Style Transfer for 3D Cell Segmentation

Donghyun Kim[1], David Denberg[1], Lisa Brown[1], Hayden Nunley[1]

[1]Center for Computational Biology, Flatiron Institute – Simons Foundation, New York, NY 10010, USA.

FLATIRON INSTITUTE

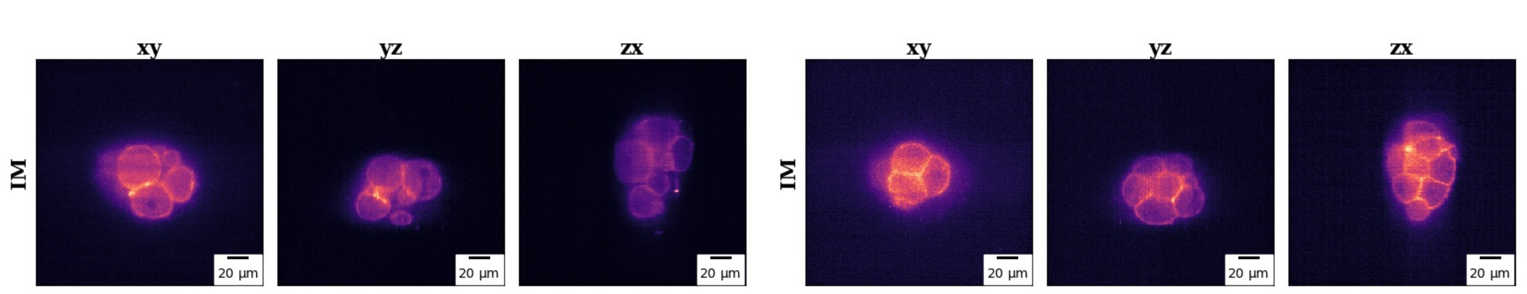
Introduction

Instance segmentation of 3D cell microscopy data is crucial for studying embryonic development. Various deep learning models have been developed for this task, such as Cellpose (Stringer et al. 2021) and EmbedSeg (Lalit et al. 2022).

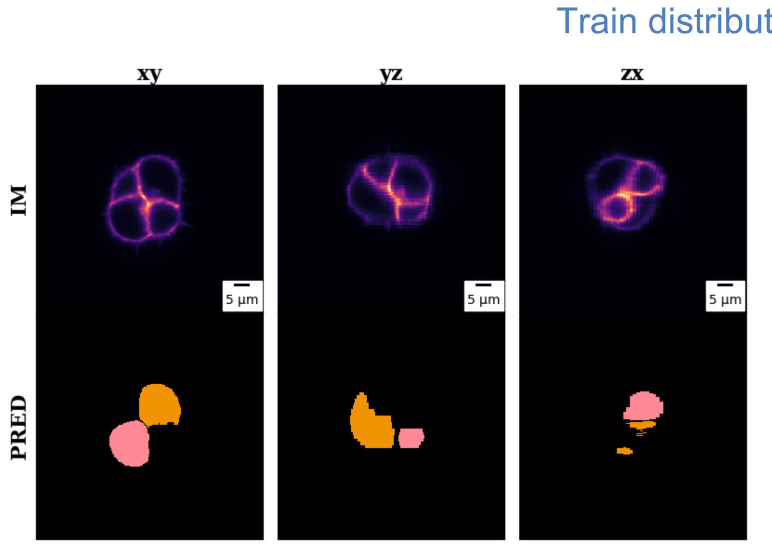
However, these models are only as good as the data they are trained on, and ground-truth annotations are difficult to obtain. Additionally, differences in experimental protocols cause images obtained in separate environments to exhibit varying data distributions. A model trained on these differing source distributions may encounter difficulties generalizing to target distributions.

We adapt style transfer methods to 3D cell microscopy data to help solve this domain adaptation problem. Style transfer fuses the content of one image with the style (e.g., colors, textures, and noise) of another.

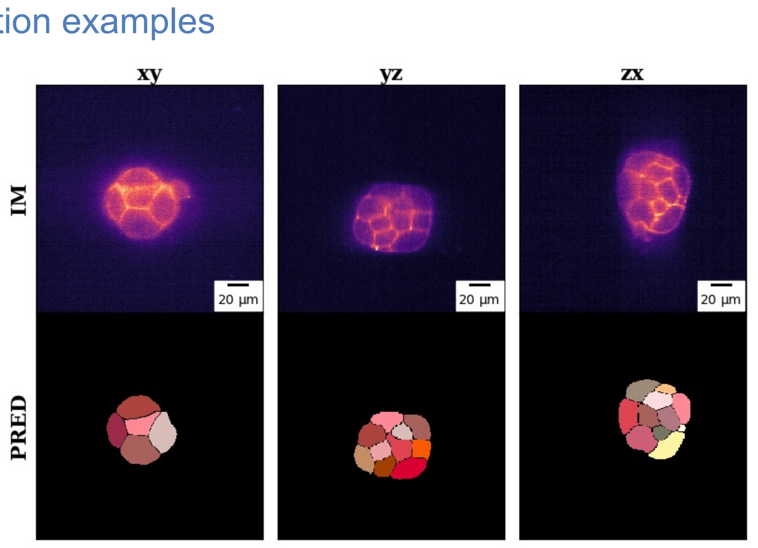
Problem Overview



Train distribution examples



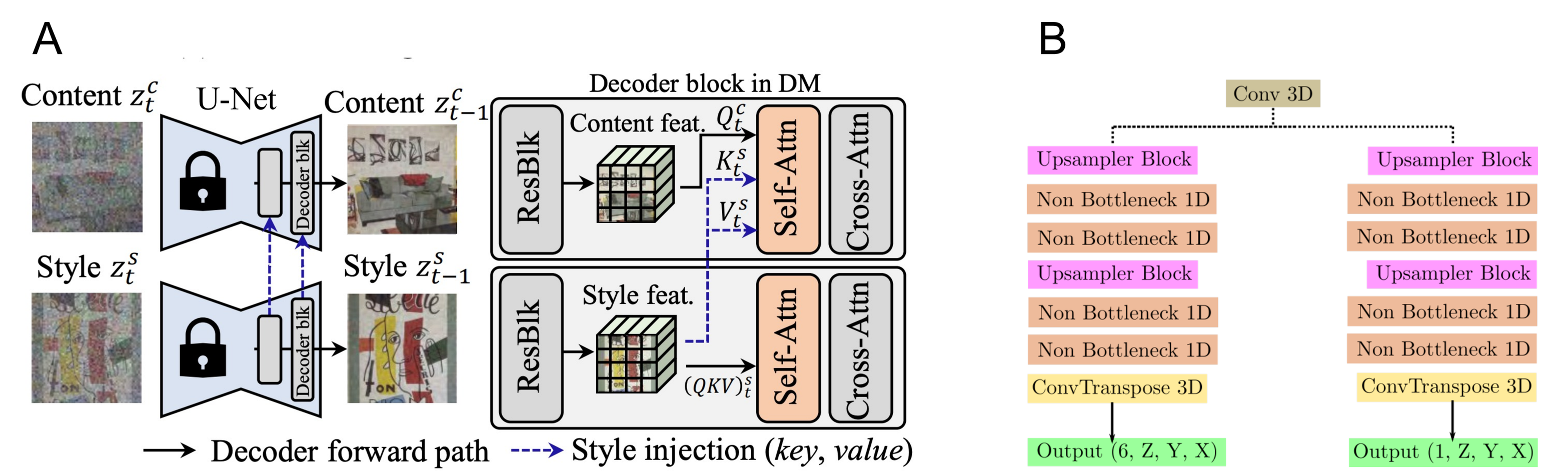
Predicted test annotations where train distribution ≠ test distribution

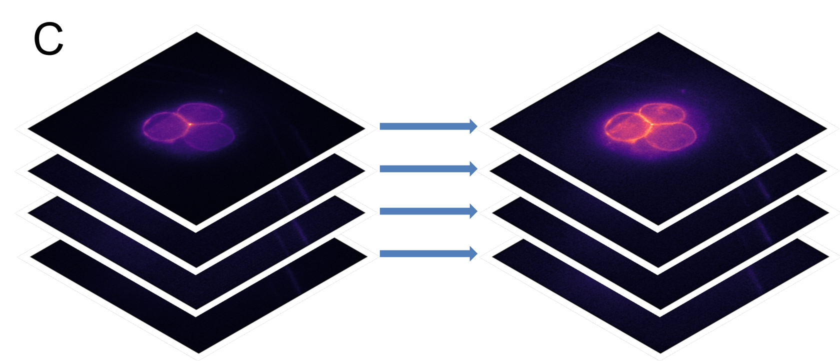


Predicted test annotations where train distribution = test distribution

Method

Inspired by CellStyle (Yilmaz et al. 2025), we adapt a style transfer method based on a large pre-trained latent diffusion model (Chung et al. 2024).





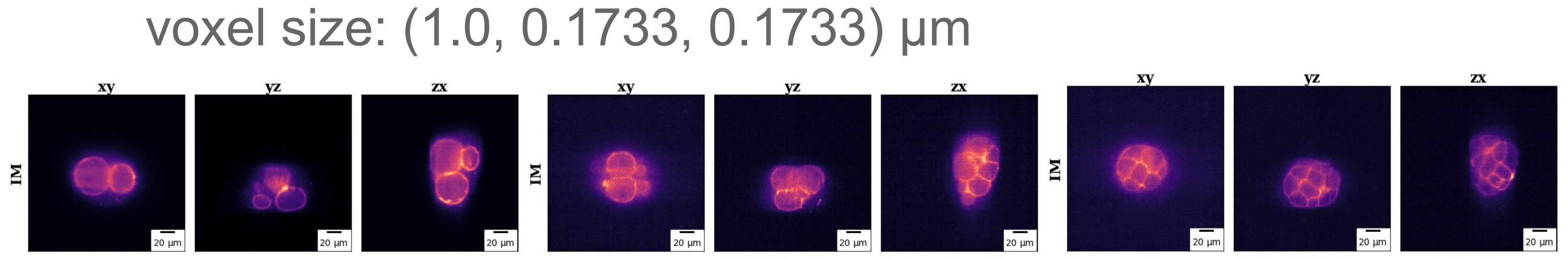
A. Style transfer method overview (Chung et al. 2024)
B. Encoder portion of network used in EmbedSeg (Lalit et al. 2022)
C. We transfer each slice of a 3D volume independently.

We use the EmbedSeg (Lalit et al. 2022) model for 3D Segmentation.
We style transfer both source and target data.

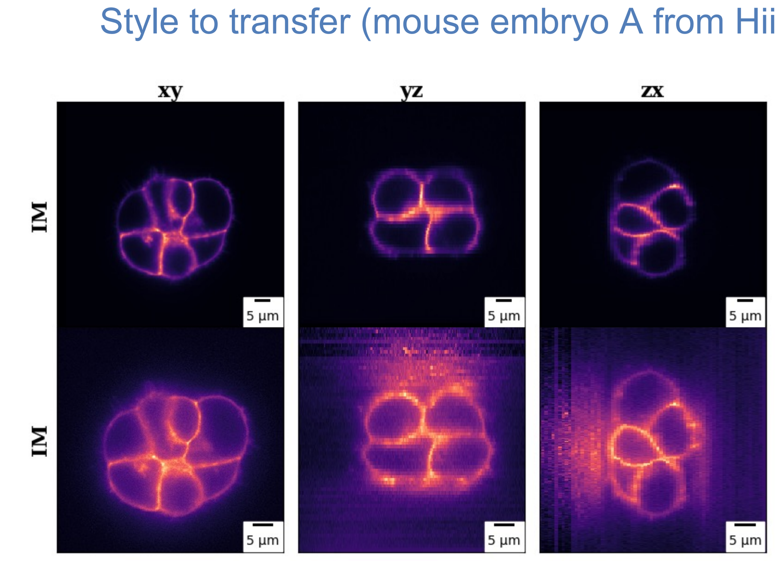
Experimental Outline

Source (Training) data: {Mouse embryo A, B from Hiiragi group}
88 volumes across developmental stage
voxel size: (1.295, 0.416, 0.416) μm

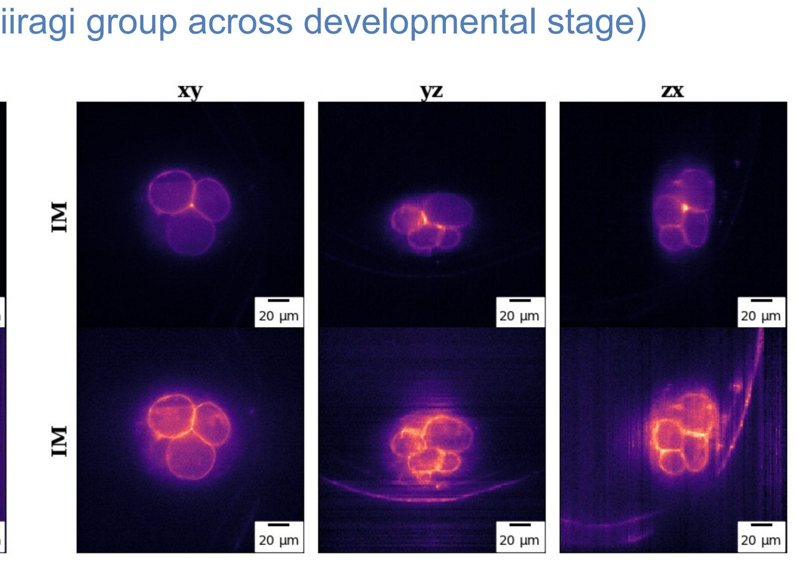
Target (Testing) data: {Mouse-Organoid-Cells-CBG};
84 volumes across developmental stage
voxel size: (1.0, 0.1733, 0.1733) μm



Style to transfer (mouse embryo A from Hiiragi group across developmental stage)



Original Mouse-Organoid-Cells-CBG (Top)
Style transferred Mouse-Organoid-Cells-CBG (Bottom)

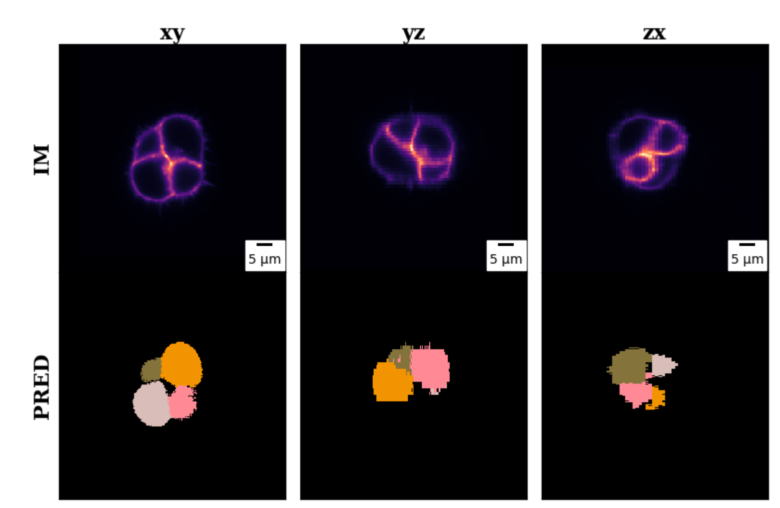


Original mouse embryo B from Hiiragi group (Top)
Style transferred mouse embryo B from Hiiragi group (Bottom)

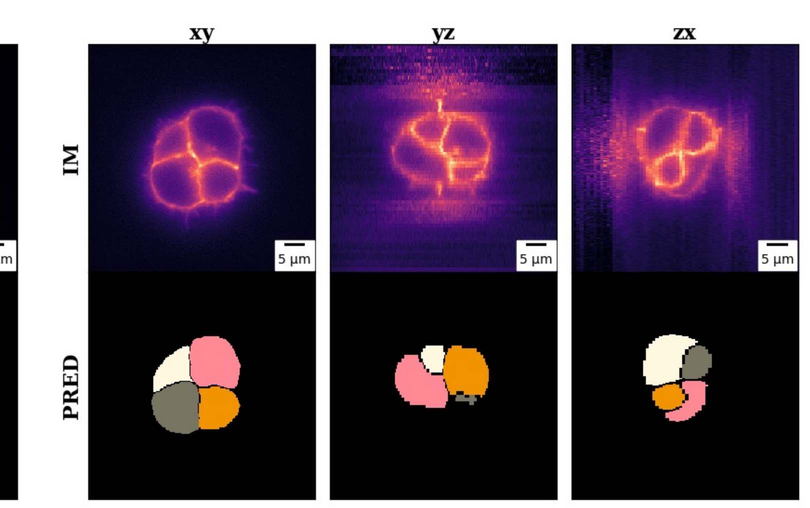
Results

Approach \ Dataset	Small target dataset	1 source dataset	2 source datasets	1 source dataset + fine tuned on small target dataset	2 source datasets + fine tuned on small target dataset
Non-Style Transfer	0.62983	0.65131	0.69955	0.77715	0.80361
Style Transfer	0.57766	**0.69545**	**0.72947**	0.78805	0.79788

Above values are IOU (Intersection over Union) averaged over the test set.



Predicted segmentations from model trained using 1 non-style transferred small target dataset



Predicted segmentations from model trained using 2 style transferred source datasets

Conclusion and Future Work

We find that 3D style transfer can improve cell segmentation accuracy, especially when ground truth annotations for target data are scarce or unavailable.

However, style transfer only improves segmentation when cells are visually similar. We also find that style transfer introduces noise for slices that do not contain any cells. This could be resolved by injecting different style features for different sections of a 3D volume.

Future work could include using style transfer to build large, pre-trained 3D segmentation models that can be immediately applied to newly imaged cells.

References and Acknowledgements

Chung, J., Hyun, S., & Heo, J. P. (2024). Style injection in diffusion: A training-free approach for adapting large-scale diffusion models for style transfer. *In Proceedings of the IEEE/CVF conference on computer vision and pattern recognition* (pp. 8795-8805).

Lalit, M., Tomancak, P., & Jug, F. (2022). Embedseg: Embedding-based instance segmentation for biomedical microscopy data. *Medical image analysis, 81*, 102523.

Stringer, C., Wang, T., Michaelos, M., & Pachitariu, M. (2021). Cellpose: a generalist algorithm for cellular segmentation. *Nature methods, 18*(1), 100-106.

Yilmaz, R., Chen, Z., Wu, Y., & Stegmaier, J. (2025). CellStyle: Improved Zero-Shot Cell Segmentation via Style Transfer. *arXiv preprint arXiv:2503.08603*.

Code repository: https://github.com/donghyunkm/3DCellSegDA

We thank the Hiiragi Grouip for providing mouse embryo data and annotations. We also thank Alf Honigmann and Anna Goncharova for the Mouse-Organoid-Cells-CBG data and annotations.