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VRCellLabeler (VCL): Immersive labeling of Platynereis embryo's cell lineage trees in Virtual Reality

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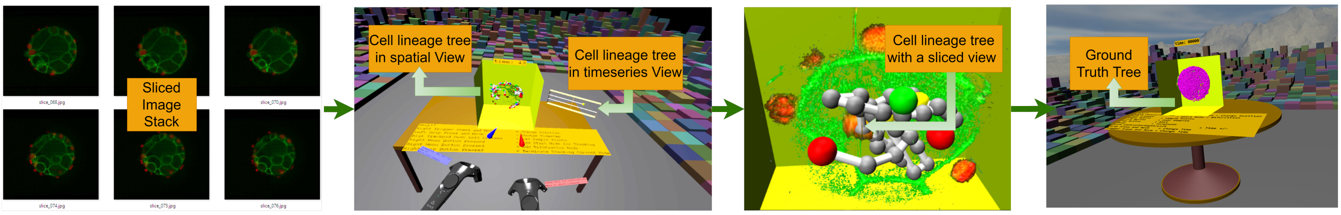

Figure 1: *Pre-processed* P.Dum.*'s developing embryo data as 2D image stack; Rendered particular cell lineage trees in both spatial and temporal view in Virtual Reality; Rendered ground truth tree for all cells using* VCL

Abstract

In biology, the study of cell lineages is used to understand tissue formation as well as the development of a complex organism and 3D microscopy data provides an overview of the dynamic formation process of cells and tissues. However, microscopic data generates an enormous amount of data that is difficult to process and contains an abundance of noise. But machine learning approach requires a lot of ground truth. For such data, ground truth is generally annotated on 2D slices, making the annotation cumbersome and difficult to validate in its 3D structure. Platynereis dumerilii *is a significant lab animal for being considered as a living fossil. VCL analyzes a large amount 3D time-lapse data of* P. Dum.*'s developing embryo cell, organized on disk into three stacks of 2D slices to support out-of-core orthogonal slicing with 90 updates per second of the slicing center and time step. On top, we build an immersive ground truth labeling tool with an intuitive and efficient Virtual Reality interface.*

CCS Concepts

• ***Data*** → *Biological, Large Scale, Microscopic;* • ***Visualization*** → *Scientific, Immersive Labeling;* • ***Hardware*** → *HTC VIVE;*

1. Introduction

P. Dum. from the Nereididae [Ver15] family is a small worm living in coastal marine waters. The cell structure of this rag worm is interesting among the scientific community for several reasons, like living in the exact environment as its million years old ancestors, re-productivity, evolution, as well as the simplest eye structure [BW09]. In general, the lineage tree captures information about the tissue-forming process and shares the common evolutionary history of cells within an organism. The study of cell lineage was initiated by *Whitman* back in 1870 [MBWW18]. From then on, the cell lineage tree has been studied by both biologists and computer scientists.

On the whole, complex organisms contain numerous cells which makes manual annotation tedious and cumbersome. Light-sheet microscopy is a highly powerful method offering high imaging speed with high spatial resolution over time [FA15] reducing the energy load. Light-sheet microscopy is being used for the development of sophisticated biological systems, predicated on imaging for the possibility to image biological structures for example - cell lineage tree, in three dimensions for extended periods by keeping the specimens untouched. But, these methods generate a large quantity of noisy data in size and images. Most of the time, data-sets generated by light-sheet microscopy range from gigabytes to terabytes with time-lapse images [ER15]. However, such data is difficult to visualize at a high frame-rate as the complete data neither fit into main memory nor in GPU memory. On the other hand, on demand data transfer from disk deteriorates the frame-rate significantly, necessitating a data streaming approach to be feasible.

To understand cell lineage of *P.Dum.* from the large amount of data efficiently, a high rendering frame-rate with smooth navigation is necessary. Our goal is to develop an immersive labeling tool *VRCellLabeler - VCL* to collaborate between biological large scale image data and visualization. *VCL* should support ground truth labeling that also demands for an efficient user interface. We chose Virtual Reality (VR) as visualization and interaction environment as it provides 3D vision and intuitive 3D interaction, amplifies human intelligence by connecting the dots between reality and data [Sko18]. Application of VR has been researched in the field of biological data analysis [KCS10], [MJ20] environmental data analysis [OMS*22] education and research [JR20] and many more. Using VR, the demand on rendering performance increases further as stereoscopic rendering at high a frame-rate with at least 90fps in addition to smooth space-time navigation. *VCL* should address the problem of visualizing light-sheet microscopic data in real-time and allow labeling cell lineage trees in VR by ensuring high rendering performance and instant out of core data updates.

2. VCL Methodology

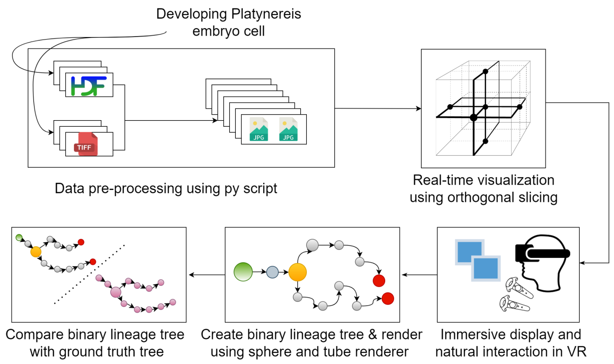

Figure 2: *Methodology of VRCellLabeler - VCL. Pre-process raw data from multiple 3D time-lapse datasets to 2D image stack using python script; Apply indirect volume visualization for real-time navigation using orthogonal slicing; Visualizes the P.Dum.'s dataset in VR using CGV C++ framework; Interactive tracing of lineage tree in VR using spheres tubes for visualizing traces on-the-fly; compare generated lineage tress with ground truth trees for validation.*

VCL aims to provide users an immersive environment that supports space and time visualization with smooth navigation. The prototype is written in C++ and uses a python script for data pre-processing. The pre-processing includes slicing of time dependent volumetric data as a 2D image stack.*VCL* is being developed using *CGV framework* [sgu21], which is a C++ based framework that allows 3D rendering, 3D visualization and offers VR support. The VR support is built directly on the OpenVR API and an emulator for VR kits is provided to foster fast development without an attached VR kit.

For real-time visualization in 3D, we used the indirect volume rendering approach as it helps to generate surface models by using volume data and this can be managed and represented efficiently. From the indirect volume visualization, we used an orthogonal slicing approach to visualize the *P.Dum.*'s embryo cells. For visualizing the 2D slice stack in real-time, first a 3D environment has been created using *CGV framework* that allows orthogonal slicing. These slices are visualized within a box extent using a rectangle renderer. The slices can be explored along space and time by navigating along x,y,z dimension and also along time by navigating along time-step. For initial control of the slices, the user will have a basic UI where the user will be able to change the 2D slices along x,y,z, and t. The 2D slices are saved on disk and cached in memory for fast retrieval, while also enabling out-of-core processing of very large volumes. For immersive interaction a VR scene has been generated based on a default scene provided by the *CGV framework*, which provides a table as the main interaction space, upon which the volume is placed including the orthogonal slices.

A lineage tree is a visual representation of cell core trajectory in *VCL*. We used binary lineage tree formation approach for creating the cell lineage tree and compared with family tree having a parent as root node, children and tree edges connecting parent & child and to follow build the edges. *VCL* contains four types of nodes that construct the lineage tree including start node as parent, bifurcation indicating potential split, sample points representing the trajectory of the cell core that does not have to be a straight line and end node. Lineage tree concept used in *VCL* does not include more than two children. The trajectory between parent to cell split or death is defined as *lifespan* – a sequence of tree edges connecting two nodes with sample points in between. When the user follows a cell, they trace the tree by inserting a point as root node or start node, and follow its path by inserting sample points in between to get the trajectory of a specific cell. In case of a split, the user follows the trajectory of one child at a time until the nucleus vanishes from the data. Then, the user will have the option to back-track to the previous split (if any) to continue tracing the trajectory of the other child. Easy automatic back-tracking is enabled by a stack-based log of user actions. Finally, the user gets a lineage tree for a cell nucleus as a combination of node points and edges. All the traced lineages can be stored in disk and can be read back from the disk. For the interaction, user needs to use an OpenVR-compatible headset and HTC Vive controllers.

3. Conclusion

The goal of this work is connecting large scale microscopic biological data to scientific visualization to build a labeling tool that facilitates efficient creation of ground truth for machine learning in the area of cell lineage study. *VCL* ensures smooth navigation along space and time while labeling the cell lineage trees with 90 fps. With further improvement, *VCL* can become a major asset for analyzing biological data and advancing our understanding of life. We therefore plan to continue this research focusing on modification of cell lineage trees, validation of *VCL* via user studies and scalability.

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References

[BW09] BW H. I.: A slightly different worm – platynereis dumerilii. https://www.

gesundheitsindustrie-bw.de/en/article/news/a-slightly-different-worm-platynereis-dumerilii, December 2009. (Accessed on 08/17/2022). 1

[ER15] EMMANUEL REYNAUD JAN PEYCHL J. H. P. T.: (2) (pdf) guide to light-sheet microscopy for adventurous biologists. https://www.researchgate.net/publication/270513802_Guide_to_light-sheet_microscopy_for_adventurous_biologists, December 2015. (Accessed on 08/17/2022). 1

[FA15] FERNANDO AMAT BURKHARD HÖCKENDORF Y. W. W. C. L. K. M. P. J. K.: Efficient processing and analysis of large-scale light-sheet microscopy data - pubmed. https://pubmed.ncbi.nlm.nih.gov/26426501/, October 2015. (Accessed on 08/17/2022). 1

[JR20] JAZIAR RADIANTI TIM A.MAJCHRZAK J. F. I. W.: A systematic review of immersive virtual reality applications for higher education: Design elements, lessons learned, and research agenda - sciencedirect. https://www.sciencedirect.com/science/article/pii/S0360131519303276, April 2020. (Accessed on 09/08/2022). 2

[KCS10] KEW-CHEOL SHIM JONG-SEOK PARK H.-S. K. J.-H. K. Y.-C. P. . H.-I. R.: Application of virtual reality technology in biology education: Journal of biological education: Vol 37, no 2. https://www.tandfonline.com/doi/abs/10.1080/00219266.2003.9655854, December 2010. (Accessed on 09/08/2022). 2

[MBWW18] MOLLIE B. WOODWORTH K. M. G., WALSH C. A.: Building a lineage from single cells: genetic techniques for cell lineage tracking - pmc. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5459401/, April 2018. (Accessed on 08/17/2022). 1

[MJ20] MOHD JAVAID A. H.: Virtual reality applications toward medical field. https://www.sciencedirect.com/science/article/abs/pii/S2213398419304294, June 2020. (Accessed on 09/08/2022). 2

[OMS*22] OYSHI M. T., MALESKA V., SCHANZE J., BORMANN F., DACHSELT R., GUMHOLD S.: Floodvis: Visualization of climate ensemble flood projections in virtual reality. https://diglib.eg.org/handle/10.2312/envirvis20221053, June 2022. (Accessed on 09/08/2022). 2

[sgu21] SGUMHOLD/CGV: Github - sgumhold/cgv. https://github.com/sgumhold/cgv, June 2021. (Accessed on 08/17/2022). 2

[Sko18] SKOLNIK S. S. A.: Connecting the dots between data and reality: Using virtual reality to visualize flooding impacts - nasa/ads. https://ui.adsabs.harvard.edu/abs/2018AGUFMPA41B..12S/abstract, December 2018. (Accessed on 09/08/2022). 2

[Ver15] VERDONSCHOT P. F.: Nereididae - an overview | sciencedirect topics. https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/nereididae, 2015. (Accessed on 08/11/2022). 1