

Turbocharged 3D Histology: Revolutionizing Medical Tissue Analysis with Automation, Light Sheet Microscopy, and Nanobodies

Pathology is crucial for human health as it provides essential insights into disease mechanisms, and histology plays a fundamental role in pathology by offering detailed cellular and tissue-level insights necessary for precise disease diagnosis and understanding pathological processes. Through digitization and automated analysis, histology has improved accessibility and usefulness for research and education. Despite these advancements, histopathology faces challenges such as technical complexities, limited tissue representation, and subjective interpretations, resulting in varying diagnostic accuracy and consistency. In the near future, our aging society and an increasing shortage of histopathologists will put additional pressure on this crucial technique.

To address these challenges, we have developed a novel 3D histology pipeline. Our approach is highly objective and reproducible, while providing significantly better coverage, higher speed and lower costs compared to 2D histology. At the core, we use light sheet microscopy to capture high-resolution 3D image data of optically cleared and fluorescently labeled tissue samples. By combining a fluorescent equivalent of the classic differential Hematoxylin and Eosin (H&E) staining with subsequent color conversion, we make our 3D histology data easily comprehensible to experienced histopathologists.

In addition, we have developed novel nanobodies against medically relevant targets to make our 3D histology pipeline even more powerful and enable the study of complex biological systems, providing insights into structures such as the vasculature. While antibodies help visualize and identify specific proteins in thin tissue sections, their use for labeling intact tissue samples is limited by subpar penetration and resulting in incomplete and uneven staining. Nanobodies, on the other hand, with their small size and high affinity, are a great match for 3D histology due to enhanced tissue penetration and precise, homogeneous labeling. By combining our nanobody labeling with the virtual H&E staining, we have at our disposal a powerful tool for medical tissue analysis. Now, we aim to put this tool into the hands of histopathologists worldwide, revolutionizing a technique of utmost importance for medicine.

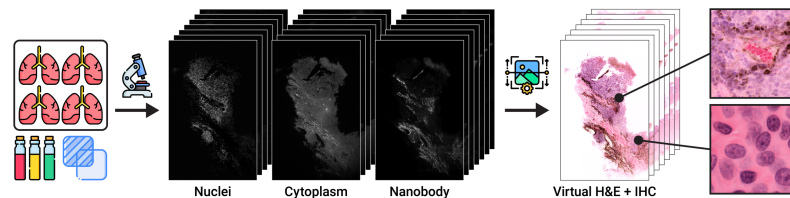


Figure 1: Overview of our 3D histology pipeline. Tissue samples are automatically fluorescently labeled and optically cleared. Image stacks are recorded using light sheet microscopy and converted into virtual histology data.

Fig.1: Overview of our 3D histology pipeline. Tissue samples are automatically fluorescently labeled and optically cleared. Image stacks are recorded using light sheet microscopy and converted into virtual histology data.

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Session Classification: Workflows for Imaging Pipeline