Vasculature Common Coordinate Framework Distance Visualizations Across Organs and Imaging Technologies

Data Analysis and Visualization
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Abstract

The vasculature forms an uninterrupted path across scales in the human body, making it an ideal choice for creating a Common Coordinate Framework of the human body. The resulting Vasculature Common Coordinate Framework (VCCF) can localize cells of different types by using the nearest blood vessel that supplies it with oxygen. As part of the Human BioMolecular Atlas Program (HuBMAP), several tools have been built for spatially registering tissue samples and connecting them with expert ontologies via ASCT+B Tables in the Human Reference Atlas (HRA) framework. Interactive data visualizations show the distributions of distances between different cell types and their closest vasculature across organs and using different technologies. Here, we present Vitessce-based visualizations of 6 organs (skin, colon, esophagus, tonsil, spleen, and lung) and three technologies (CODEX, Cell DIVE, CyCIF) from five different data providers. All datasets were RUI-registered (or are in the process of) and can be explored within the context of the 3D human body in the Exploration User Interface. We conclude with a discussion of planned extensions of the analysis and visualization workflows to cover disease (e.g., tumor cells) and hierarchical cell neighborhoods.

Spatially registering human tissue samples in the HuBMAP EUI

The spatial size, location, and rotation of tissue specimen are manually registered using the Registration User Interface (https://humanatlas.io/registration-user-interface) in coordination with data providers. All RUI-registered tissue blocks can be explored in the Exploration User Interface (EUI, https://apps.humanatlas.io/eui, **Fig. 1**) [1].

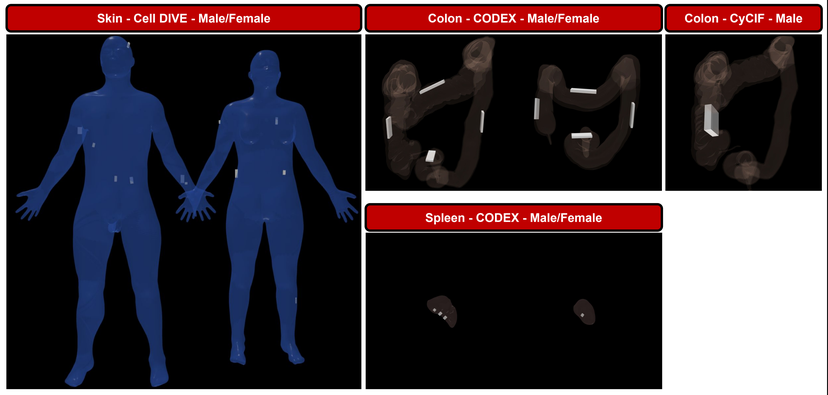

Figure 1. Exploration User Interface screenshots showing skin (**Fig. 3**) and colon plus spleen tissue registrations (**Fig. 4**).

Considerations for using the vasculature as a cell coordinate system

A Vasculature Common Coordinate Framework has been proposed to map all 37 trillion cells in the human body in a way that addresses its multiscale nature [2]. The vasculature seamlessly connects the macro-, meso-, and micro-scales of the body and hence provides an ideal pathway to assign “zip codes” to these cells in order to localize them, see **Fig. 2**. Ghose S., Ju Y., et al. [3] looked at the distance distributions between different immune cell types and the closest endothelial cells in 3D reconstructed tissue samples from adult human skin tissue using Cell DIVE, see **Fig. 3**. This enabled an in-depth analysis of different distance distributions focussed on the effects of UV sun exposure and aging in three dimensions.

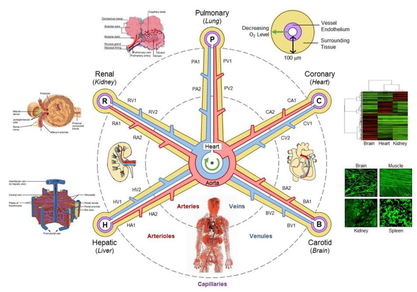

Figure 2. Vasculature Common Coordinate Framework, from [2].

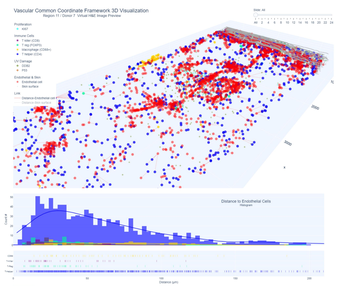

Figure 3. 3D VCCF Visualizations of skin Cell DIVE data, from [3].

Expanding VCCF visualizations to other tissue types and imaging technologies

The visualization workflow has been generalized to cover more tissue types and assay type technologies from different data providers. Furthermore, the open-source visualization tool Vitessce [4,5] can now be used to explore 2D VCCF visualizations within the HRA Portal. **Fig. 4** shows first results on colon (CODEX [6]) dataset from Stanford University, spleen (CODEX [7,8]) datasets from University of Florida and Johns Hopkins University, tonsil (CODEX [9]) and esophagus (CODEX [9]) from Stanford University, lung (CODEX) from University of Rochester Medical Center, and colon (CyCIF [10]) from Harvard Medical School (HTAN). Additional datasets using imaging technologies such as Xenium, MIBI-TOF and confocal microscopy have been visualized but are not shown here as primary data is not yet published.

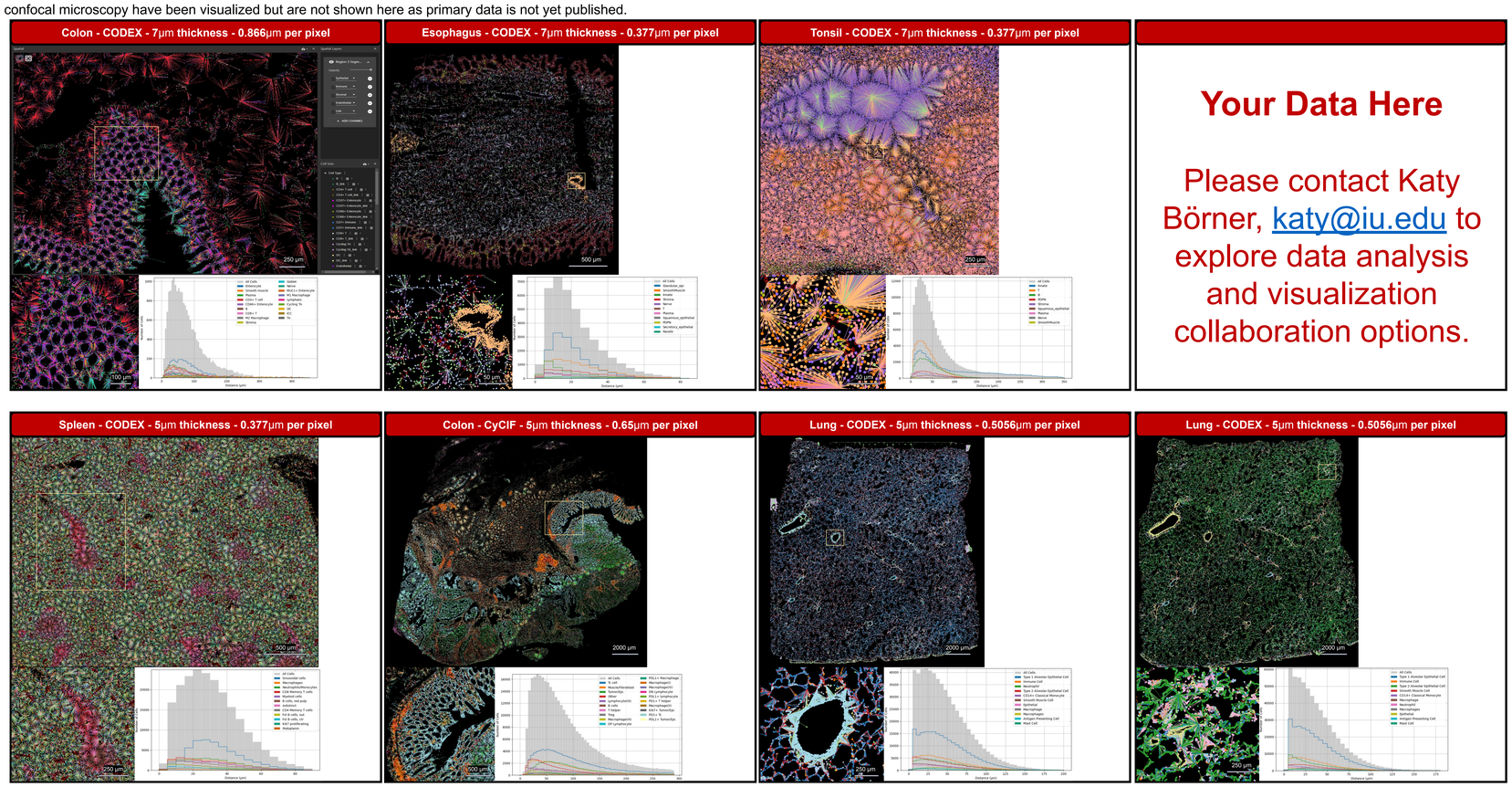

Figure 4. VCCF Visualizations of seven datasets across organs and imaging technologies.

Future Directions, References, and Acknowledgements

Future Directions

Going forward, we plan to extend these analyses to additional tissue types and technologies. If you are interested to collaborate, please share a table with 2D or 3D coordinates (cell centroids) and assigned type of each cell (see **Table 1**). We are in the process of mapping cell types to ASCT+B tables and CL.

x	y	z	Cell Type
555	756	4	Endothelial cell
765	231	3	B cell
356	235	7	T cell

Table 1. Required data format example.

In close collaboration with different HuBMAP and HTAN tissue data providers, we will enhance the visualization workflows based on user needs, e.g., to support more in-depth analyses of the vascular system in correlation to different cell types across organs; making it possible to pick “anchor” cell types to visualize distance to cell types other than endothelial cells; adding scale bars, legends, and distance distribution histograms within the Vitessce viewer; visualizing 3D data in Vitessce as shown in **Fig. 3** and analyzing distances for a selected cell, cell type, or cell neighborhood (e.g., FTU); to add imaging data and turn specific image channels on/off; and compute quantifications of cell-type colocalization as a function of the z-plane in 3D datasets.

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