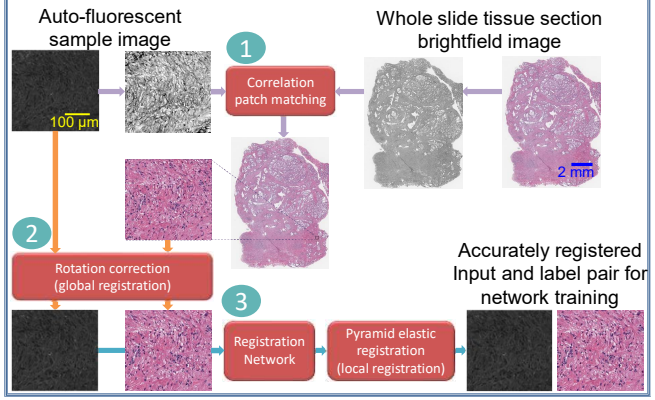


Image Alignment

Accurate co-registration of the images is required for the network to be trained successfully, as it requires knowledge of which pixels in each image correspond to those in the other.

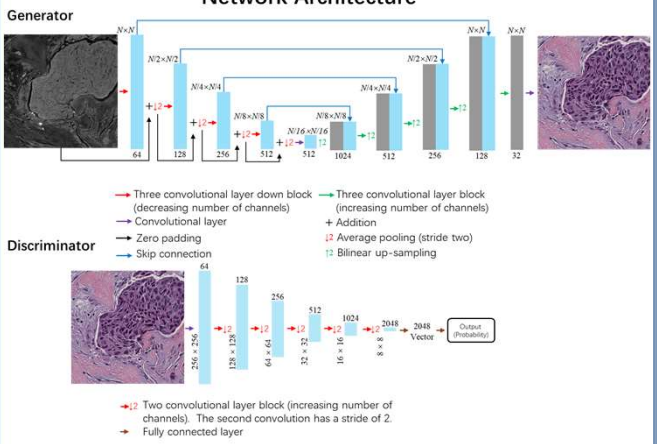
1. Find corresponding sections of the unstained and stained images.
2. Correct misalignments using a global matching algorithm.
3. Achieve subpixel matching by iteratively breaking the images into smaller and smaller blocks and co-registering each block.



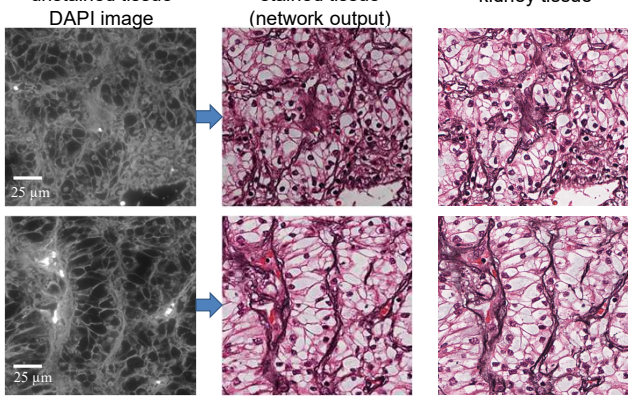
Generative Adversarial Network

The virtual staining is performed using a convolutional neural network. A generative adversarial network is used during training to help achieve sharp, high quality images.

Network Architecture



Results

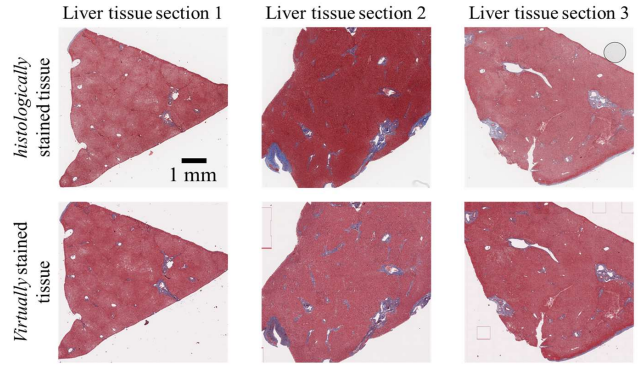


Examples of the virtual stains are shown, demonstrating the efficacy of the virtual staining technique at the cellular level. Virtual stains were also validated by pathologists using 15 different tissues where they:

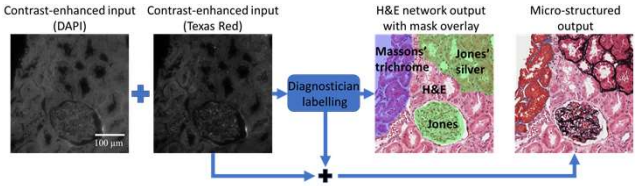
- On average rated the virtual stains to be the same quality the histological ground truth stains
- The pathologists were able to correctly diagnose diseases in the virtually stained tissues.

Additional benefits

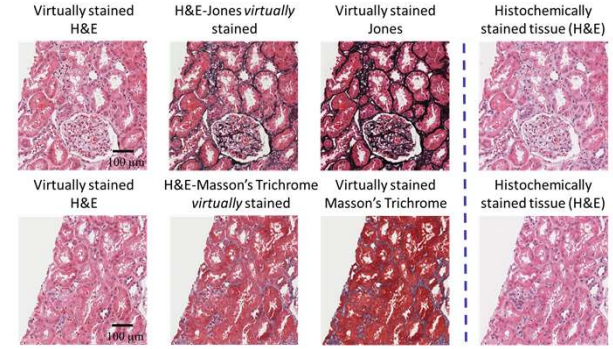
- **Virtual staining enables stain normalization – ensuring that the stains are consistent across tissue sections.**



- **Different stains can be applied to different sections of the tissues.**



- **Stains can be digitally blended, combining multiple virtual stains.**



Reference: Rivenson Y., et al. Virtual histological staining of unlabeled tissue autofluorescence images via deep learning. Nat. Biomed. Eng. (2019)
Zhang Y., "Digital synthesis of histological stains using micro-structured and multiplexed virtual staining of label-free tissue," Light (2020)

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