Image Translation

Shalin Mehta
Computational Microscopy Platform

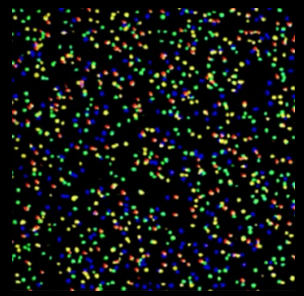
CHAN ZUCKERBERG
Biohub San Francisco

@mattersOfLight

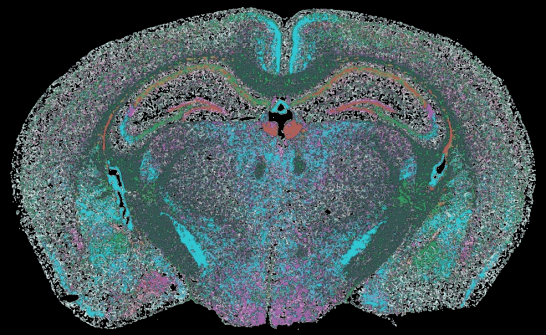
www.czbiohub.org/comp-micro/

DL@MBL
Aug 25, 2025

Imaging: foundational modality for biology



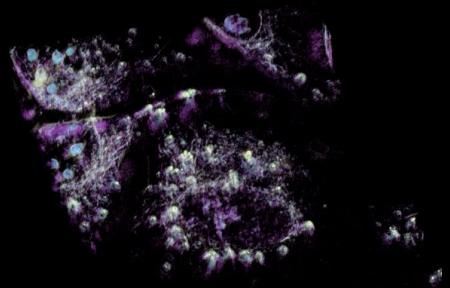
genome



transcriptome

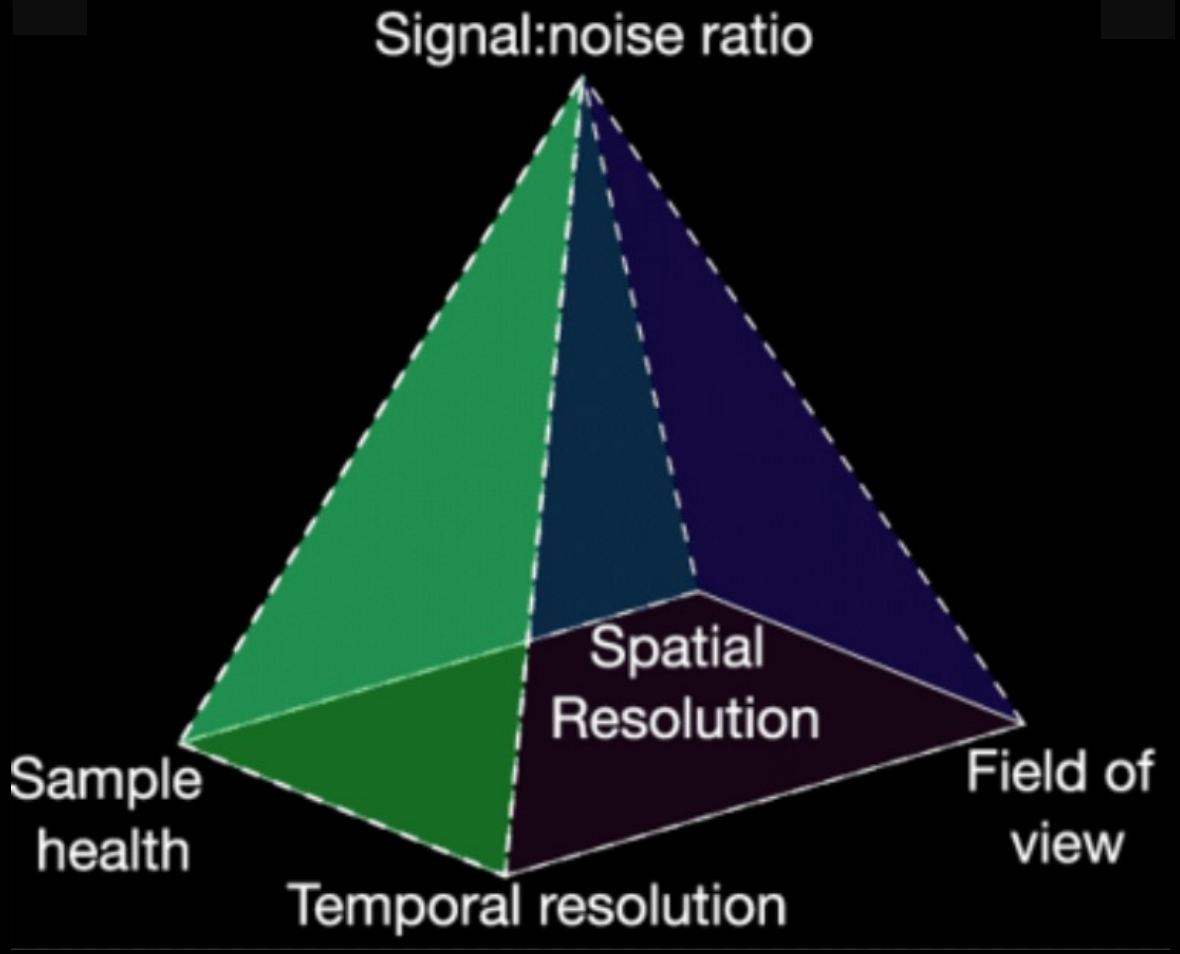
proteome

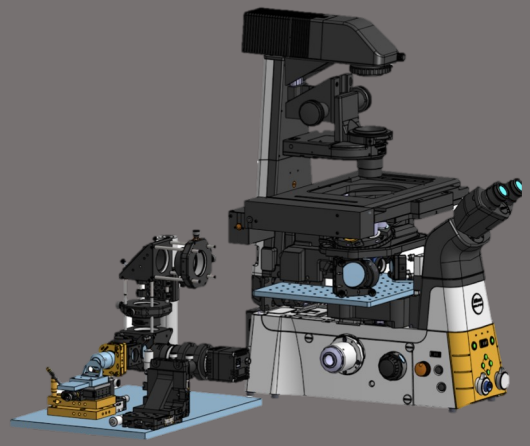
structure



function

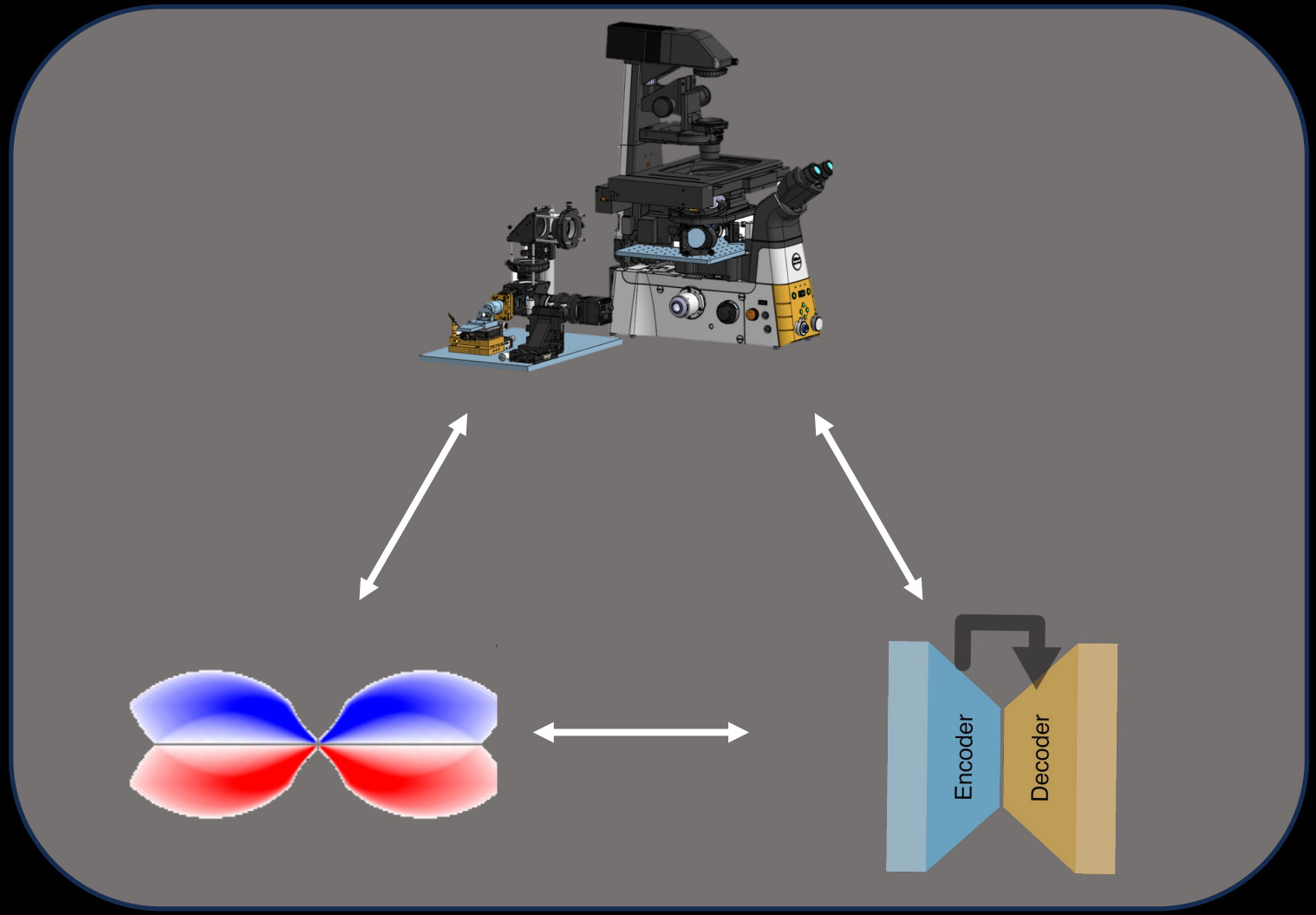
Multiplexing is hard just with optics!



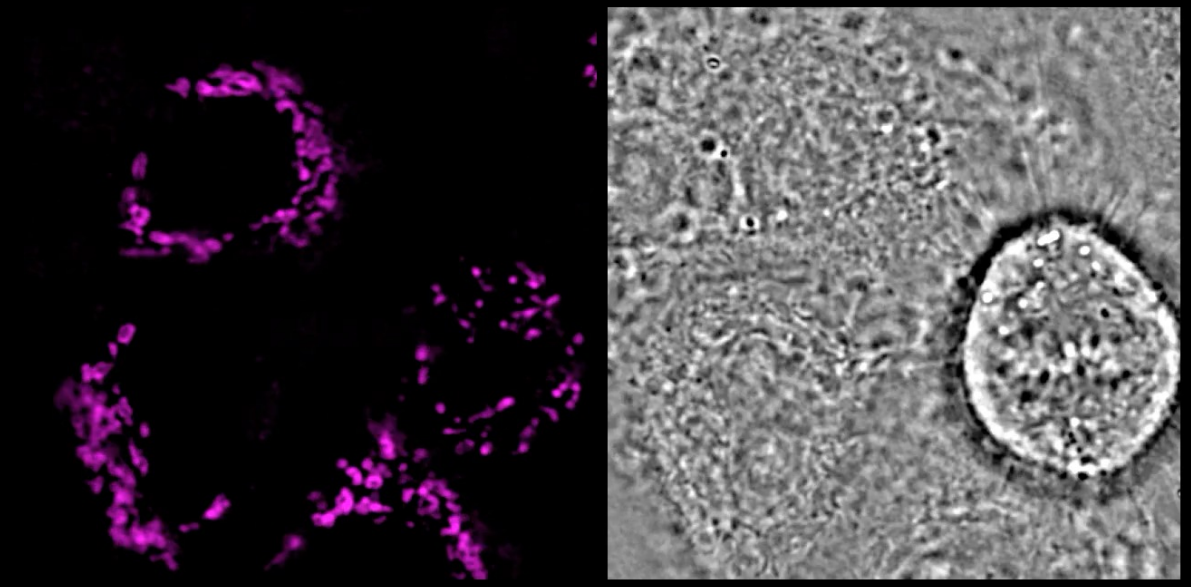


per Channel
per Perturbation

Computational microscopy relaxes constraints



correlative live imaging



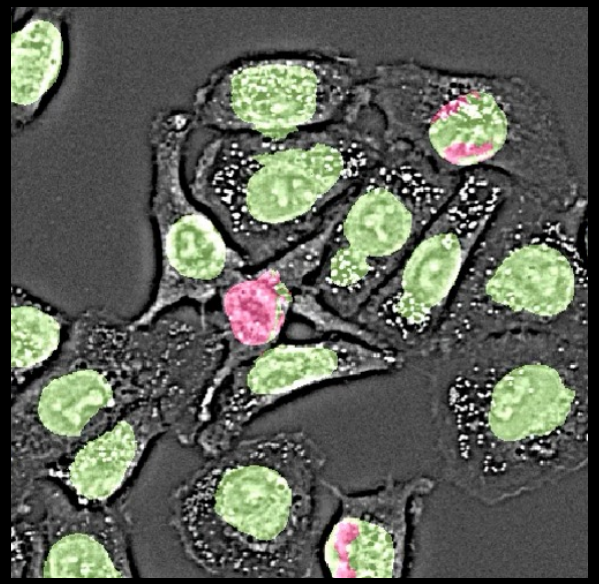
Guo et al., eLife 2020
Ivanov et al., Biomed. Opt. Exp., 2022
Yeh et al. Nature Methods, 2024
Ivanov et al., PNAS Nexus, 2024

mehta-lab / **recOrder**

mehta-lab / **waveorder**

czbiohub-sf / **shrimPy**

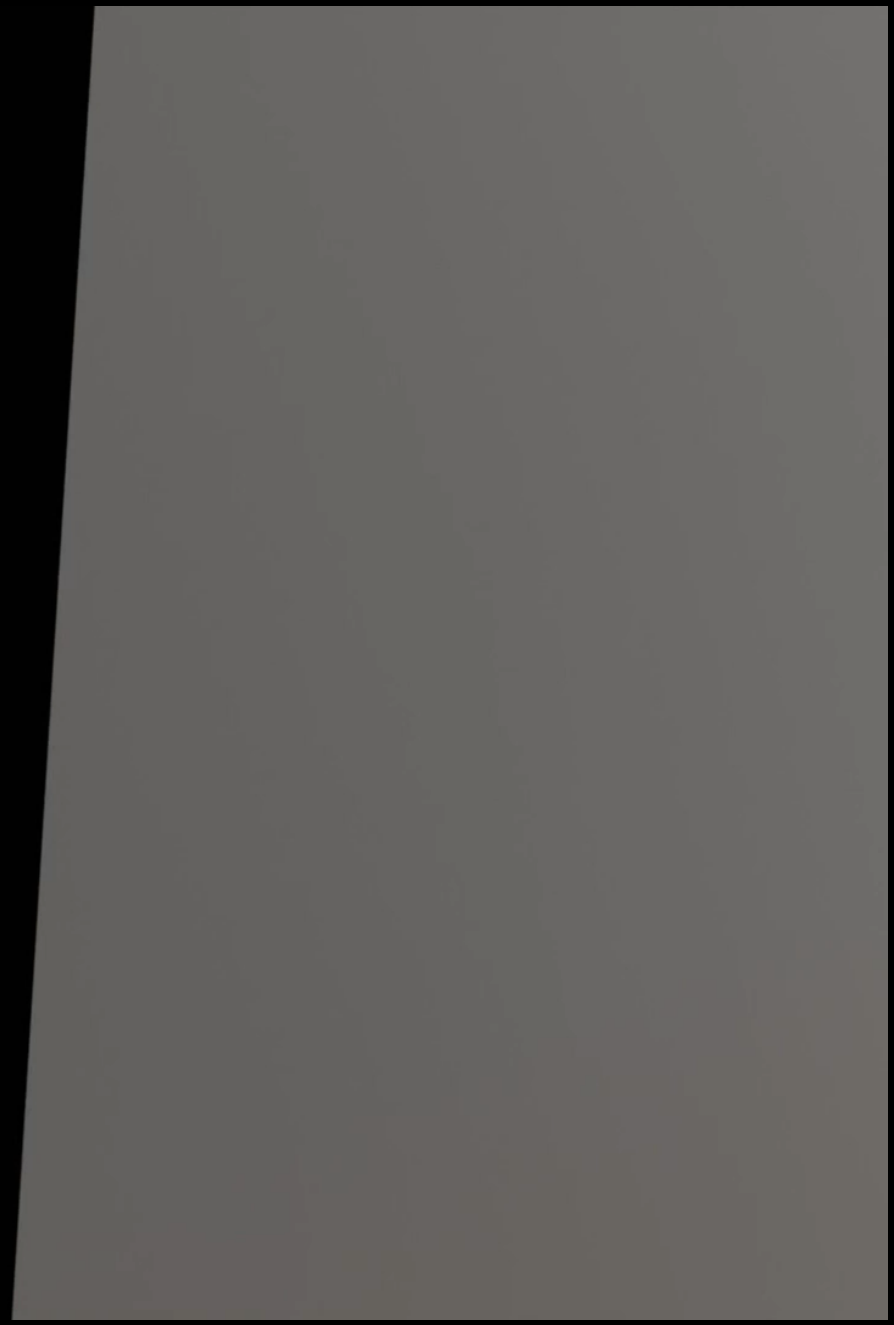
learning cell dynamics



Guo et al., eLife 2020
Wu et al., Mol. Biol. Cell, 2022
Ivanov et al., PNAS Nexus, 2024
Liu et al., bioRxiv 2024

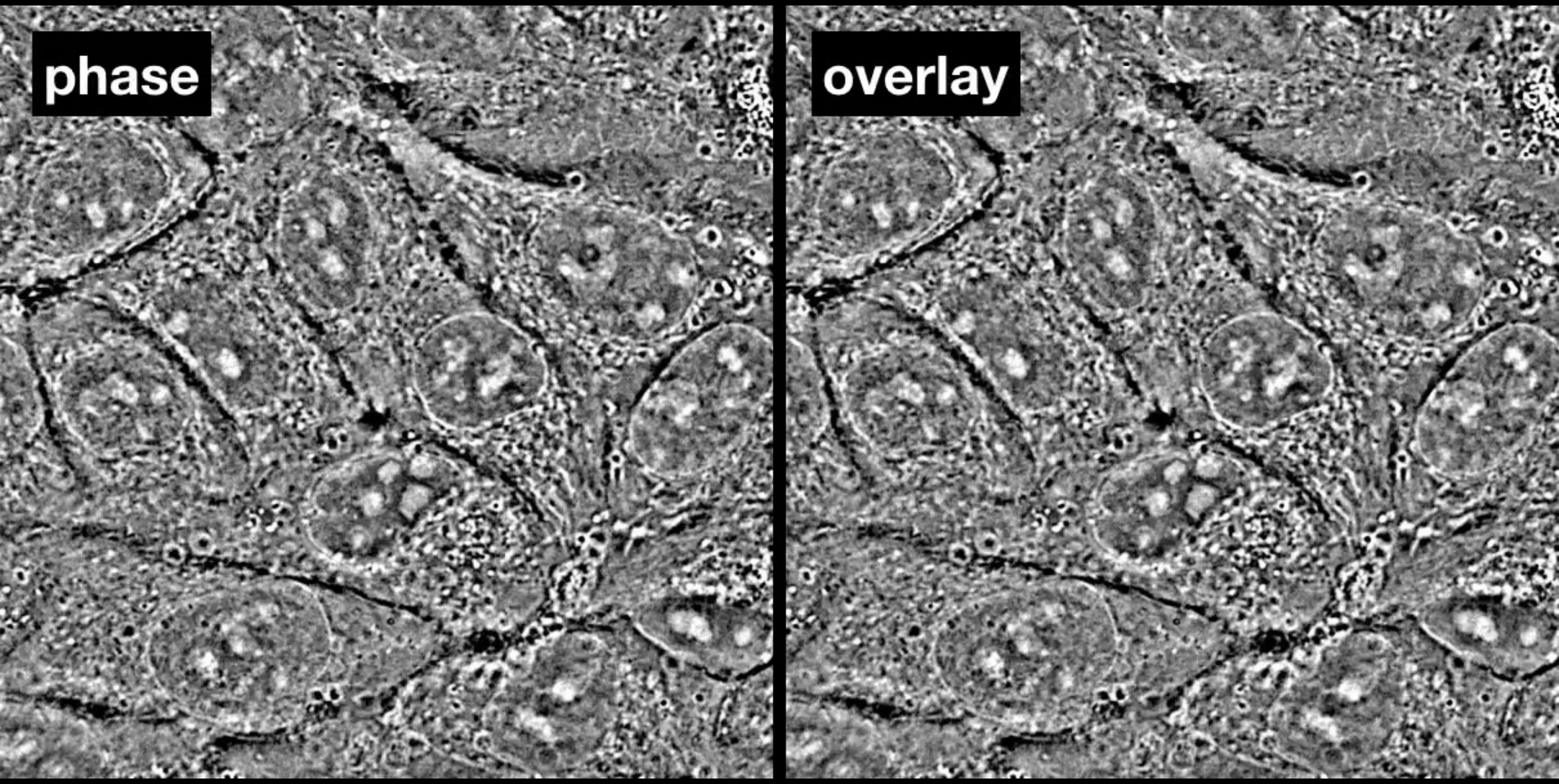
mehta-lab / **VisCy**

czbiohub-sf / **iohub**



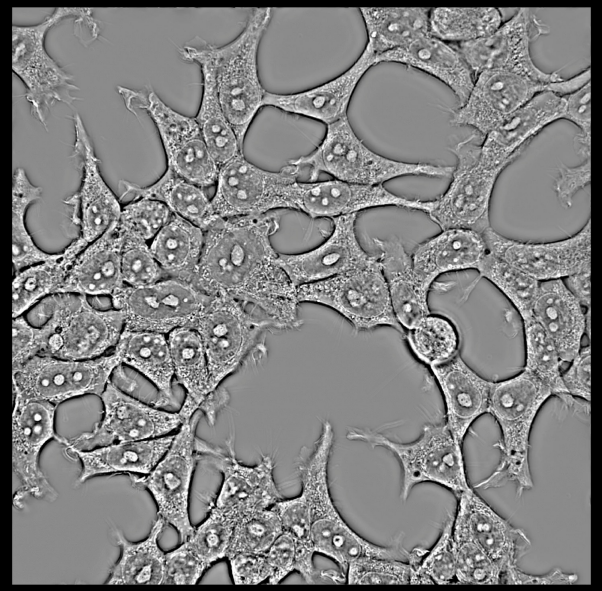
Guo et al., eLife 2020

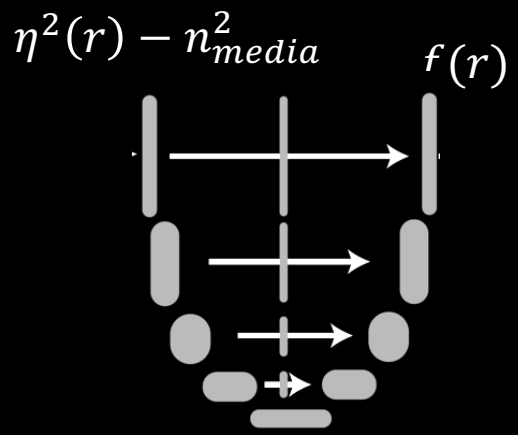
Ivanov et al. PNAS Nexus 2024


phase
overlay

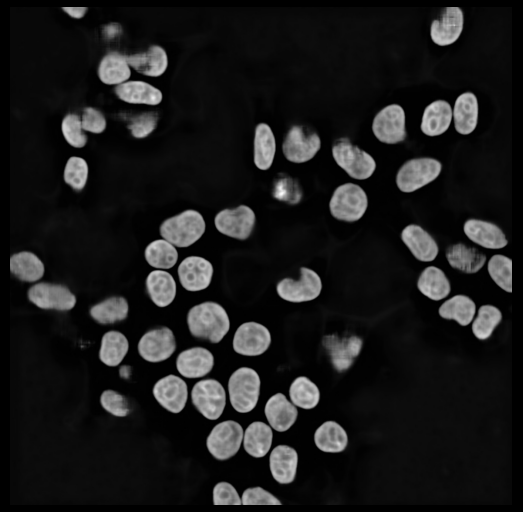
Robust virtual staining of landmarks

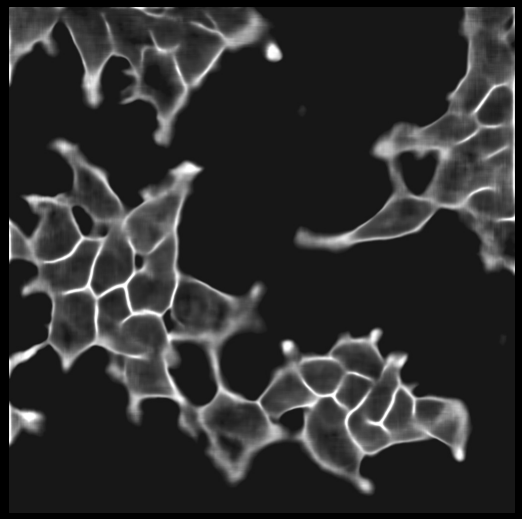
local permittivity





fluorophore density






Ziwen Liu


Eduardo Hirata-Miyasaki


Soorya Pradeep


Ivan Ivanov


Talon Chandler


Christian Foley


Johanna Rahm


Chad Liu

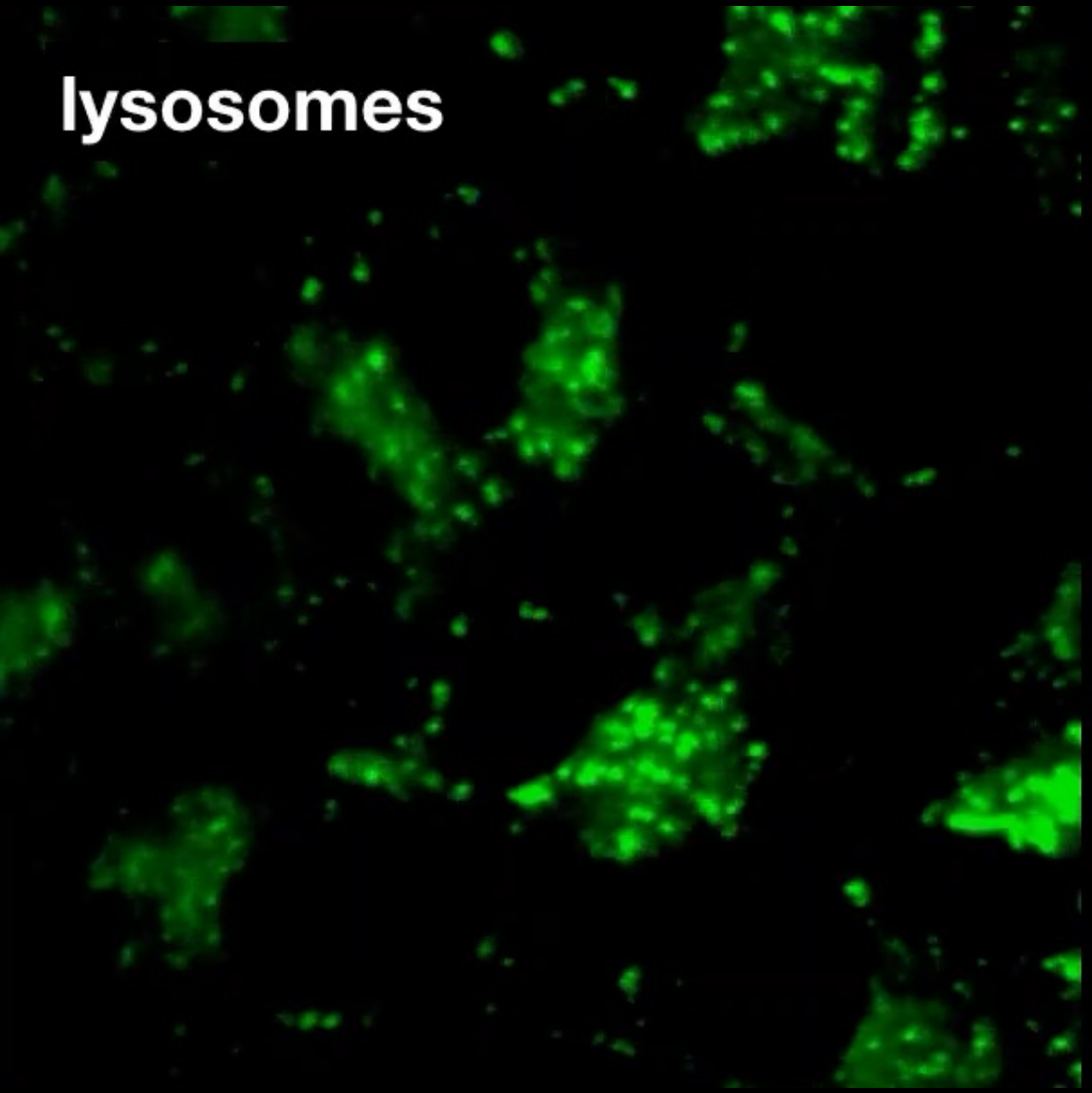

Manu Leonetti

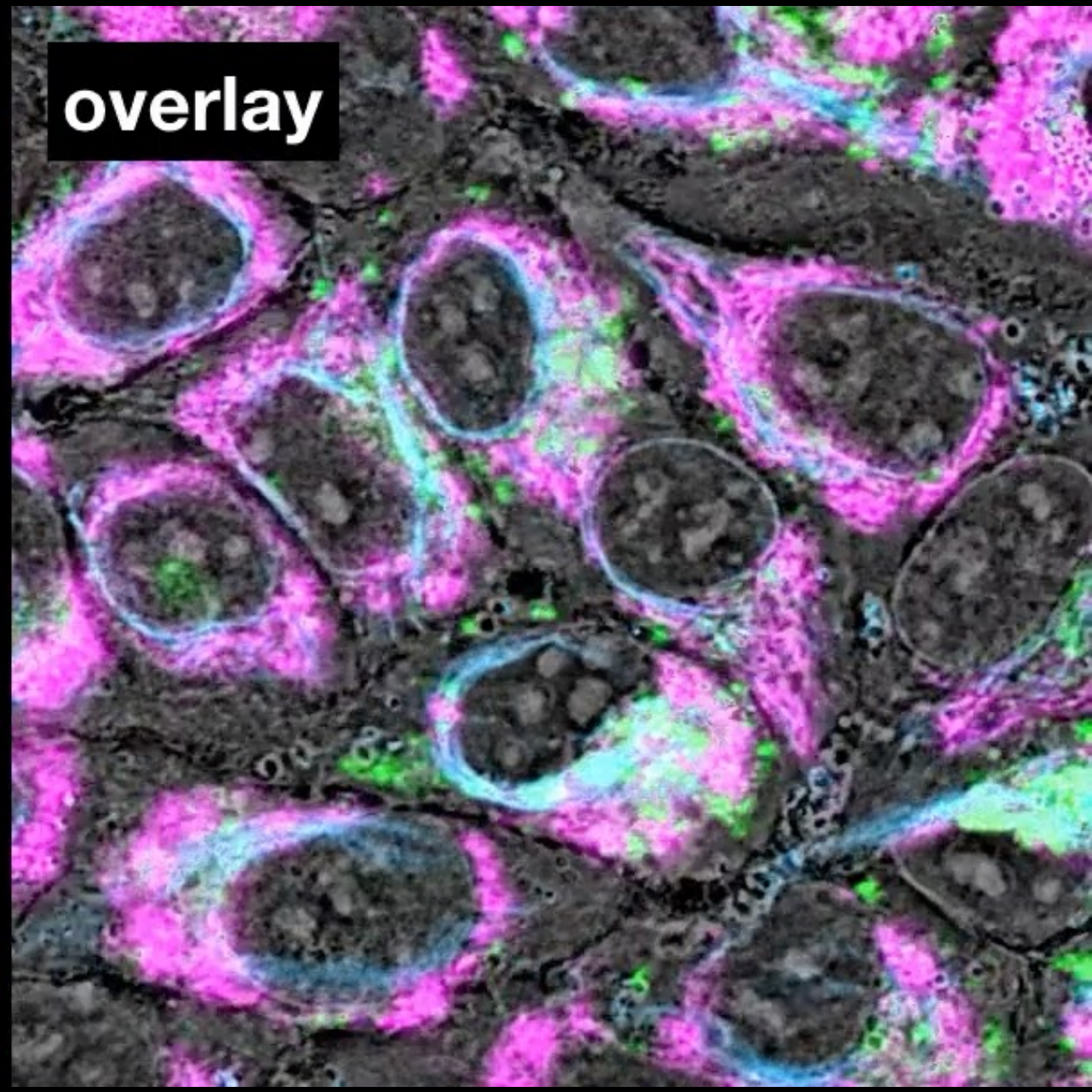

Hunter Woosley


Carolina Arias

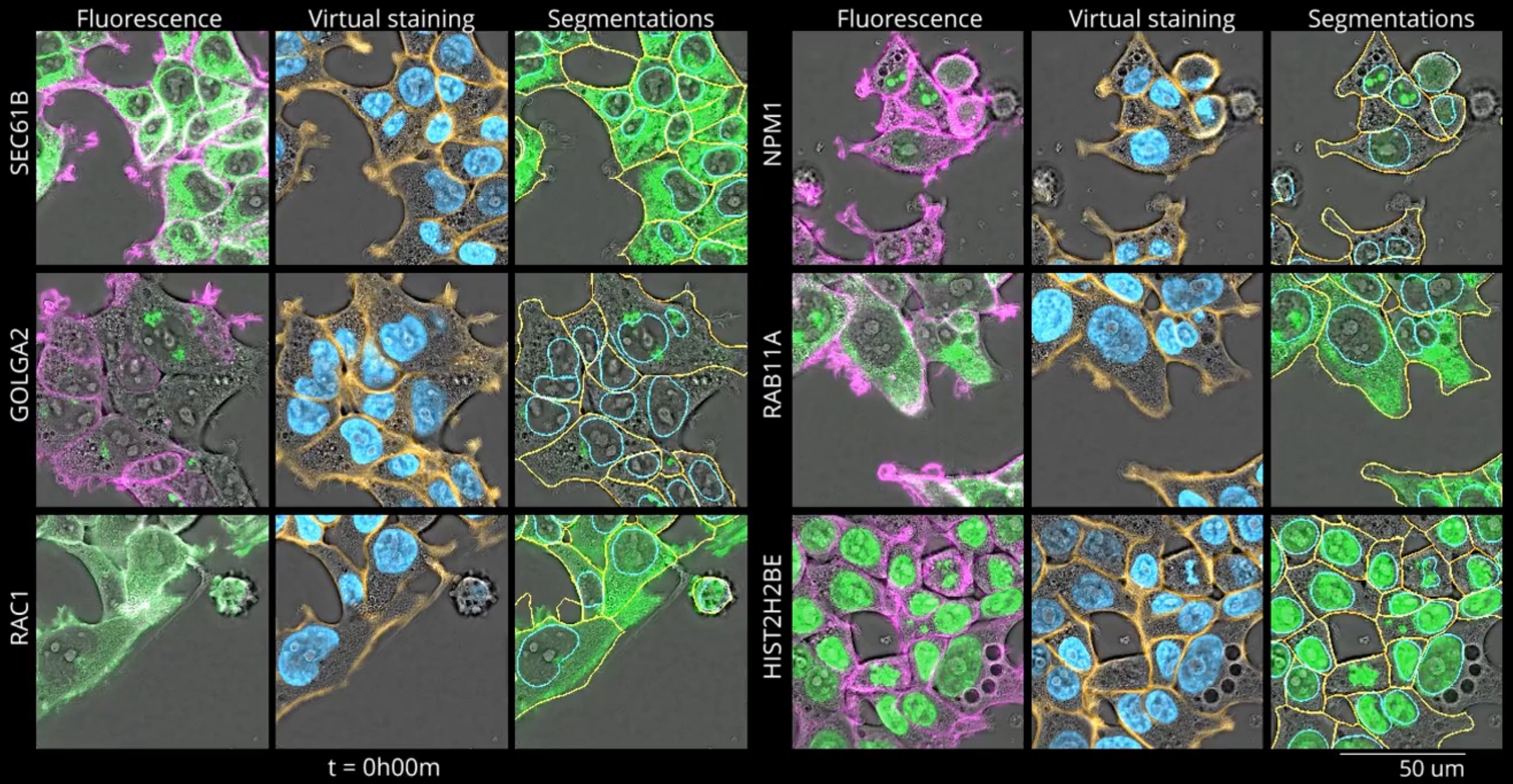

Ranen Aviner

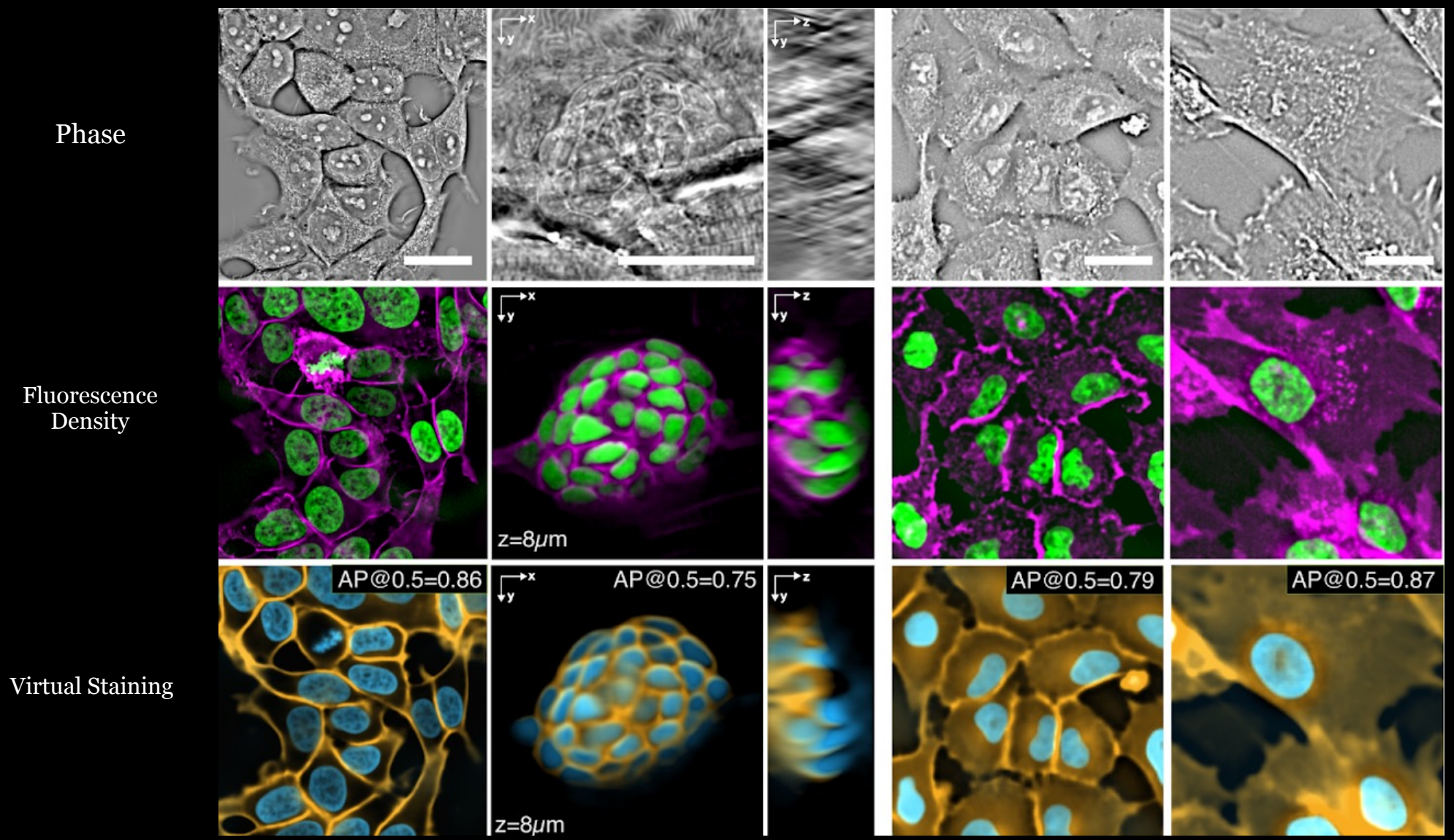

Adrian Jacobo



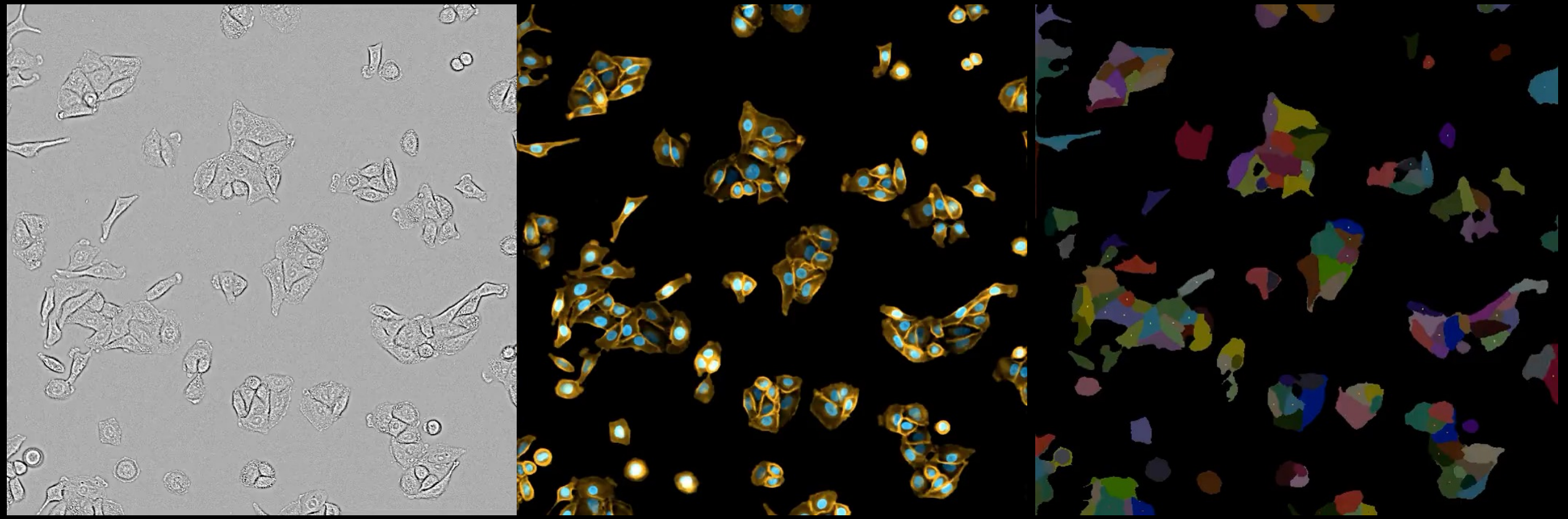


Ivanov et al. PNAS Nexus 2024


Fluorescence
Virtual staining
Segmentations
Fluorescence
Virtual staining
Segmentations
SEC61B
NPM1
GOLGA2
RAB11A
RAC1
HIST2H2BE
t = 0h00m
50 um



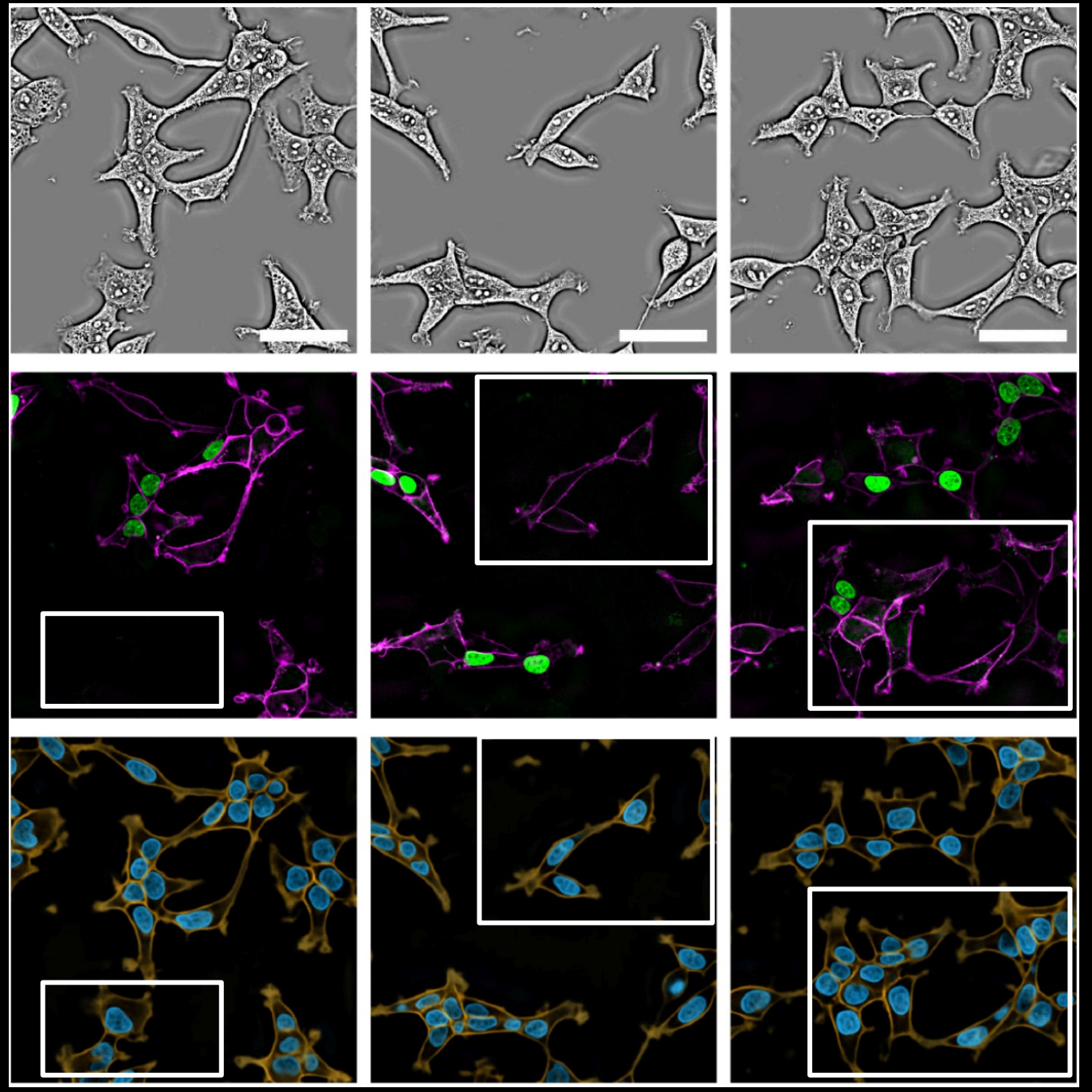
...across cell types



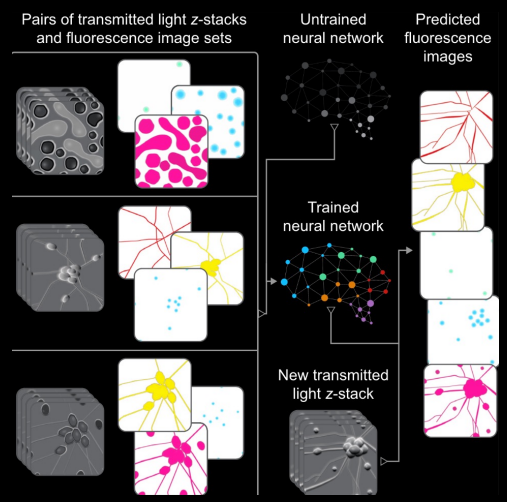
...across cell states

Bragantini et al., bioRxiv, 2024

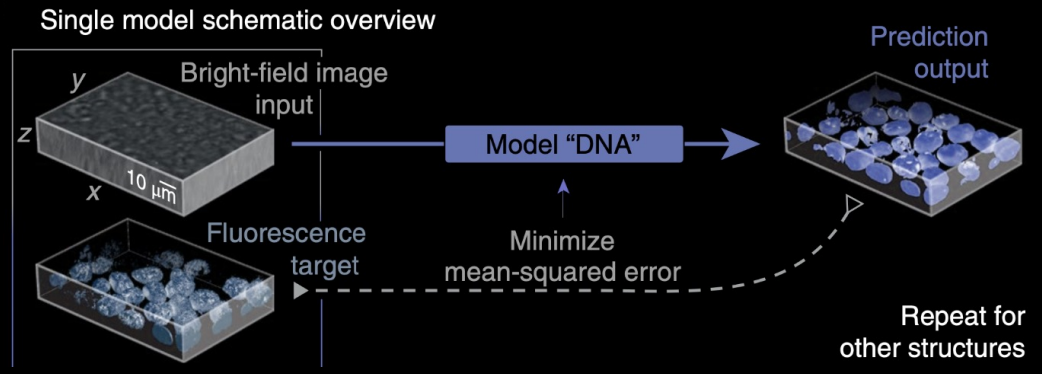
More robust than experimental stain



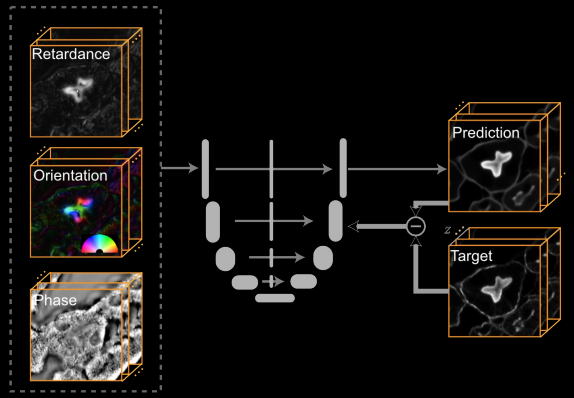
Liu et al., bioRxiv, 2024



2D In silico labeling (Inception)
(Christiansen et al., Cell 2018)

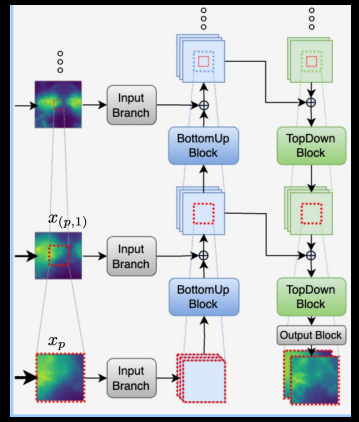


3D Label-free determination (3D U-Net)
(Ounkomol et al., Nature Methods, 2018)



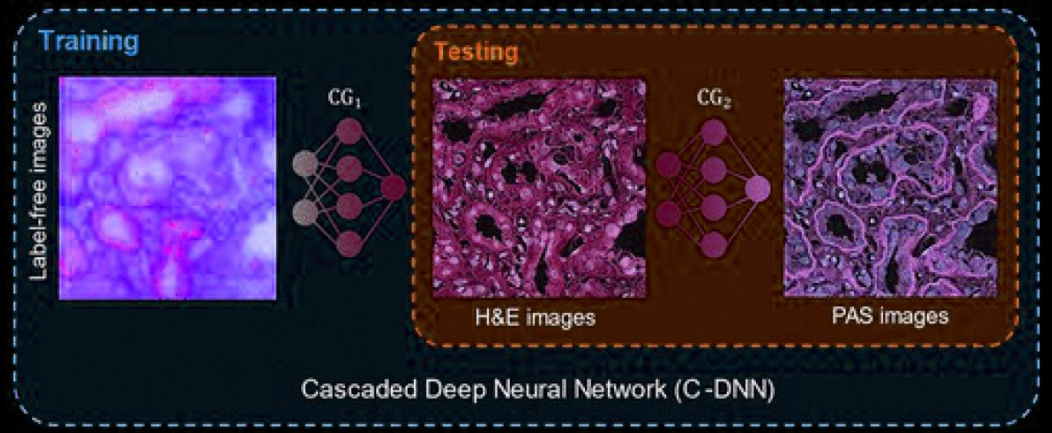
3D image translation (2.5D U-Net)
(Guo et al., eLife, 2020;
Liu et al., bioRxiv, 2024)

2D Pix2Pix (conditional GAN)
(Zhu et al., ICCV 2017; Isola et al., CVPR 2017; Tonks arXiv 2024)

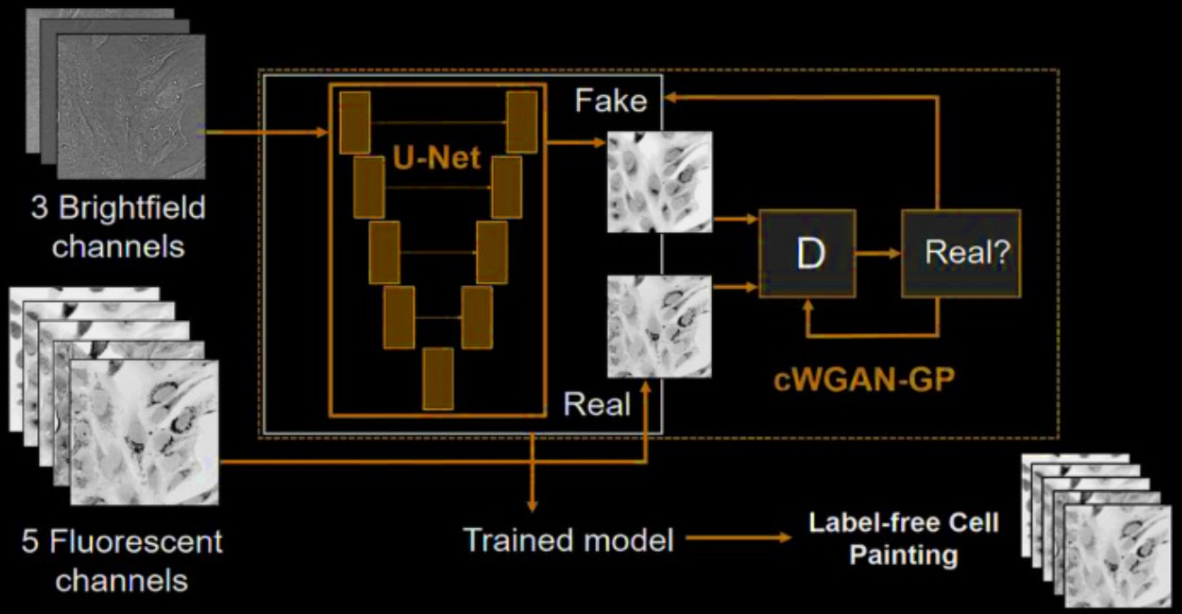


2D image splitting (HVAE)
Ashesh ICCV 2023

virtual histology & live cell painting

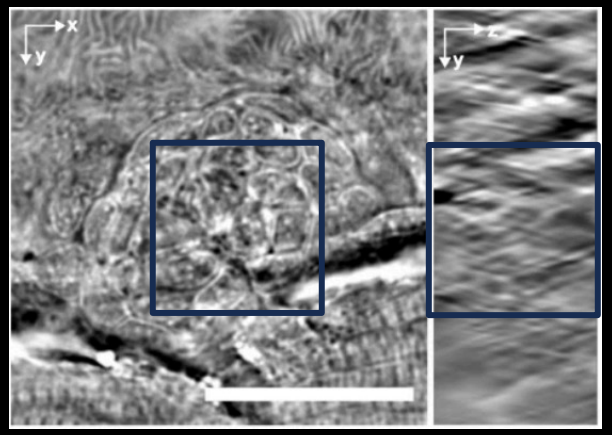


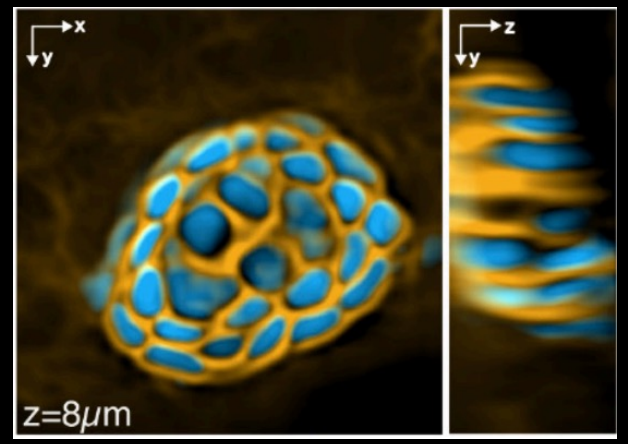
Yang…Ozcan ACS Photonics, 2022

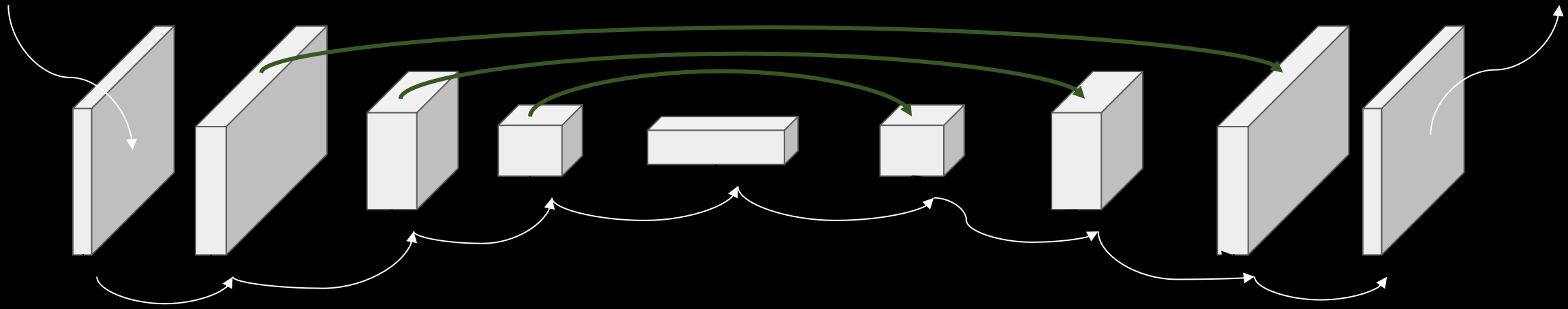


Oscar…Wang (AstraZeneca R&D), Scientific Reports, 2022

3D U-Net







3D input

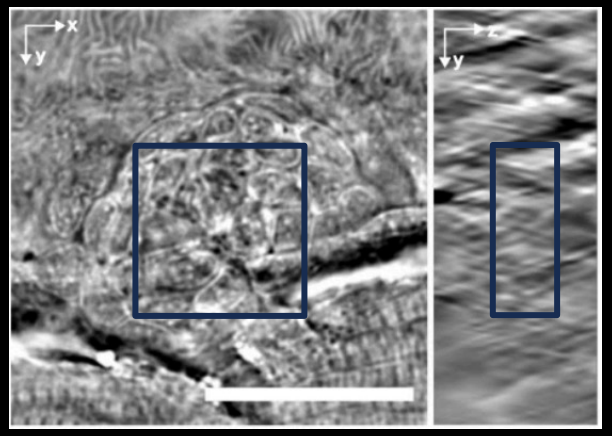
3D channels

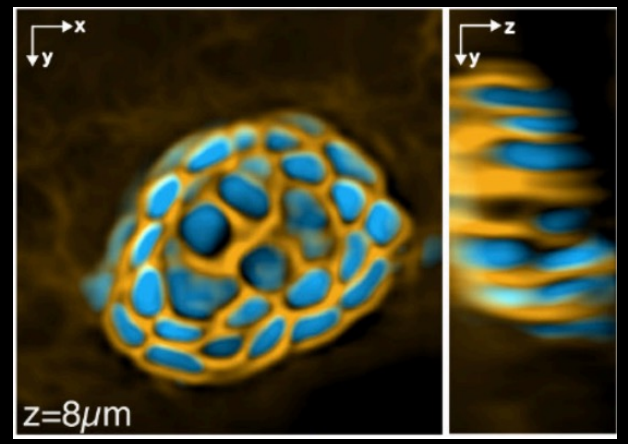
3D channels

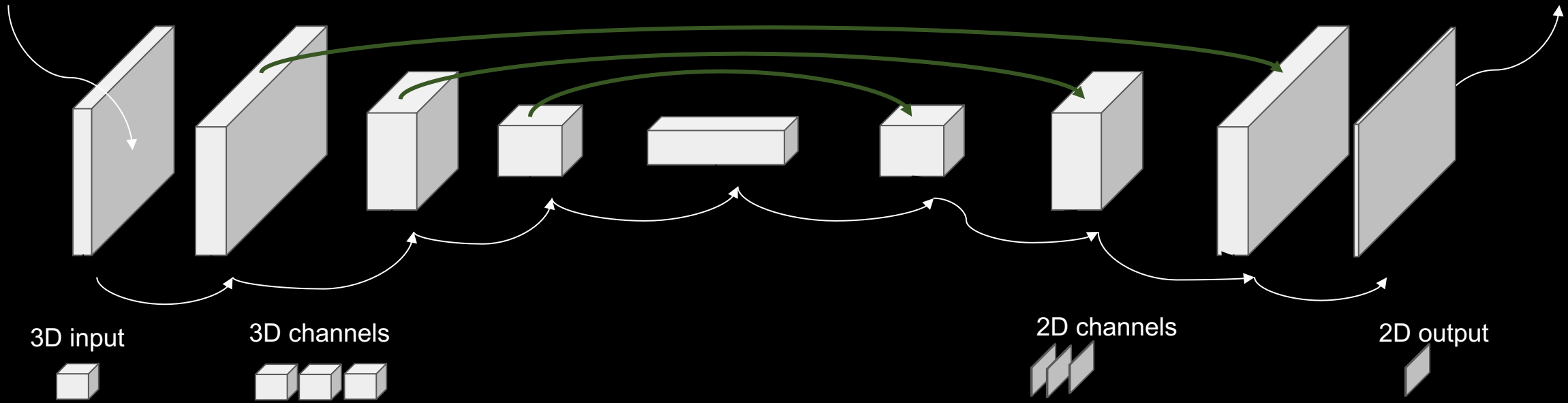
3D output

LOT to fit on the GPU

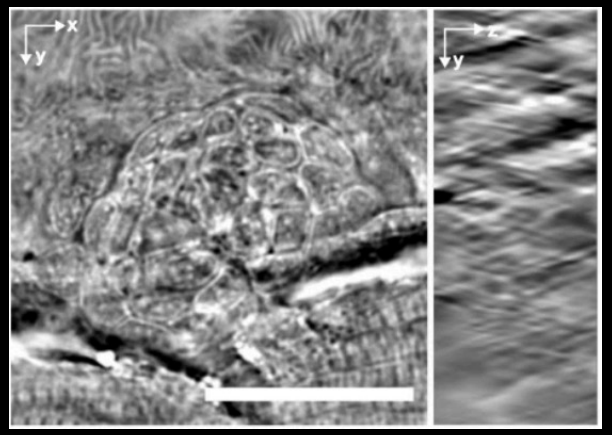
2.5D U-Net

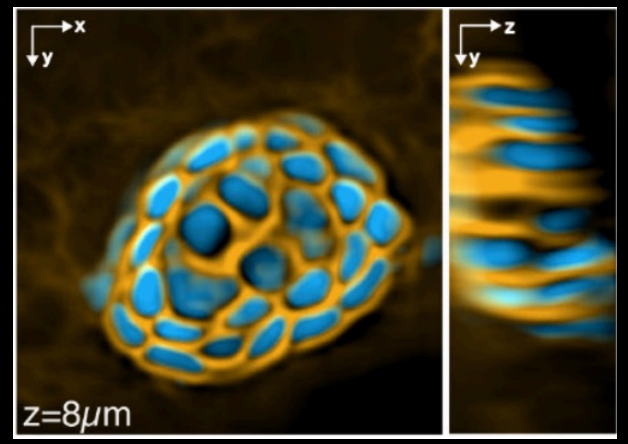






UNeXt





Z→C

C→Z

2D or 3D input

2D channels

2D channels

2D or 3D output

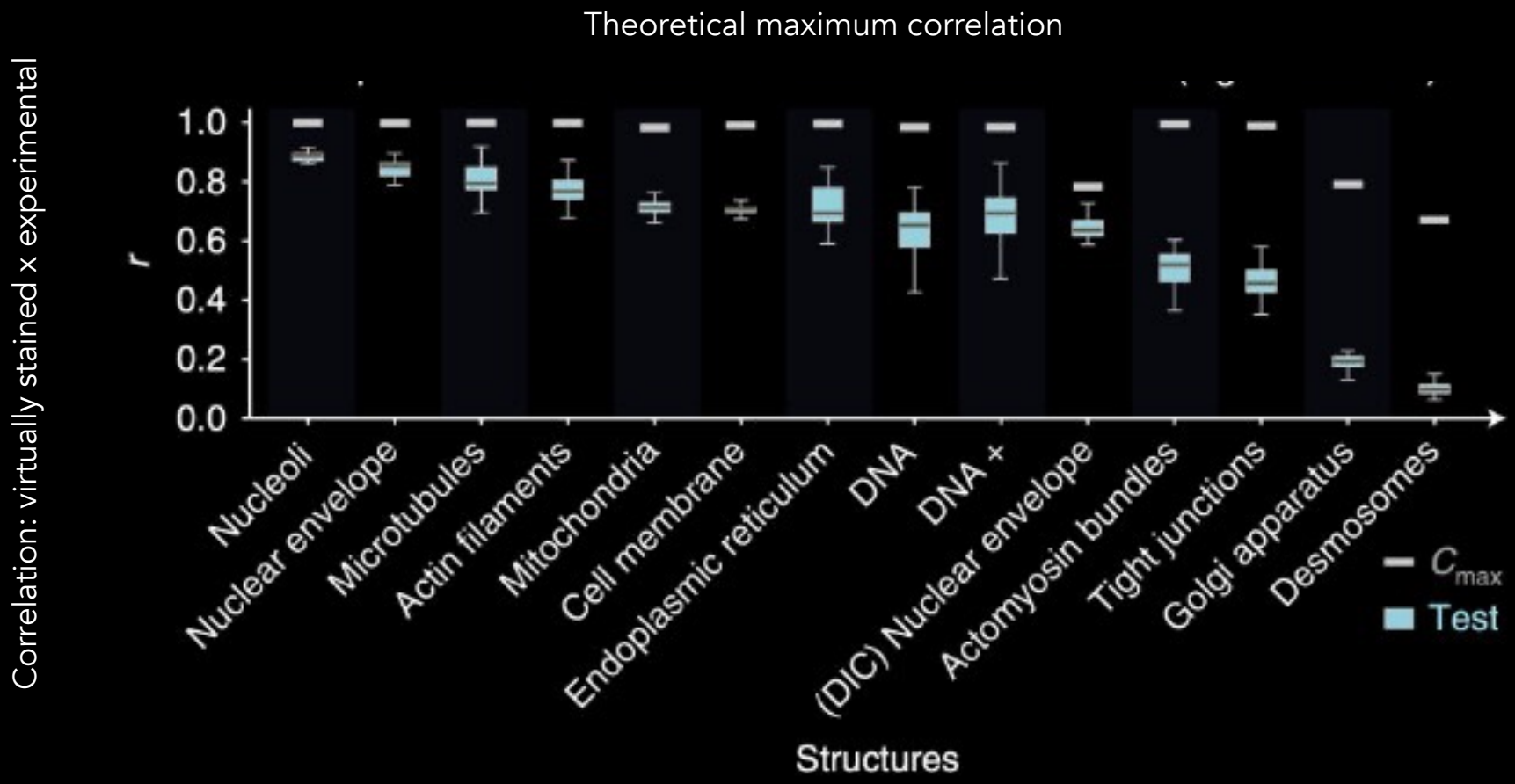
Table 1

In silico labeling in selected publications.

Reference	Paper title	Label-free modality	#Dimensions	Cell types	Subcellular structures	Term used	Deep learning network architecture	Evaluation metrics
Ounkomol et al., 2018 [11]	Label-free prediction of three-dimensional fluorescence images from transmitted light microscopy	bright-field, DIC	3	HEK-293, HT-1080, hiPSC	(+) microtubules, nuclear envelope, nucleoli (~) DNA, ER, cell membrane, actin filaments, mitochondria (–) desmosomes, actomyosin bundles, Golgi apparatus, tight junctions	label-free prediction	U-Net	PCC
Christiansen et al., 2018 [12]	In silico labeling: Predicting fluorescent labels in unlabeled images	bright-field, phase contrast, DIC	3	human motor neurons from iPSCs, primary rat cortical cultures, human breast cancer line	nuclei + neurons/ dendrites/dead cells/ membrane/axons	In silico labeling	multiscale sub-networks (towers) and one or more pixel-distribution-valued predictors (heads)	PCC, ▲ (see legend)
LaChance and Cohen 2020 [13]	Practical fluorescence reconstruction microscopy for large samples and low-magnification imaging	phase contrast, DIC	2	MDCK, KC, HUVEC	(+) nuclei (~) actin, cell–cell junctions	FRM (Fluorescence reconstruction microscopy)	U-Net	PCC, P, ▲▲ (see legend)
Wang et al., 2021 [14]	Global voxel transformer networks for augmented microscopy	Same as Ounkomol et al., 2018				augmented microscopy	U-Net with attention	PCC
Cheng et al., 2021 [15]	Single-cell cytometry via multiplexed fluorescence prediction by label-free reflectance microscopy	multimodal reflectance microscope	2	HeLa	(+) DNA, actin, endosome (–) Golgi apparatus	digital labeling	U-Net	PCC
Jo et al., 2021 [16]	Label-free multiplexed microtomography of	QPI	3	NIH3T3, CRL-1658, COS-7, HEK 293, HeLa, astrocytes	(+) actin, mitochondria, lipid droplets, plasma	in silico labeling	NAS, U-Net	PSNR, PCC, SSIM

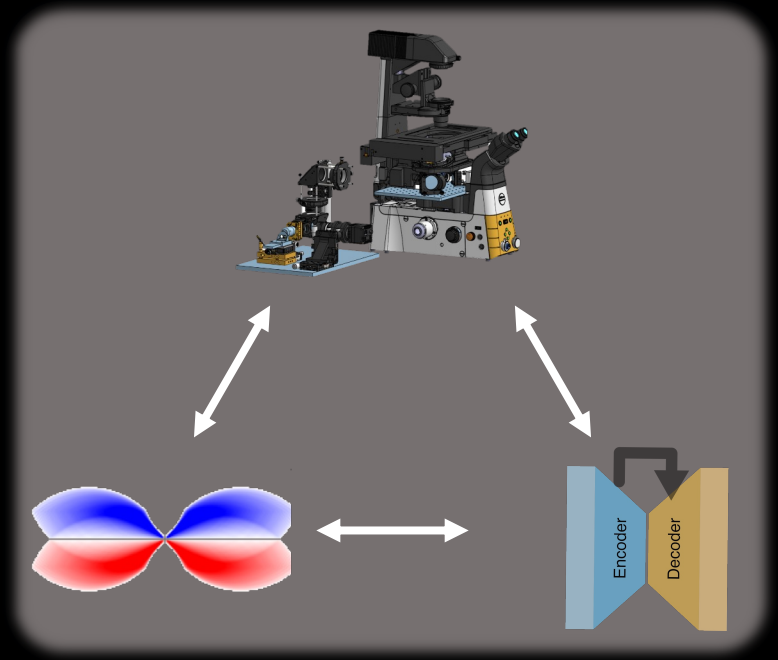
Elmaman, Ben Nevada, Zaritsky, Current Opinion in Cell Bio 2024

consistency of label-free encoding



Ounkomol et al., Nature Methods, 2018

Neural networks often don’t generalize across imaging systems or cell types …



Physics-based inverse algorithms:

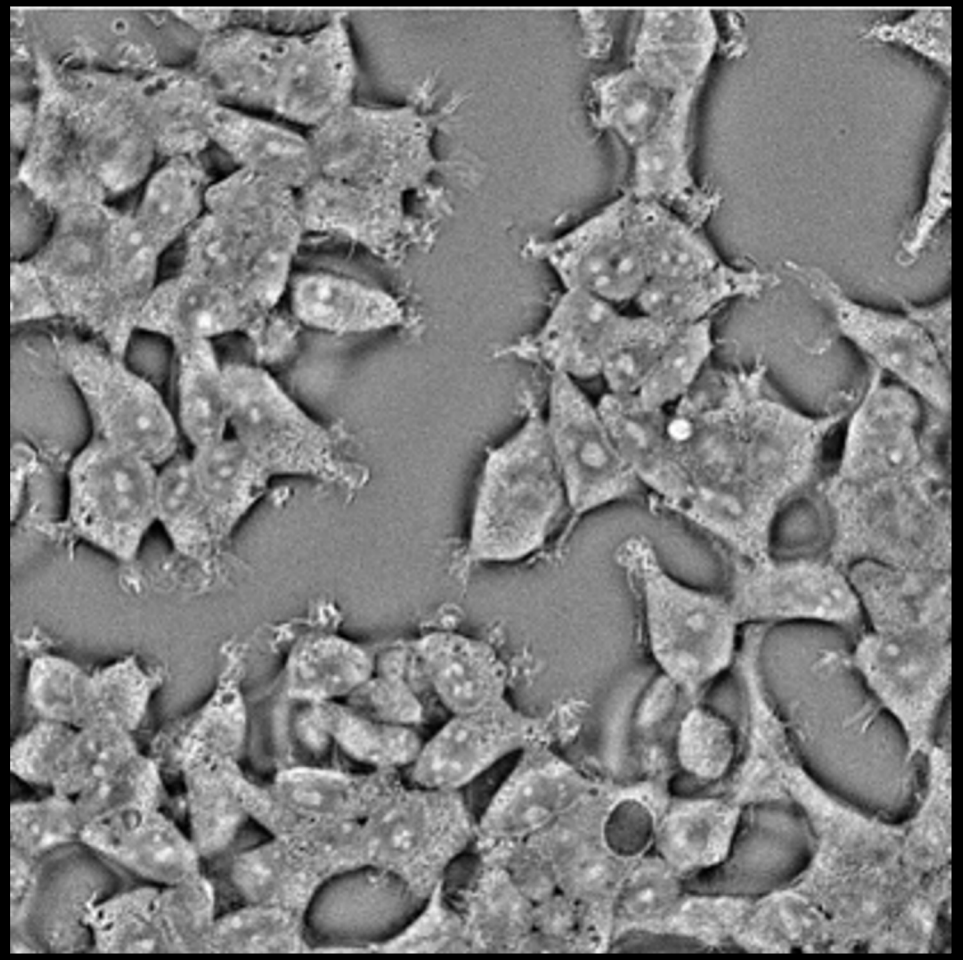
- Cells and tissues that scatter once
- Diverse imaging configuration

Learned models:

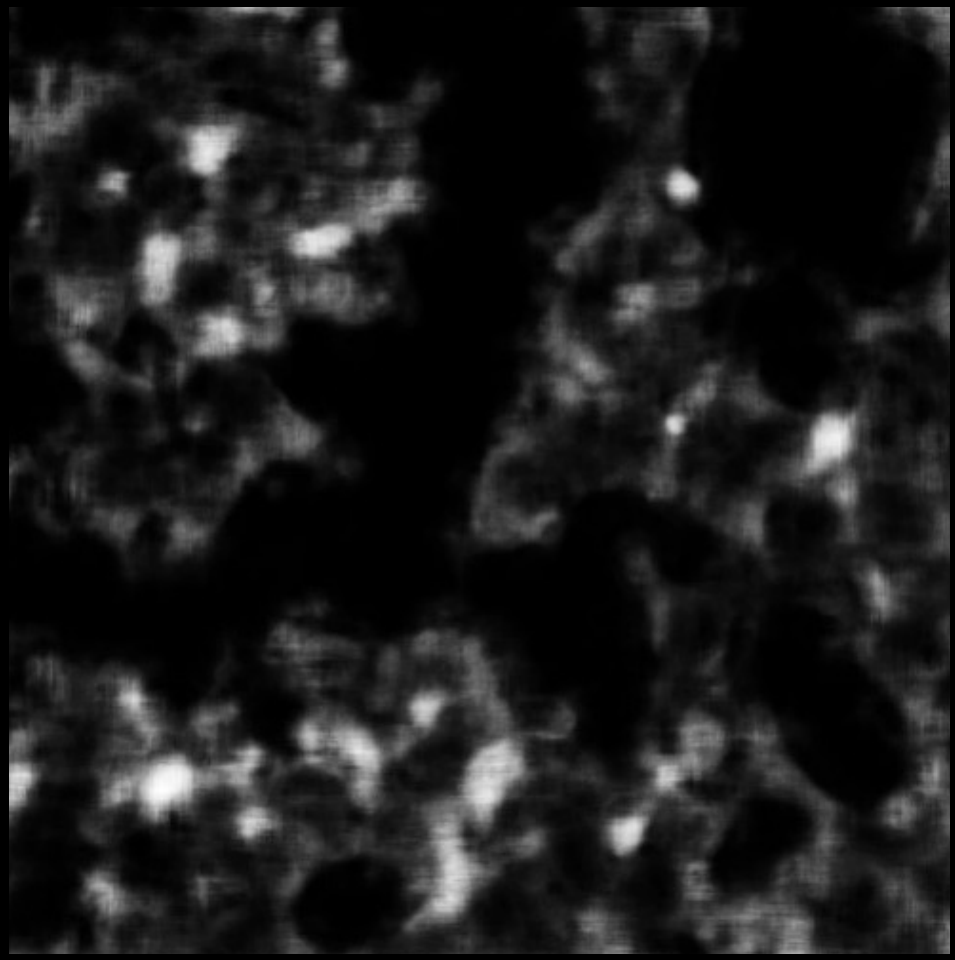
- Cells and tissues *in distro*
- Specific imaging configurations

Generalization across imaging conditions

Different noise than training data

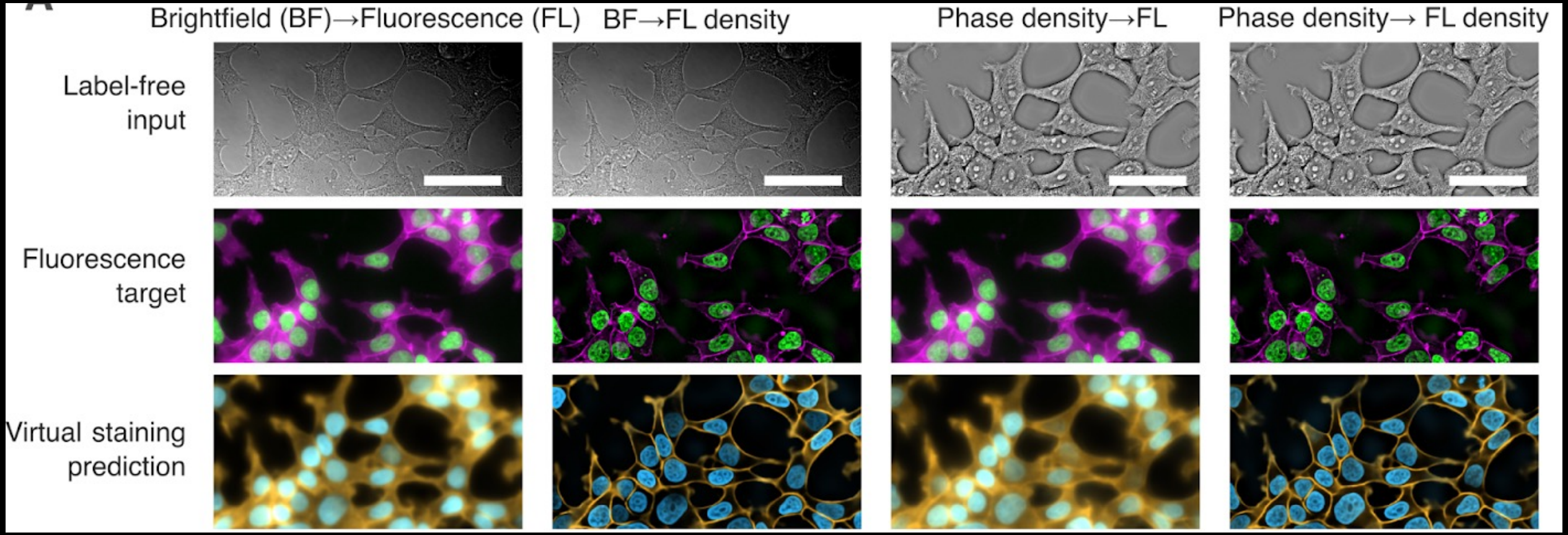


Prediction of nuclei

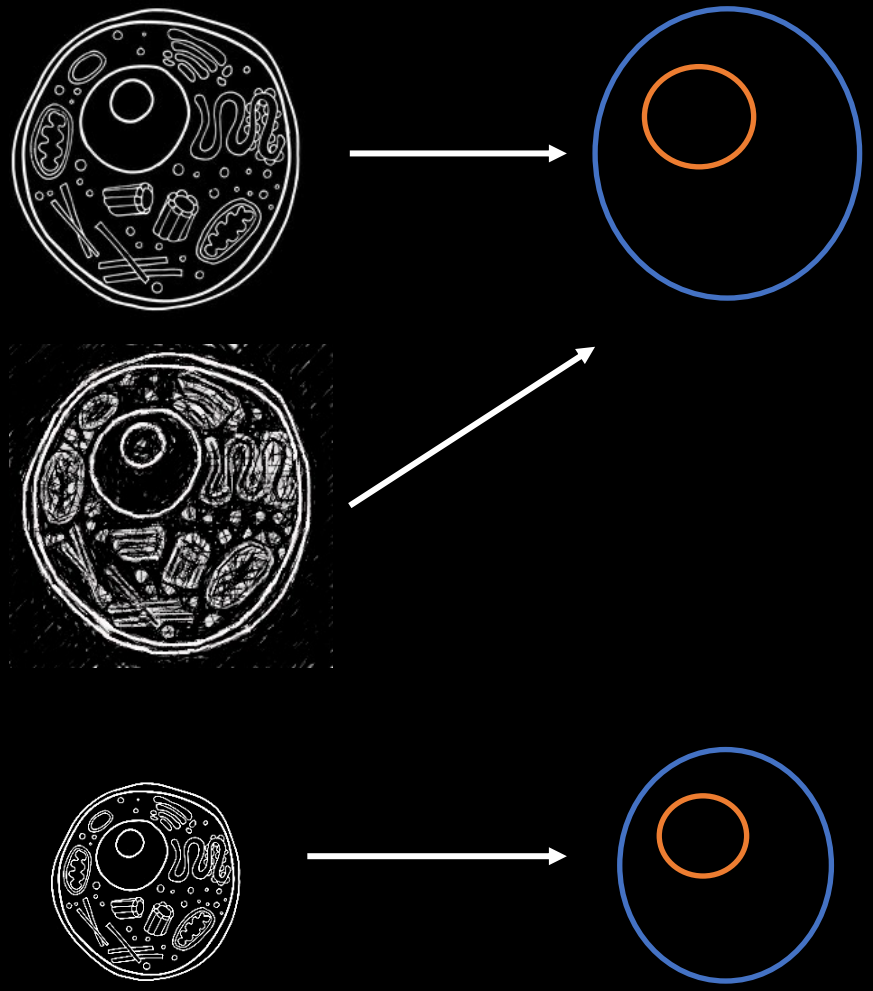


Towards robust virtual staining …

deconvolution improves accuracy



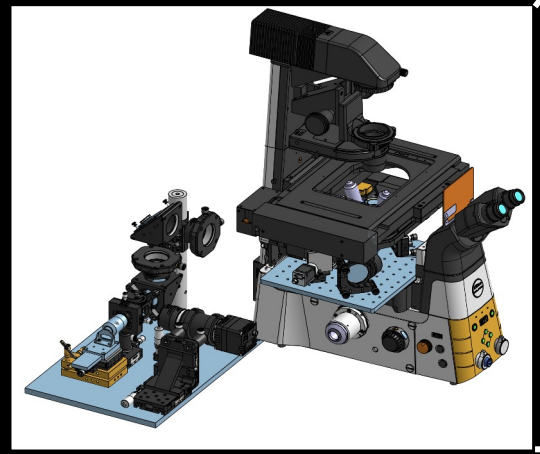
augmentations to the rescue!

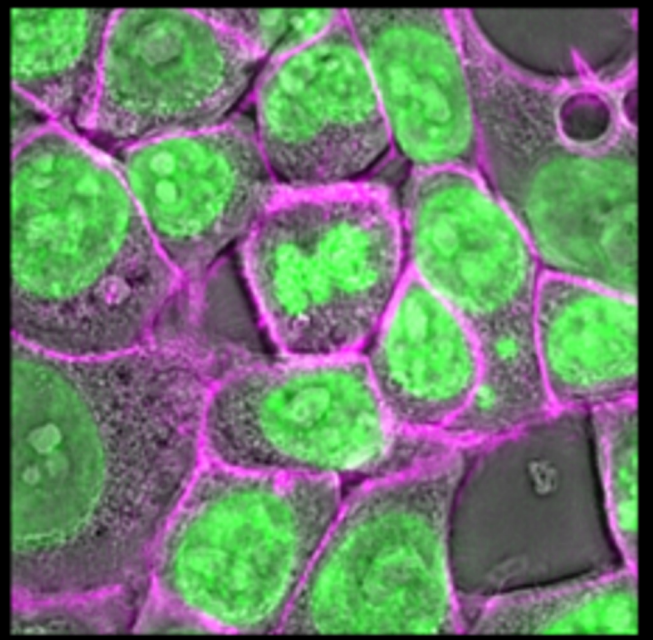


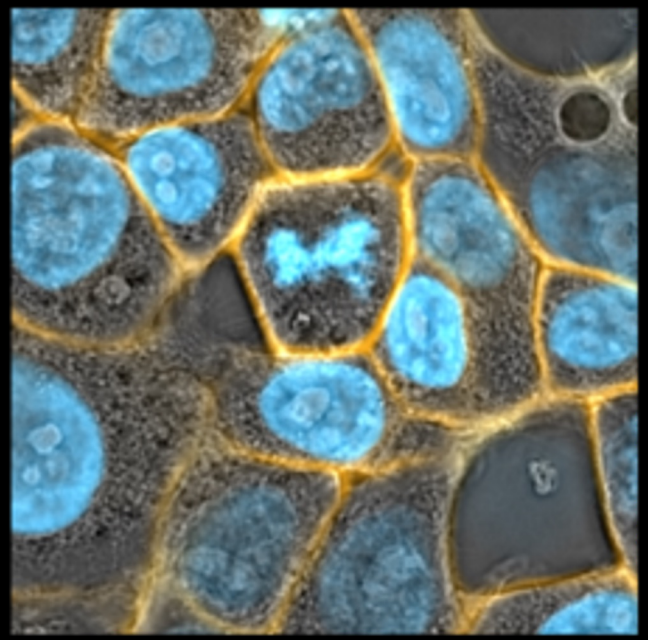
generalization across microscopes

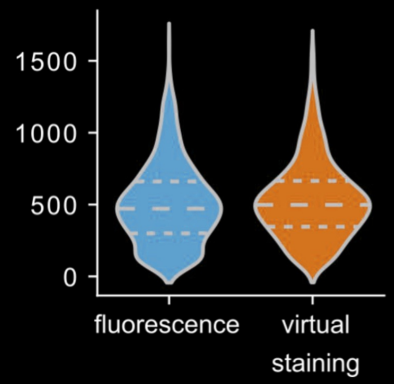
Training data from scope 1

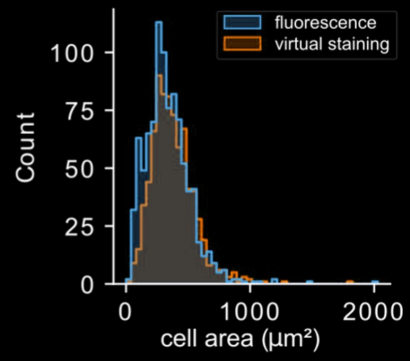
Test data from scope 2



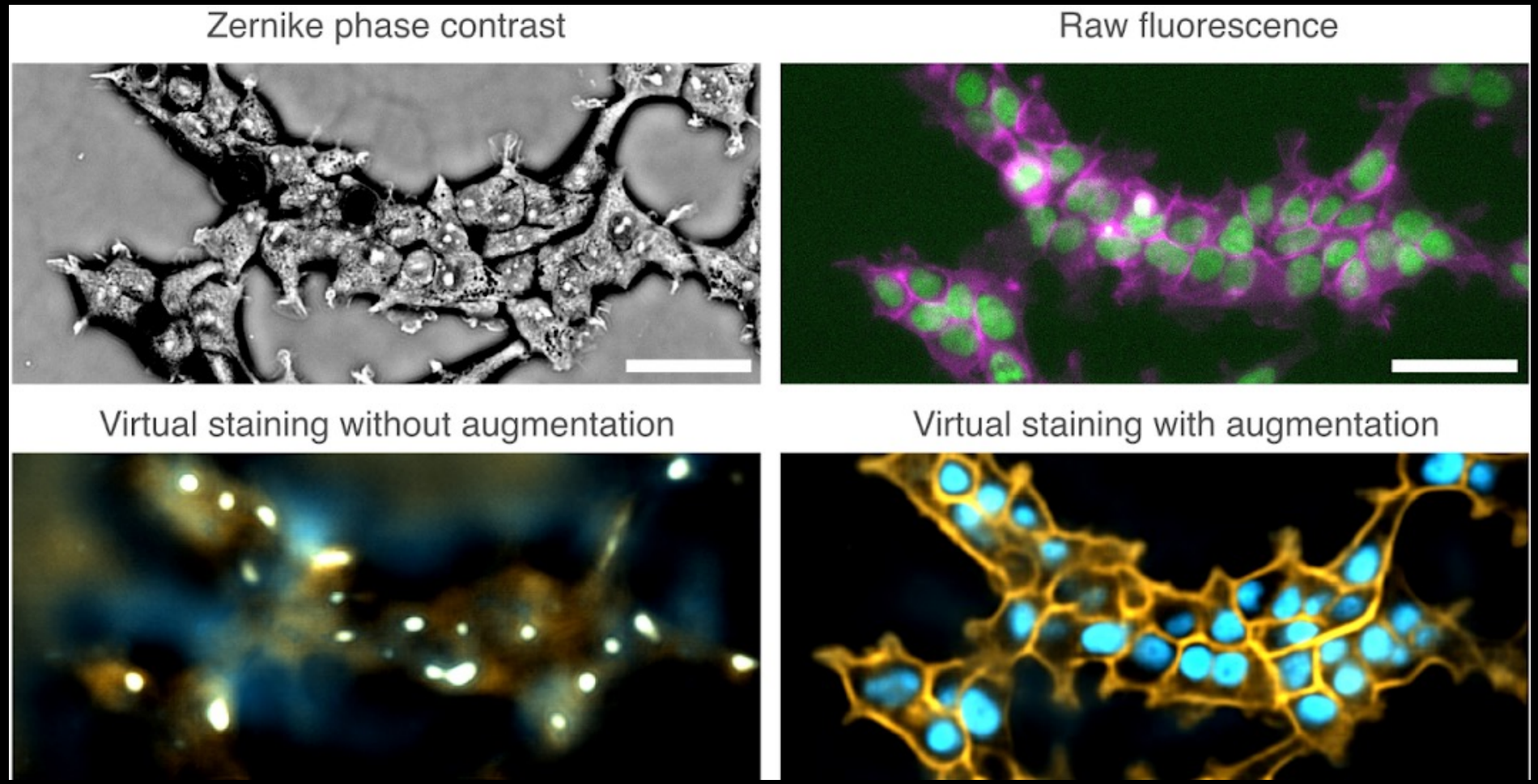




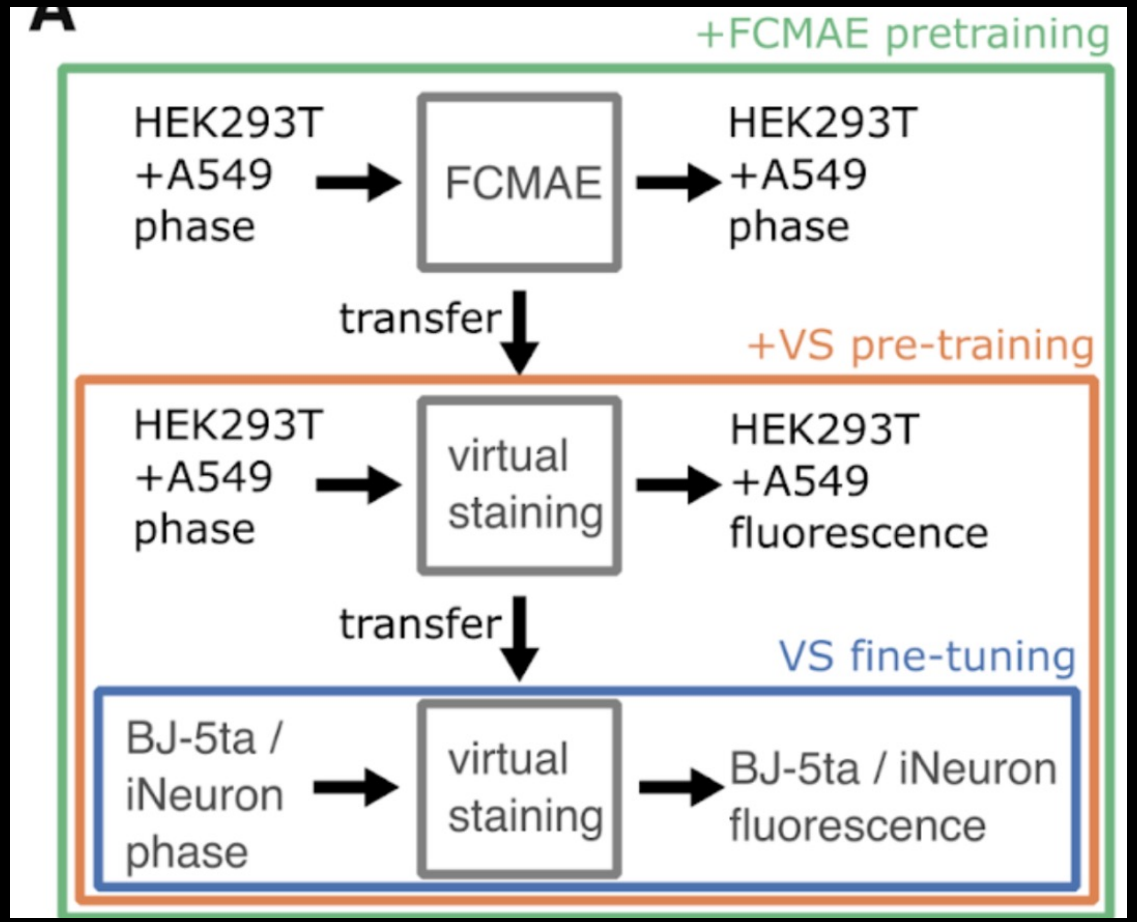


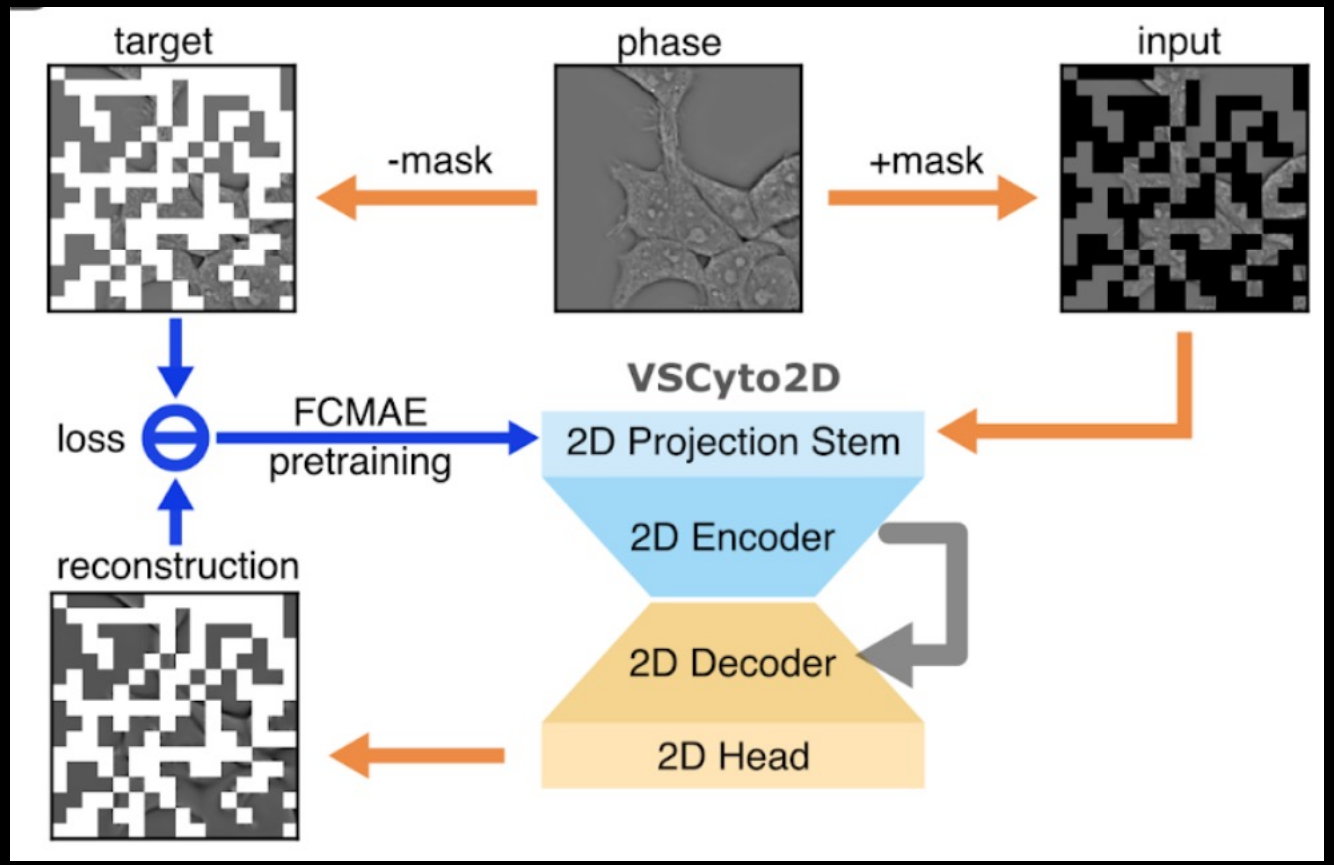


Zero-shot generalization to new contrast



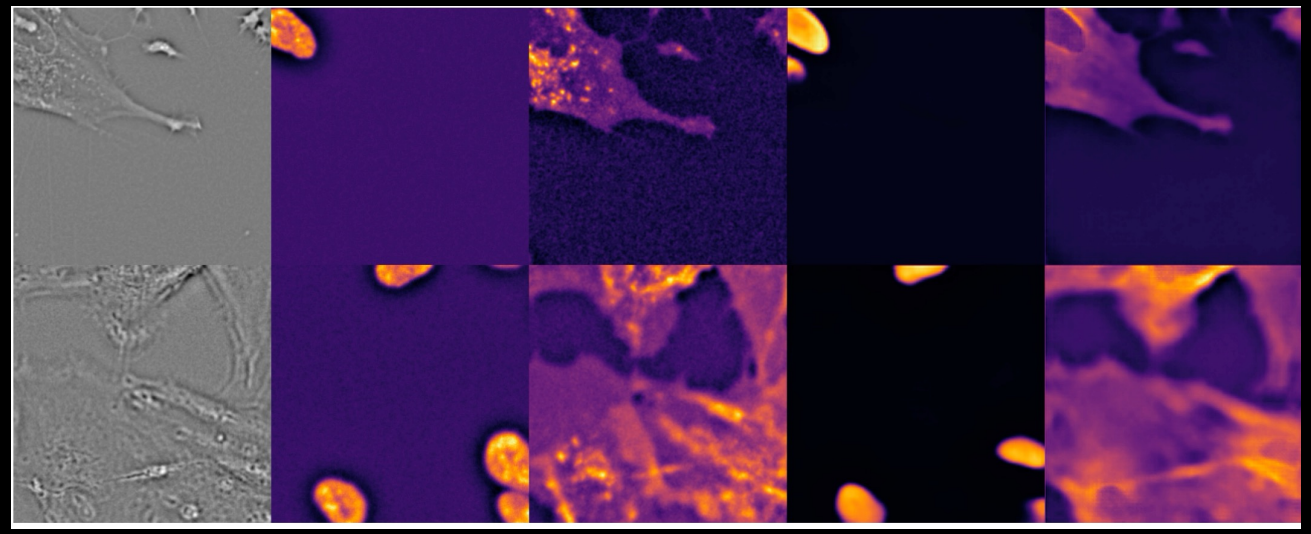
generalization across cell types



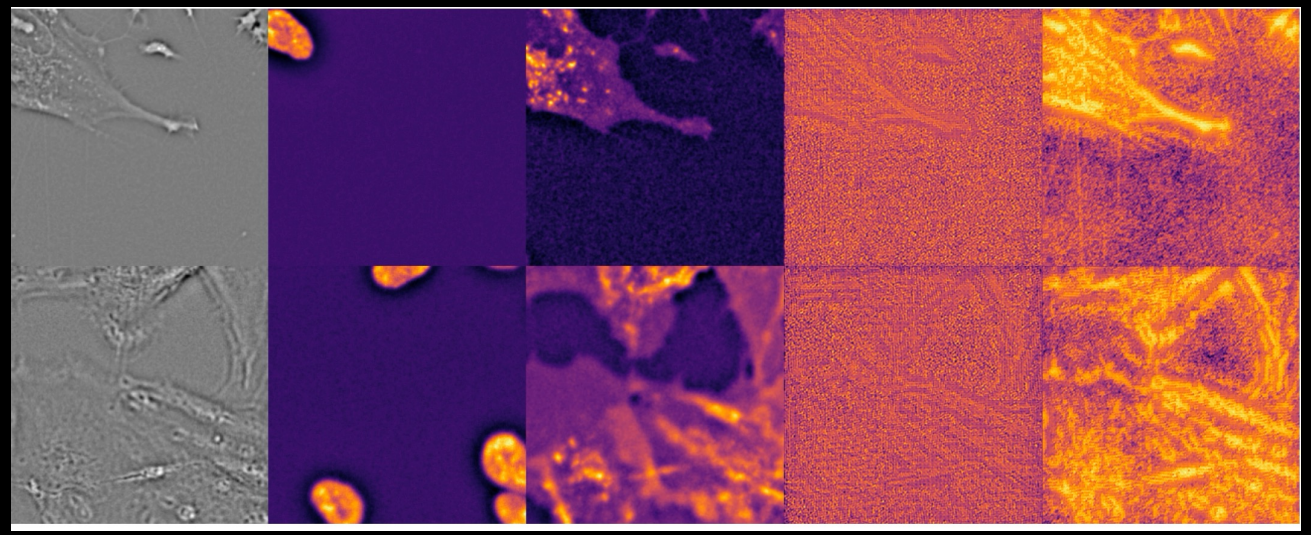


Pretraining for few-shot generalization

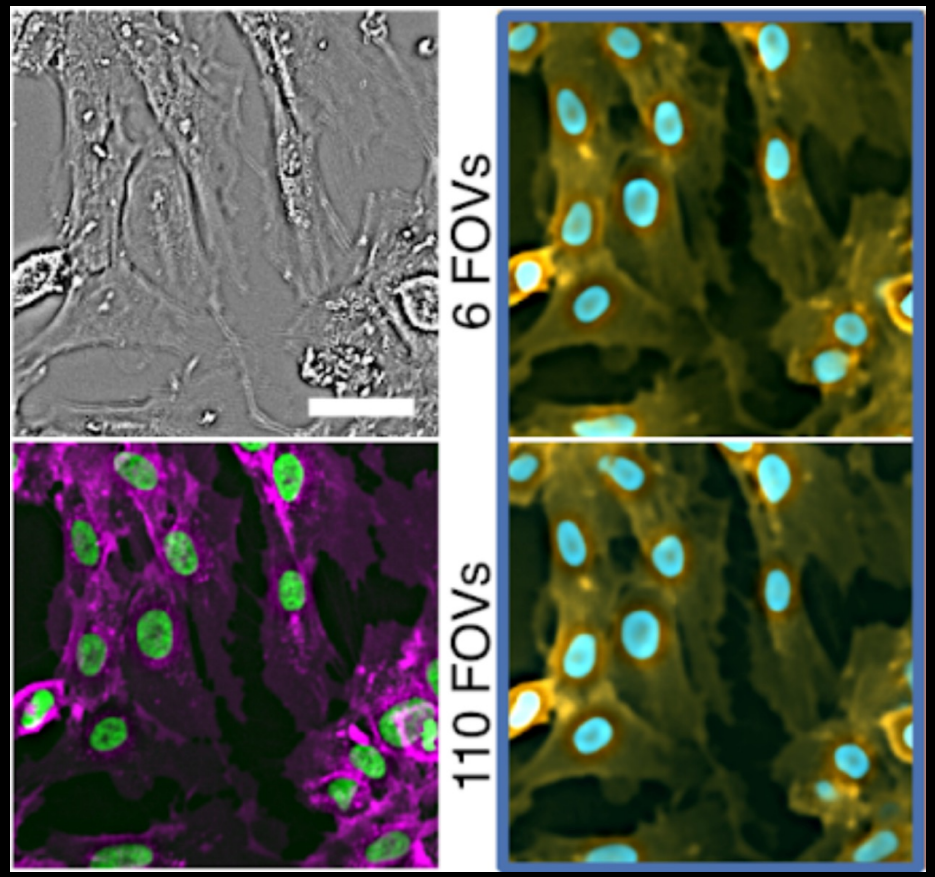
Pretrained + fine-tuned

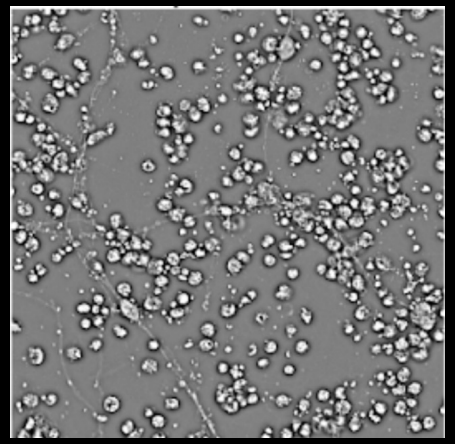


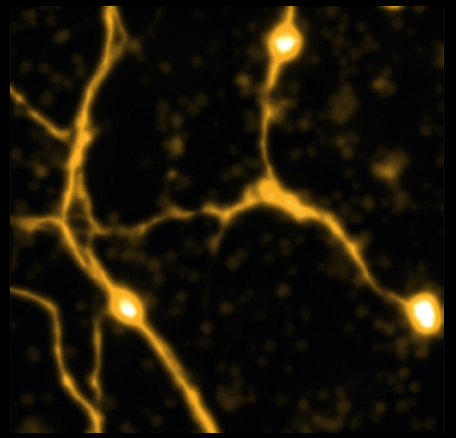
Trained from scratch

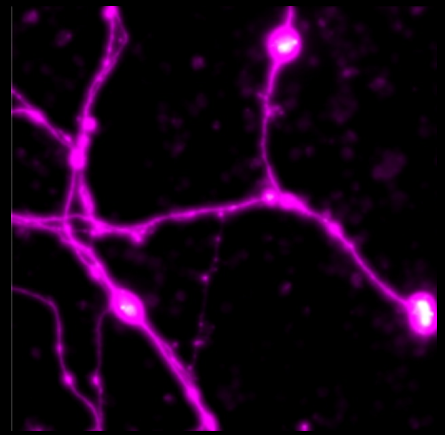


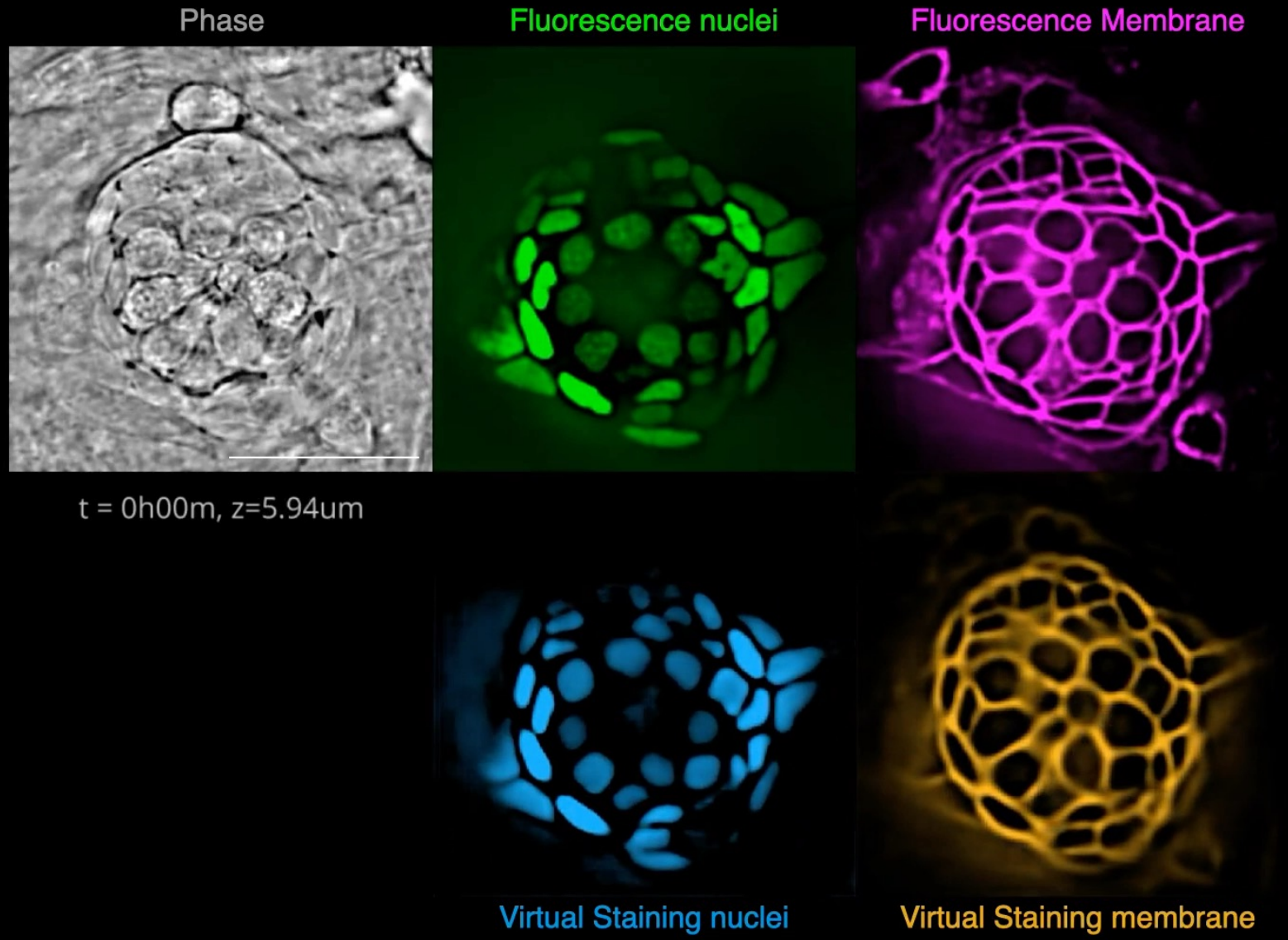
generalization across cell types







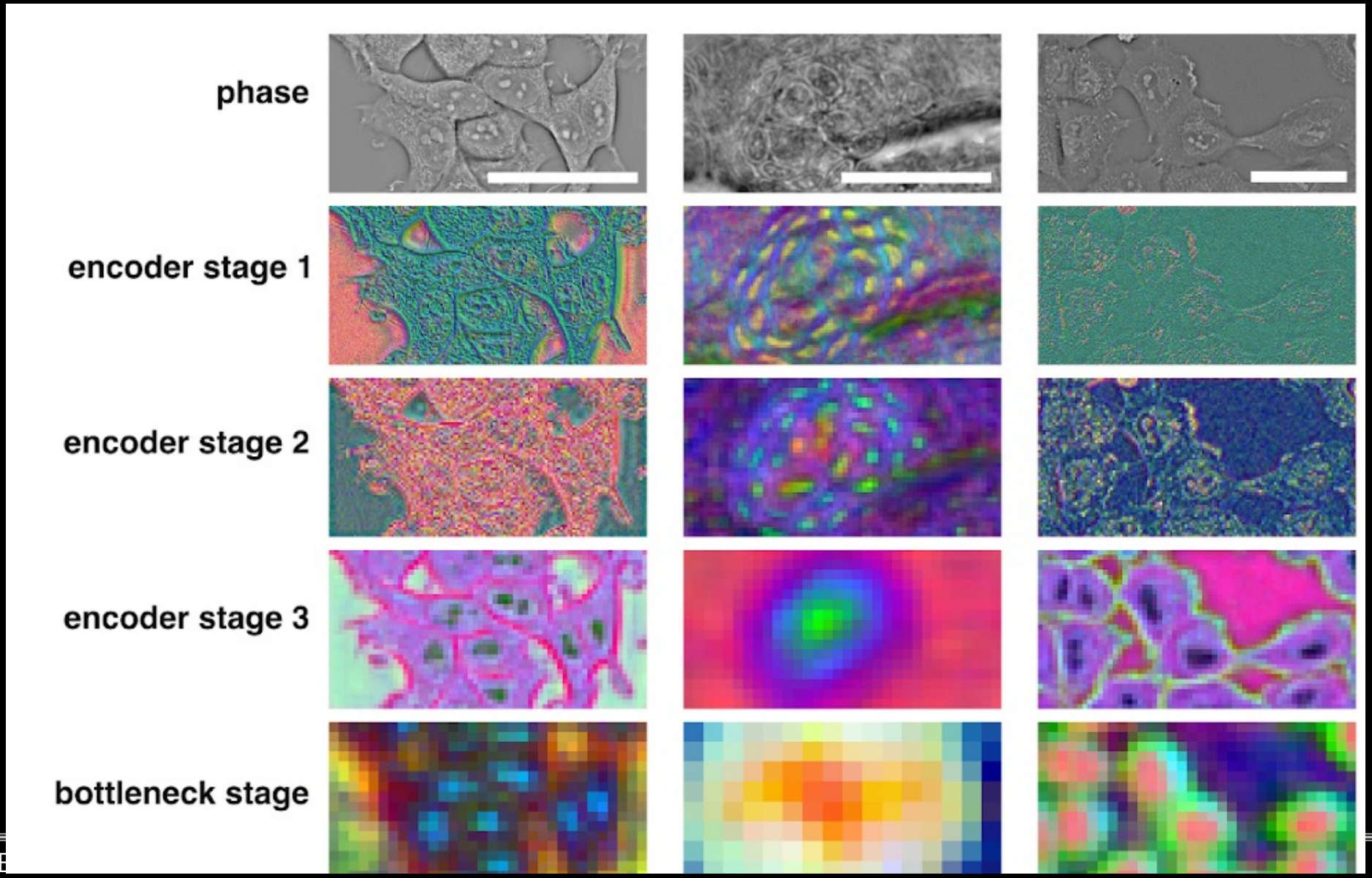




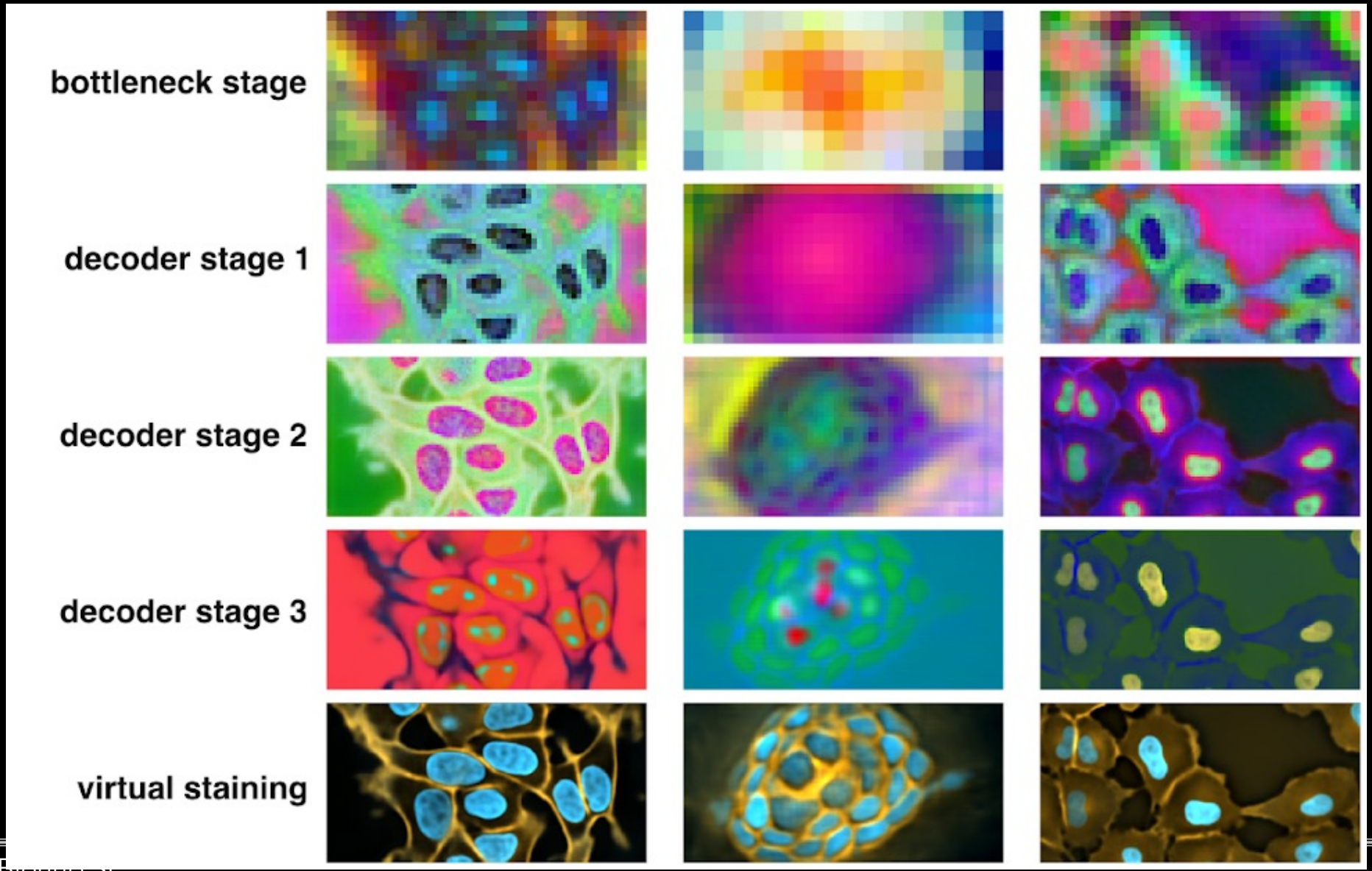
...fine tune with sparse supervision

Liu et al., bioRxiv, 2024

Multi-scale representation

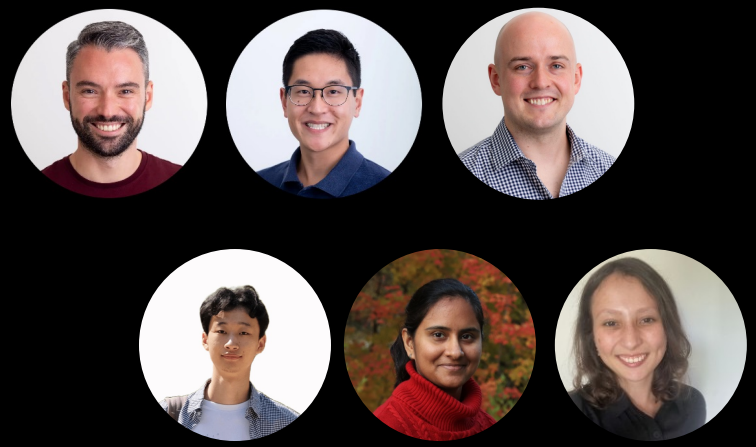


Multi-scale representation



Thank you!

Computational Microscopy



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Collaborators