

Image Translation

Shalin Mehta,
Computational Microscopy Platform

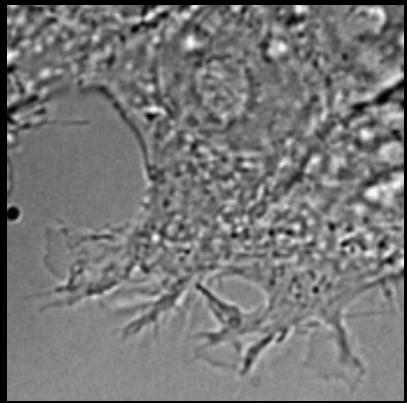


@mattersOfLight

www.czbiohub.org/comp-micro/

Deep Learning @ MBL
Aug 28, 2022

Agenda



computational
imaging

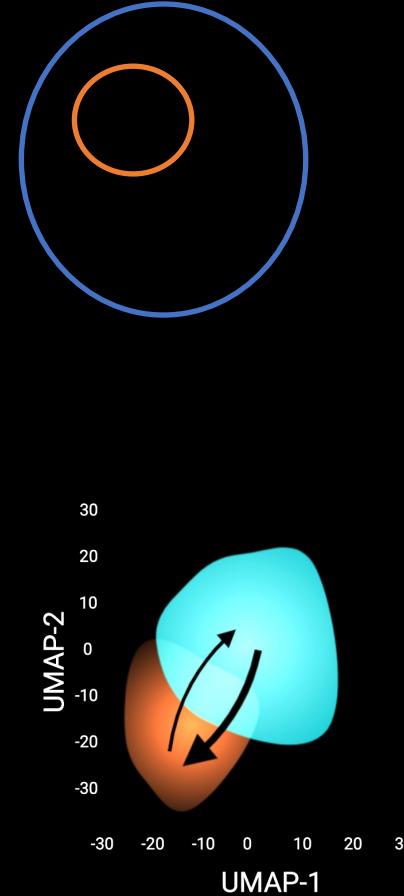


x

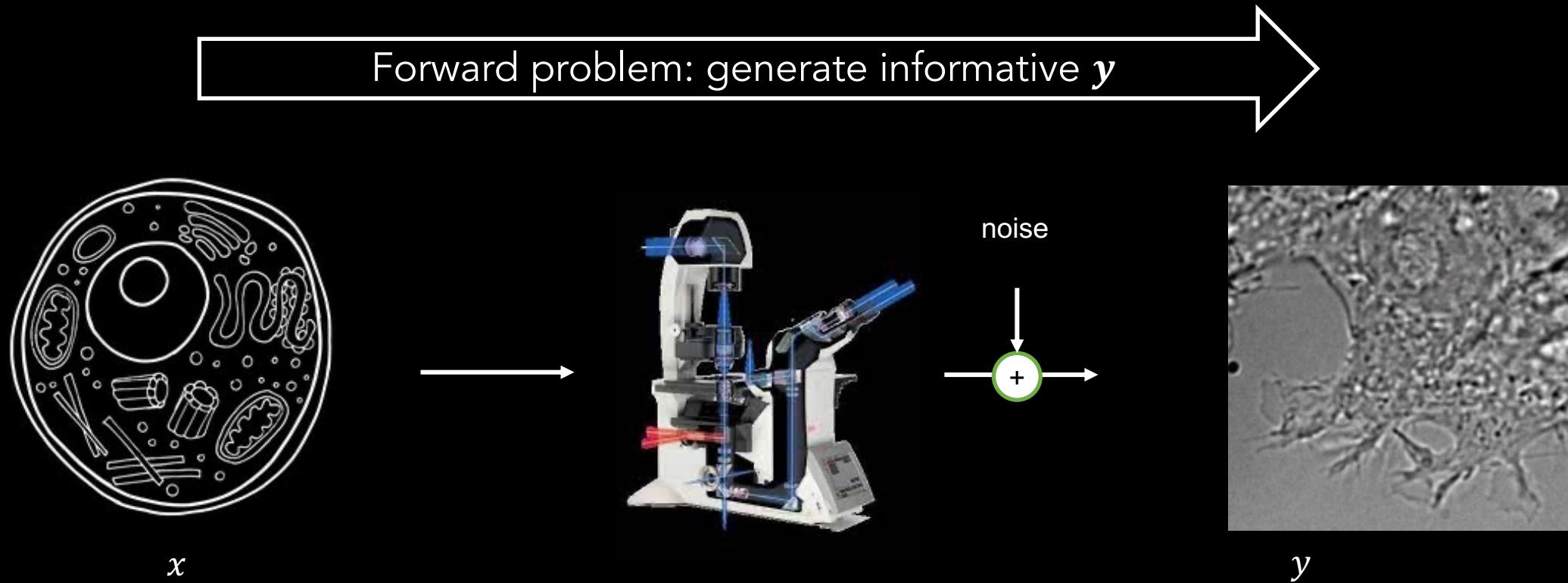
$$y = H_j x S_i + n$$

image
translation

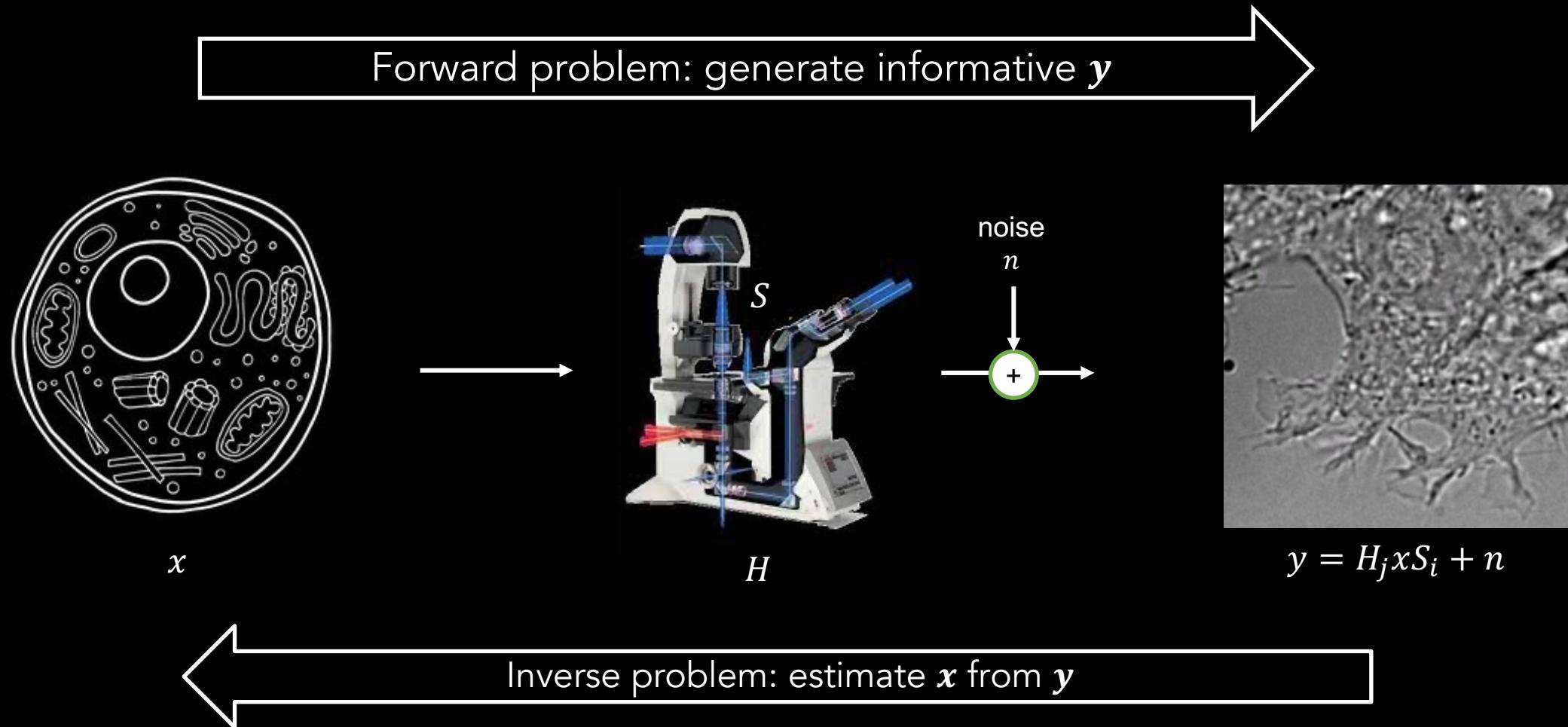
representation
learning



classical imaging

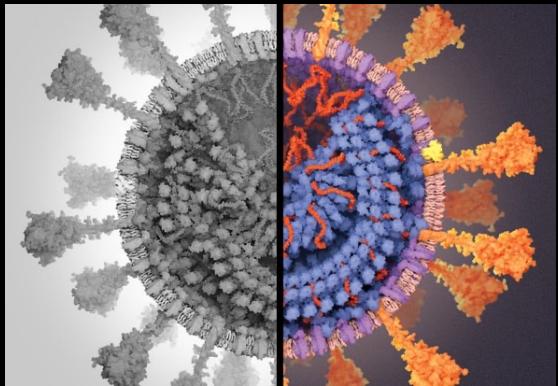


computational imaging

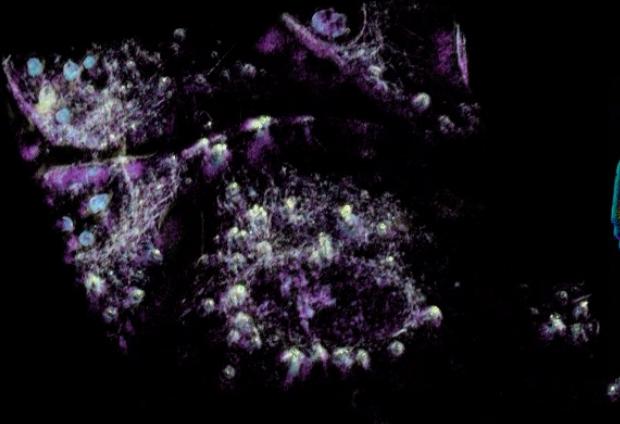


computational label-free imaging

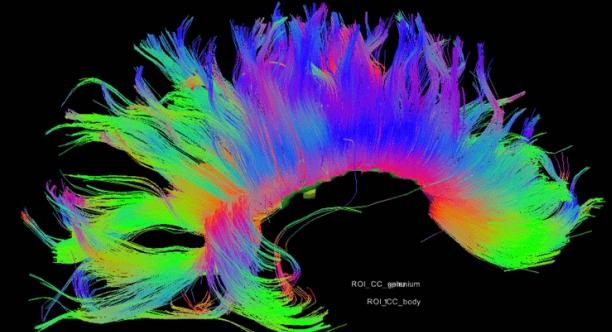
Cryo-EM



Quantitative label-free microscopy



Diffusion tensor imaging (DTI)



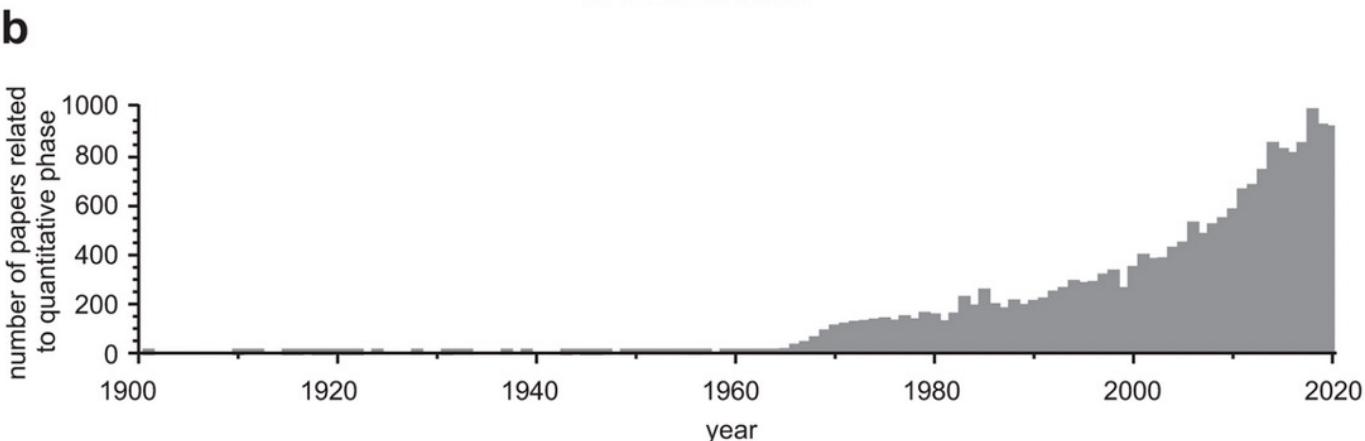
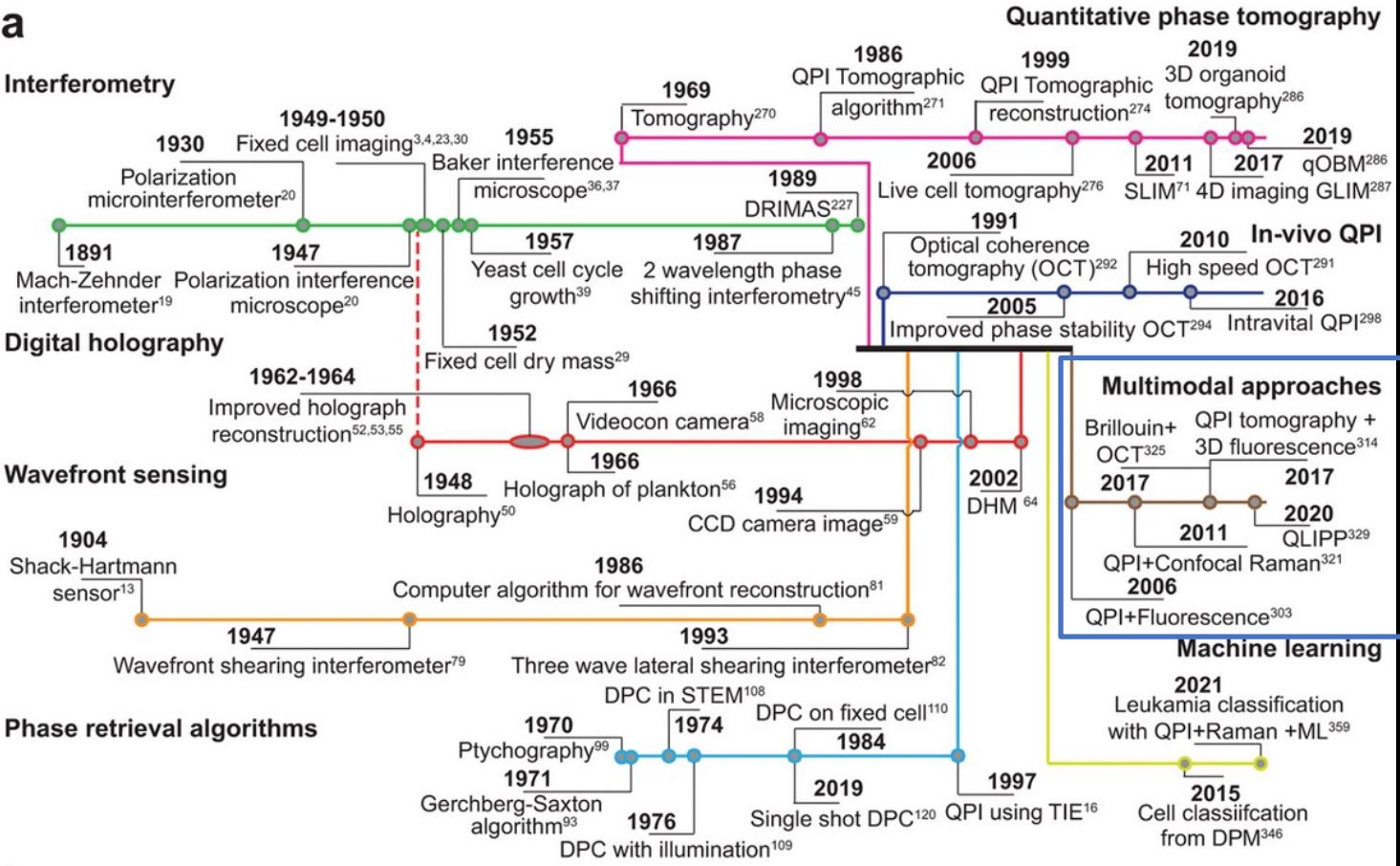
→ scale

Molecular

cellular

tissue

organ



Nguyen, Pradeep et al, 2022.
In Press, ACS Nano,

classical label-free imaging



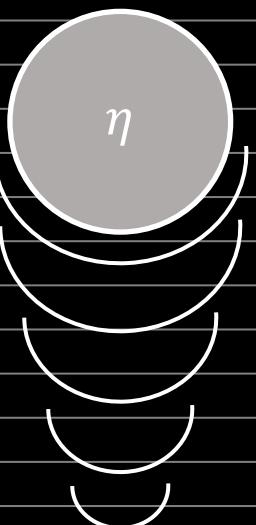
David Rogers, 1950



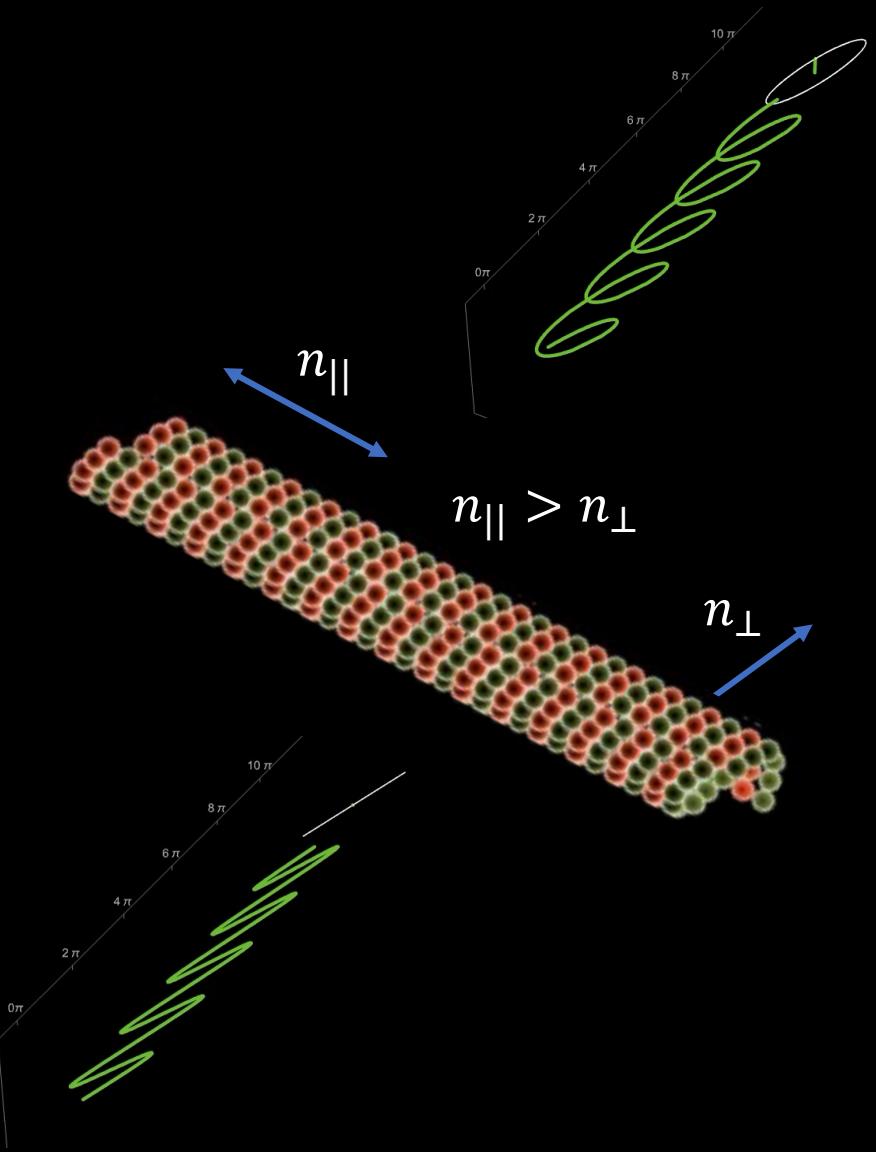
Inoue, Chromosoma 1951

phase

η_{media}



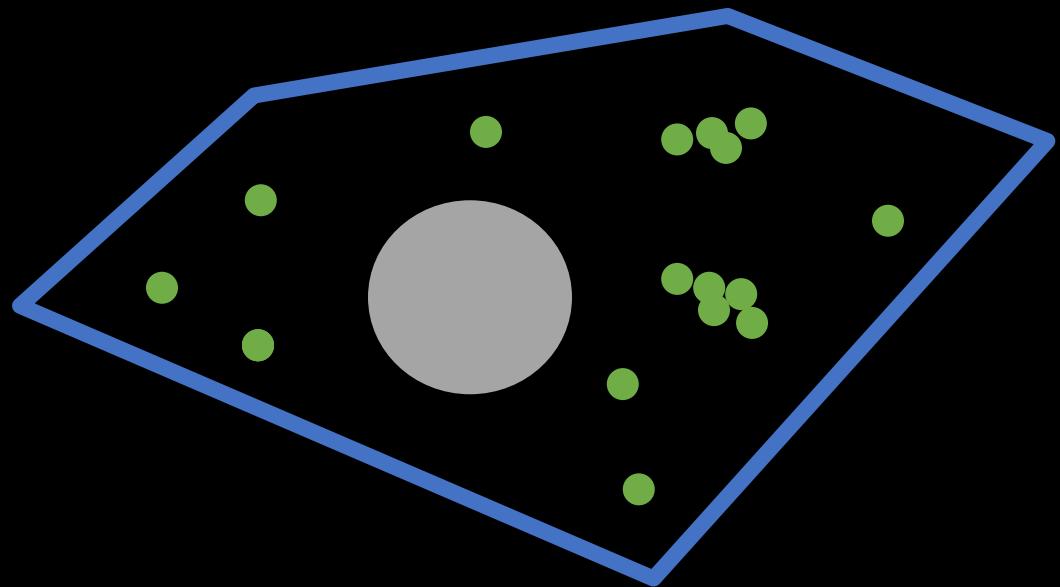
retardance



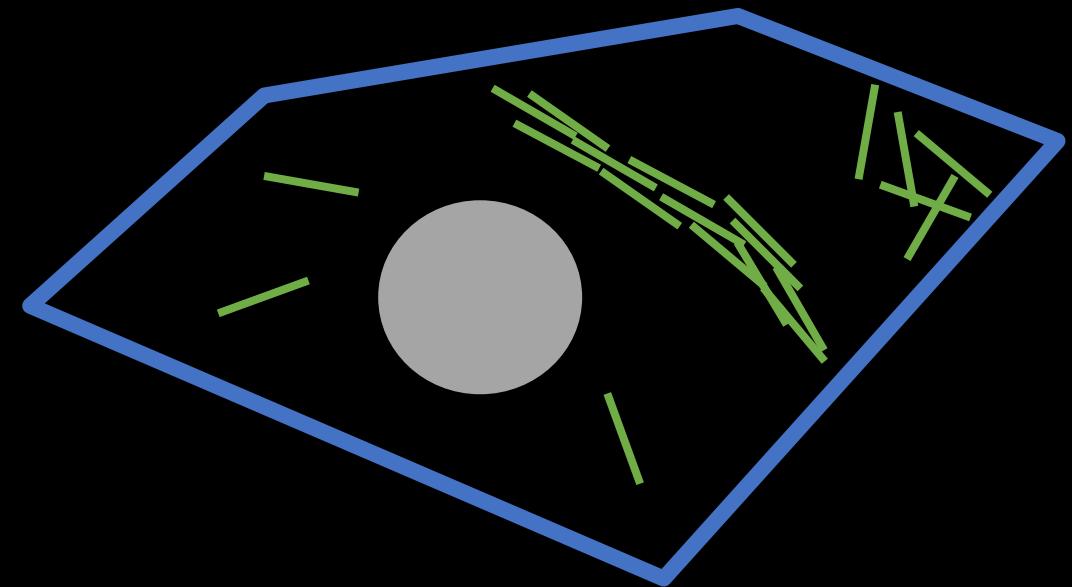
from AQLM 2022

“biological architecture is tensorial”

Rob Phillips

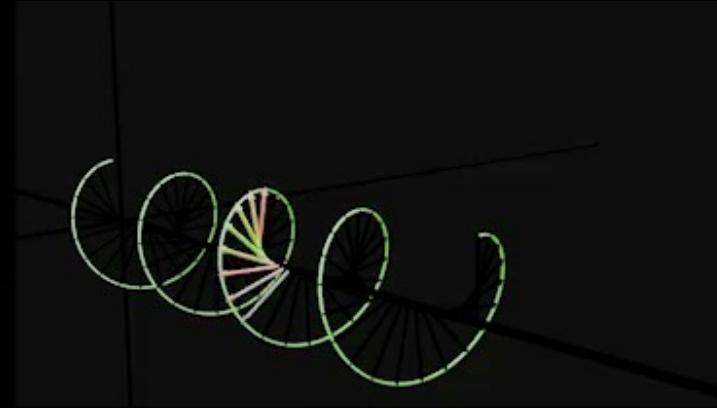
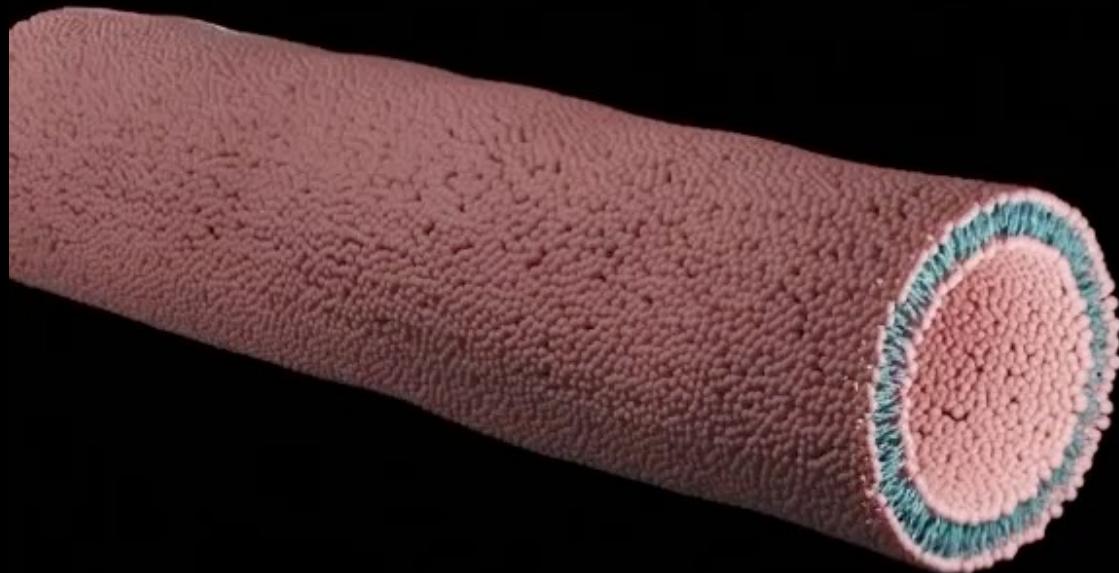


spatial architecture

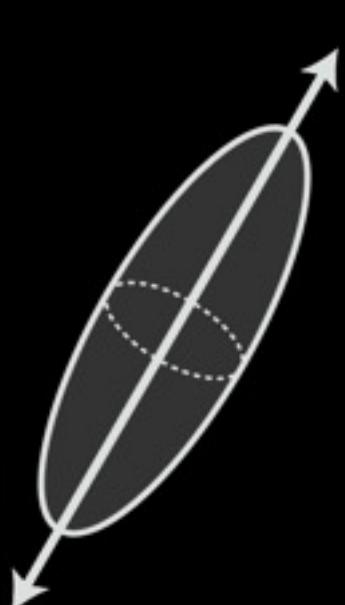


spatio-angular architecture

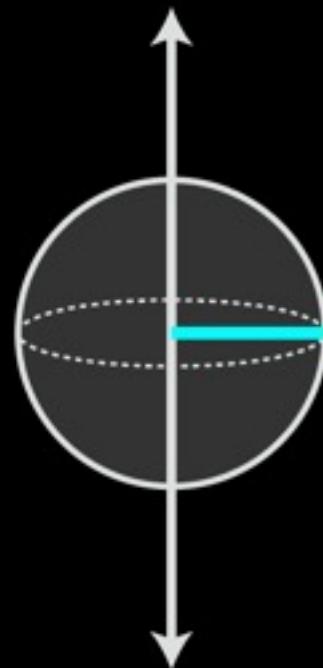
permittivity tensor



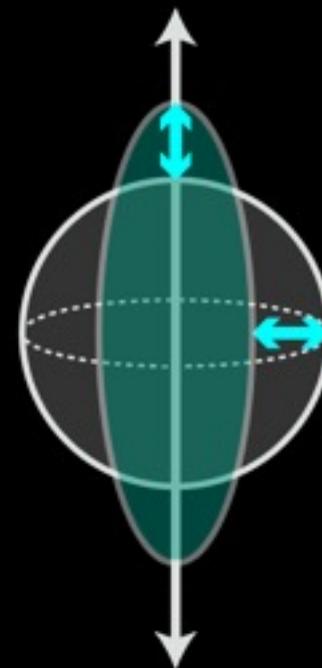
permittivity
tensor



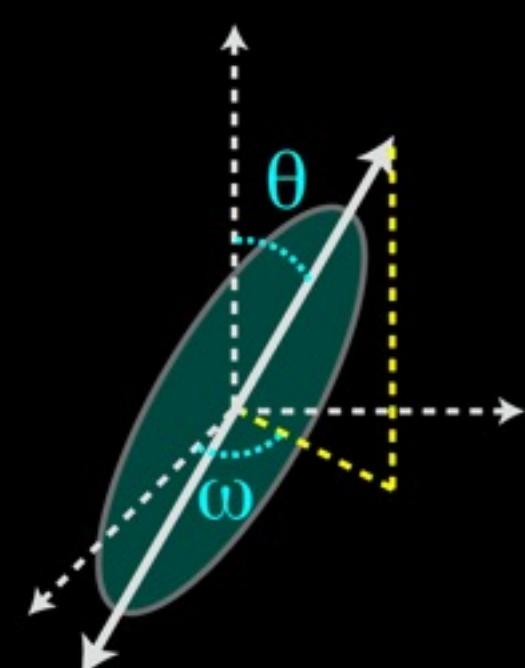
mean
permittivity



differential
permittivity



3D orientation



=

+

+

reports

biomolecular density

identifies

nuclei, nucleoli, vesicles,
mitochondria, vacuoles, ...

biomolecular anisotropy

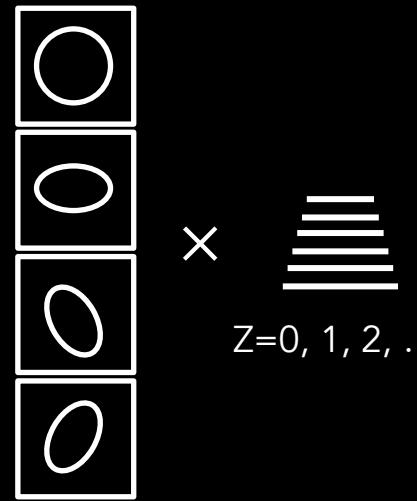
vesicles, spindle, plasma membrane, ECM, myofibril, axons,
...

biomolecular orientation

Current line of spatio-angular computational imaging methods

QLIPP

6 volumes per minute

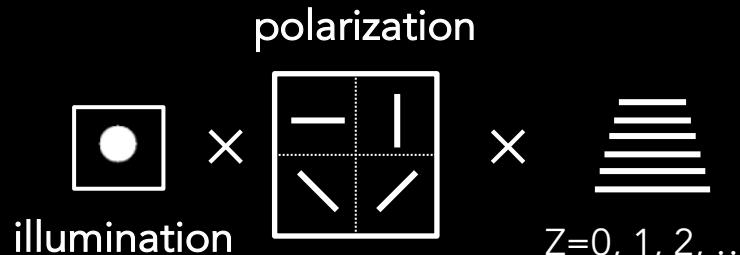


most sensitive

Guo, Yeh, Folkesson et al. eLife 2020

miPolScope

60 volumes per minute

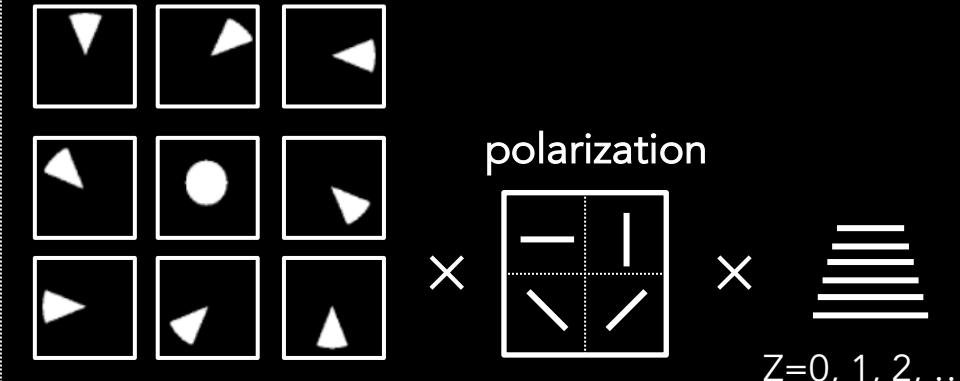


fastest

Ivanov et al. Biomed. Opt. Exp. 2022

PTI

1 volume per minute

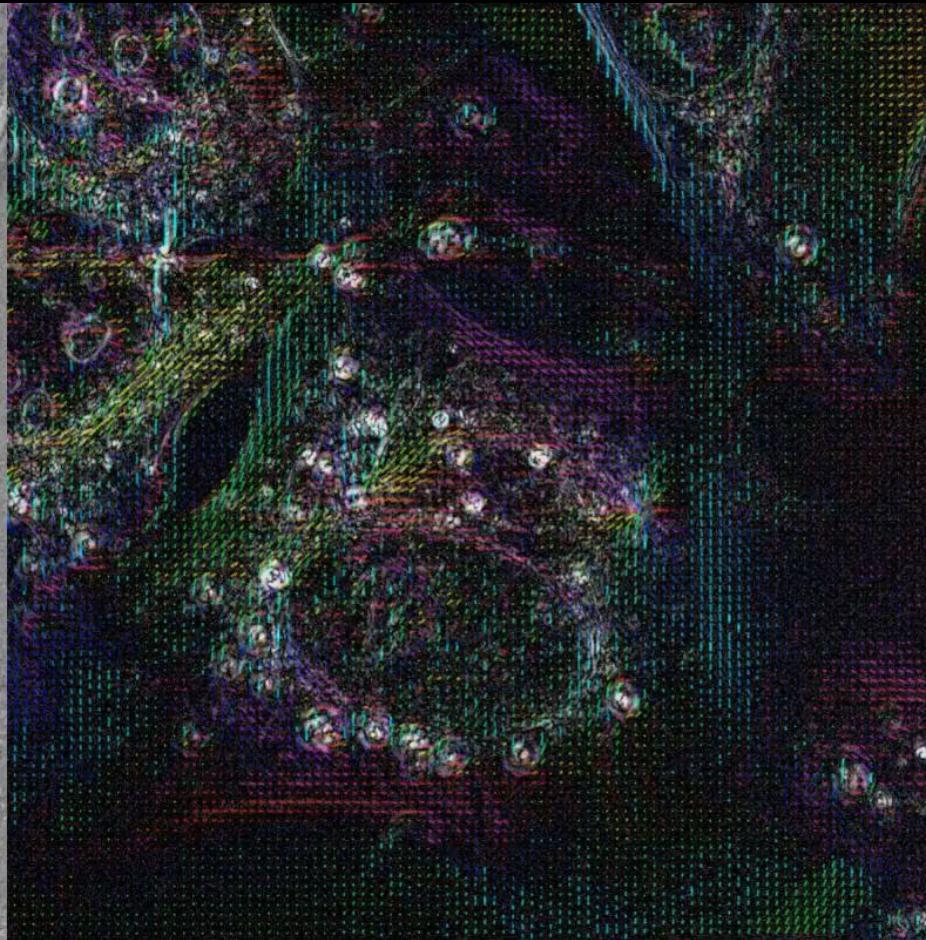
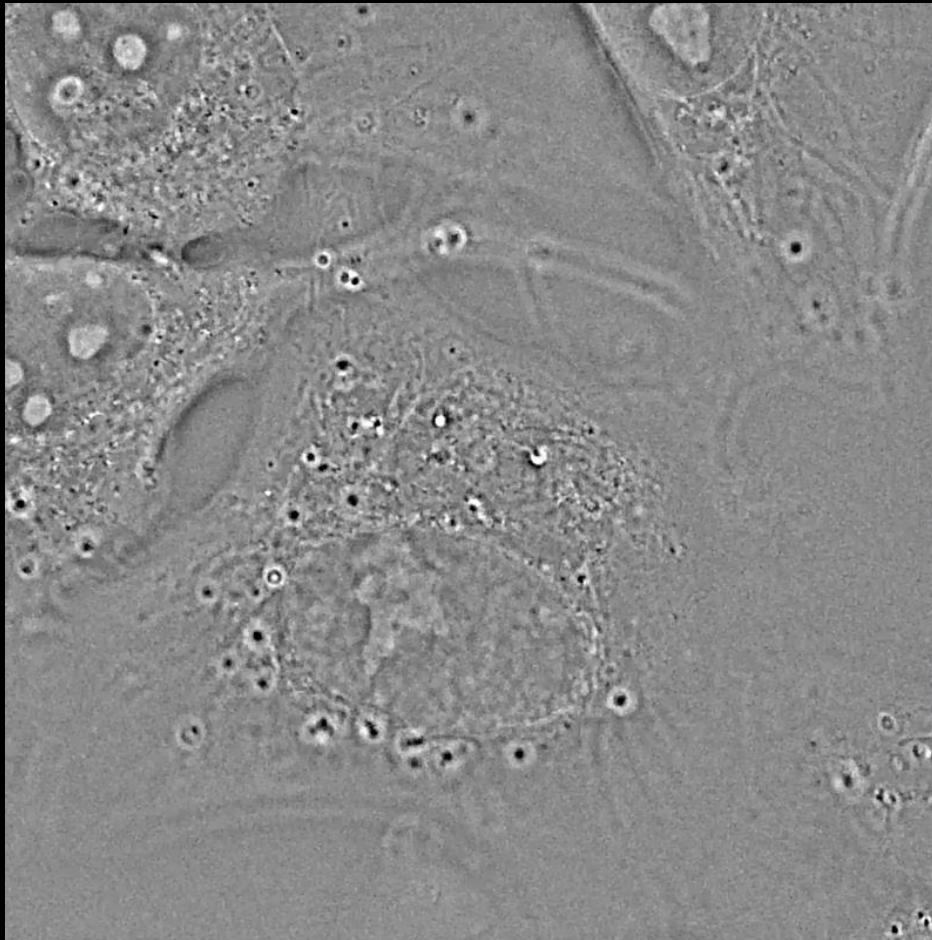
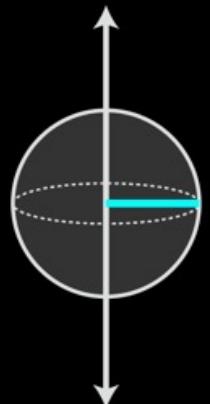


highest resolution

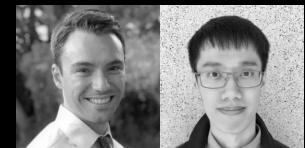
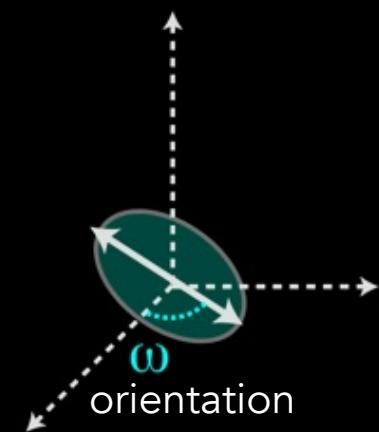
Yeh et al. bioRxiv 2020 (soon to be published)

QLIPP: sensitive

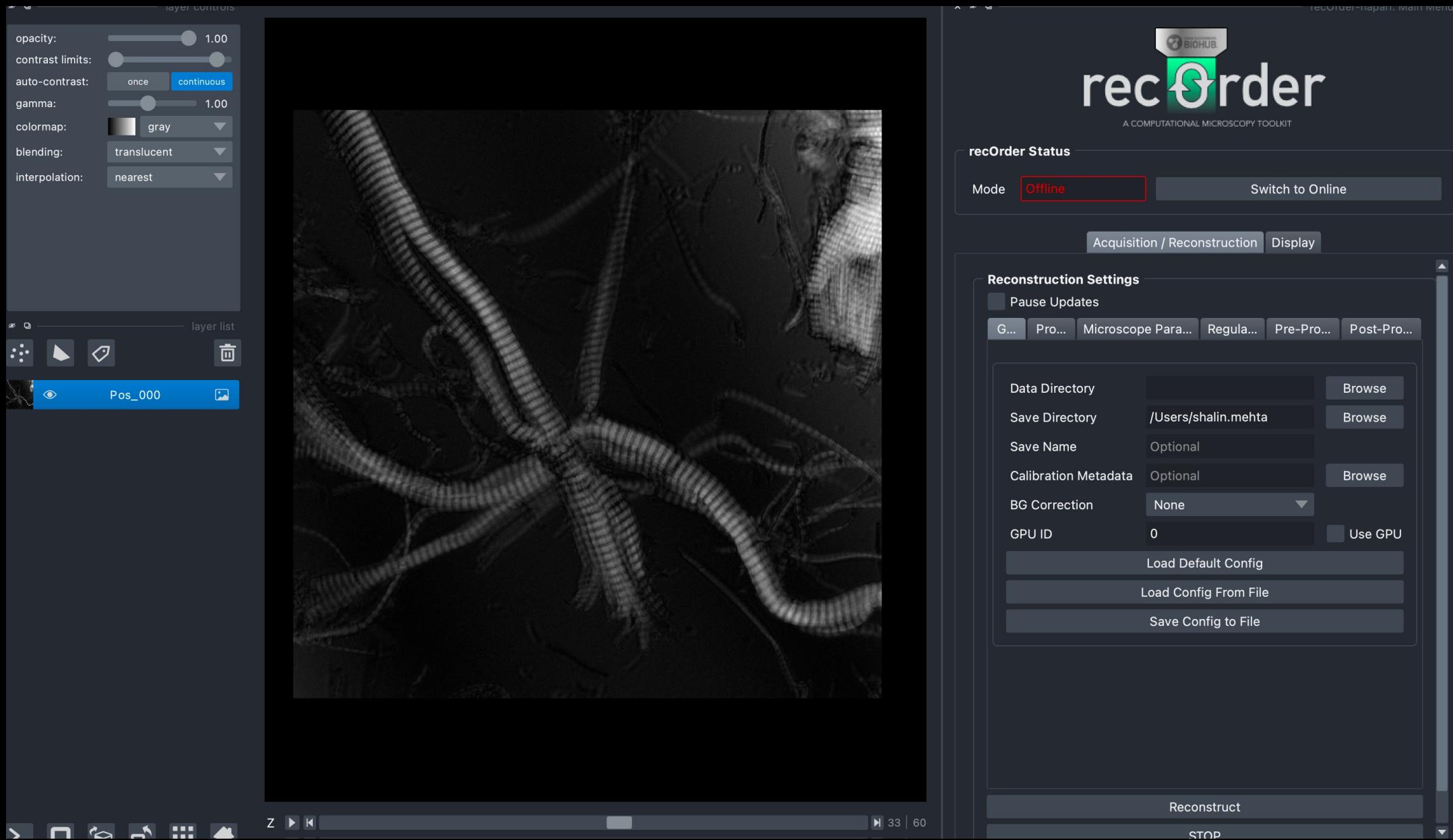
phase



retardance



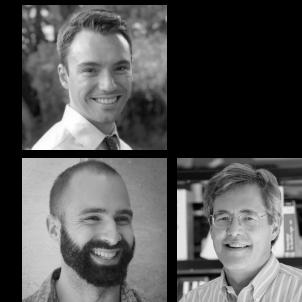
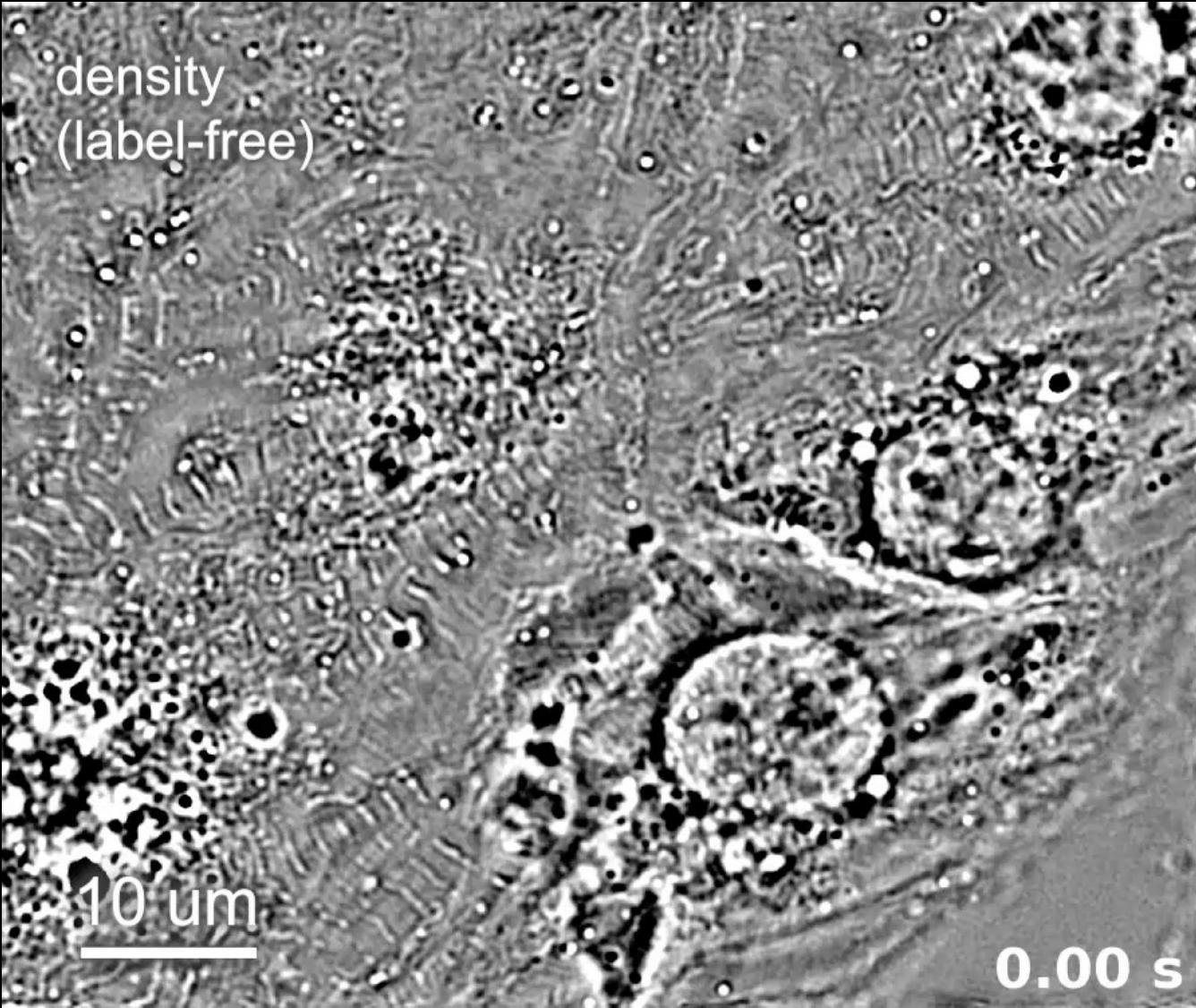
Quantitative label-free imaging with phase & polarization



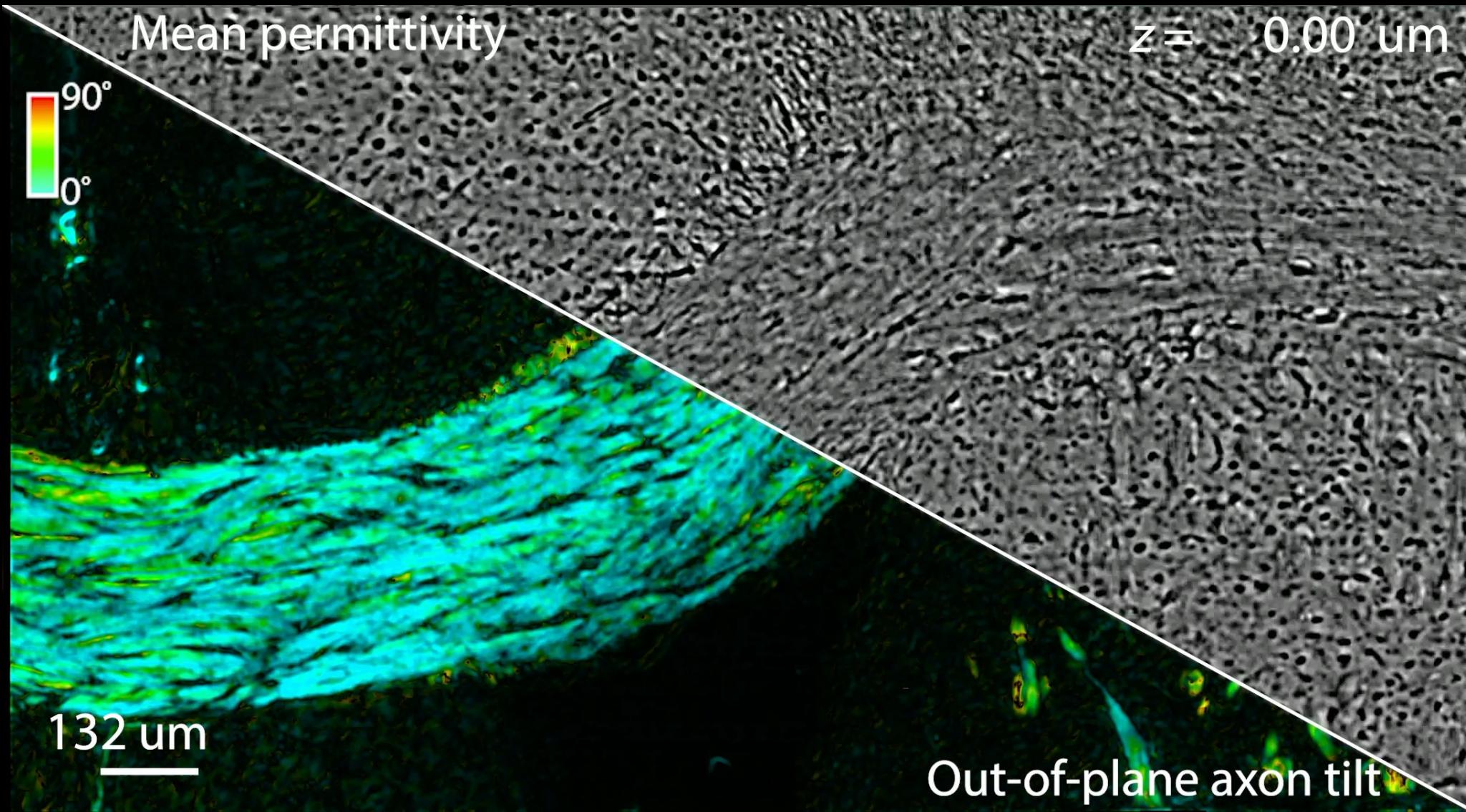
pip install recorder-napari

<https://www.napari-hub.org/plugins/recOrder-napari>

miPolScope: fast



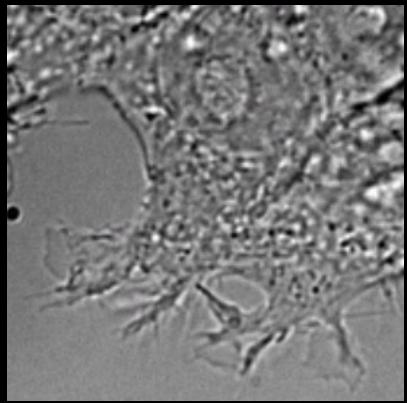
PTI: highest resolution



permittivity tensor imaging - hardware

Before setting up...

Agenda



$$y = H_j x S_i + n$$

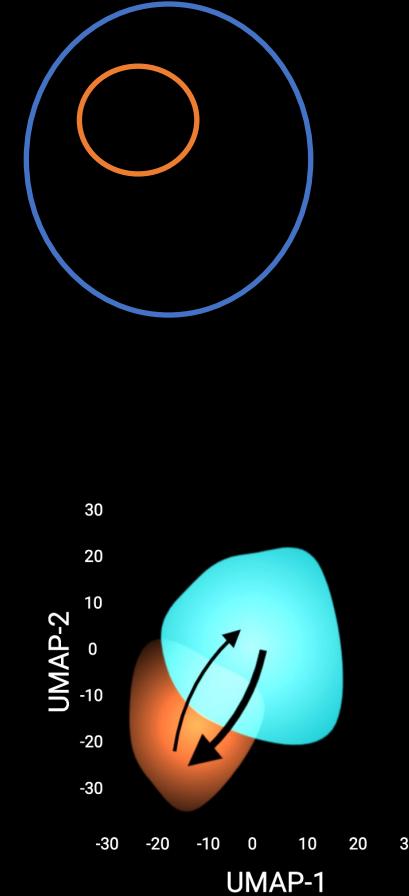
computational
imaging



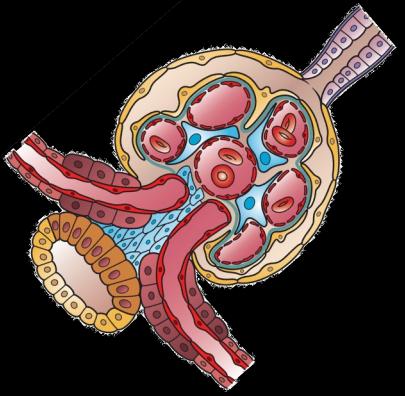
x

image
translation

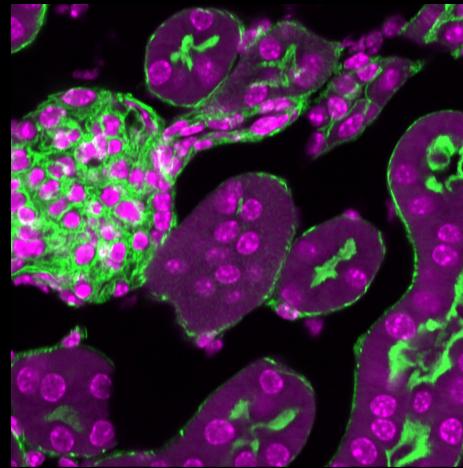
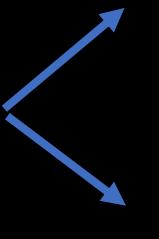
representation
learning



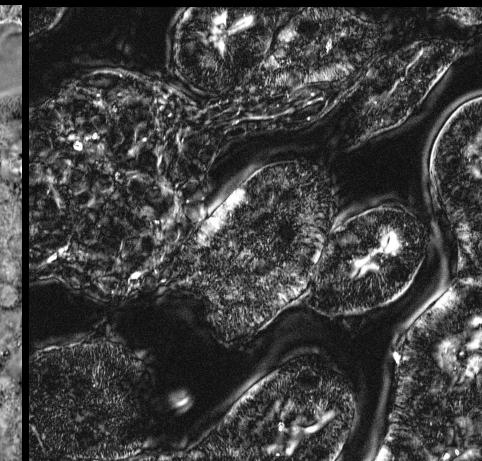
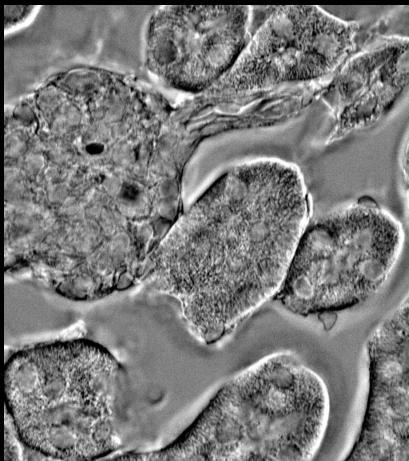
Virtual staining



glomerulus in kidney

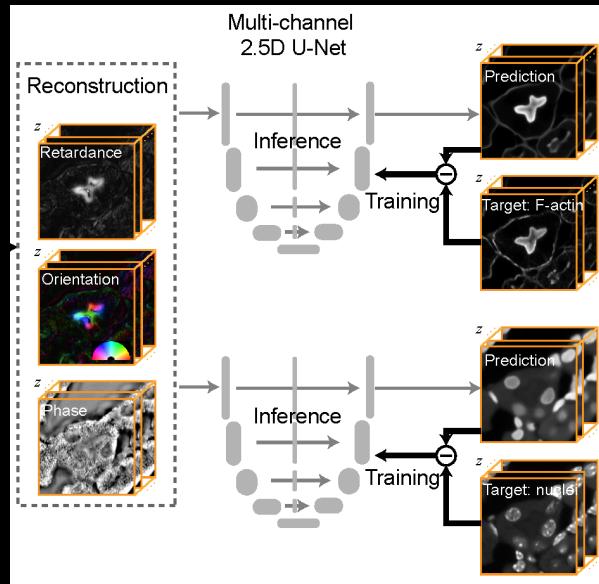


DL

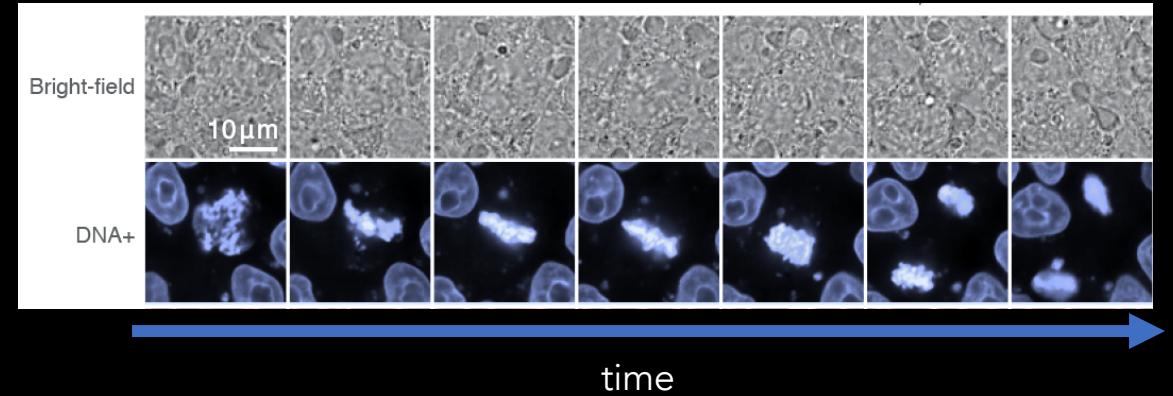


Artwork by Holly Fischer
<https://commons.wikimedia.org/w/index.php?curid=24367132>

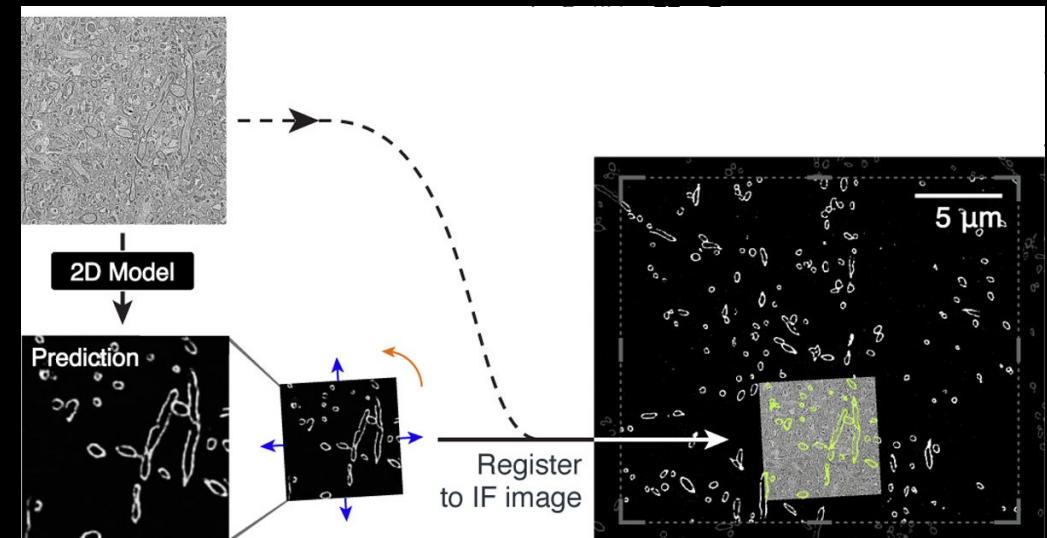
Computational multiplexing



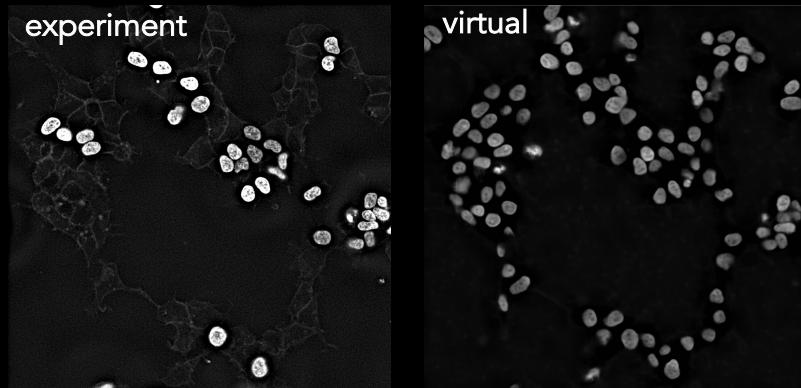
Virtual live cell labeling



Cross-modality registration



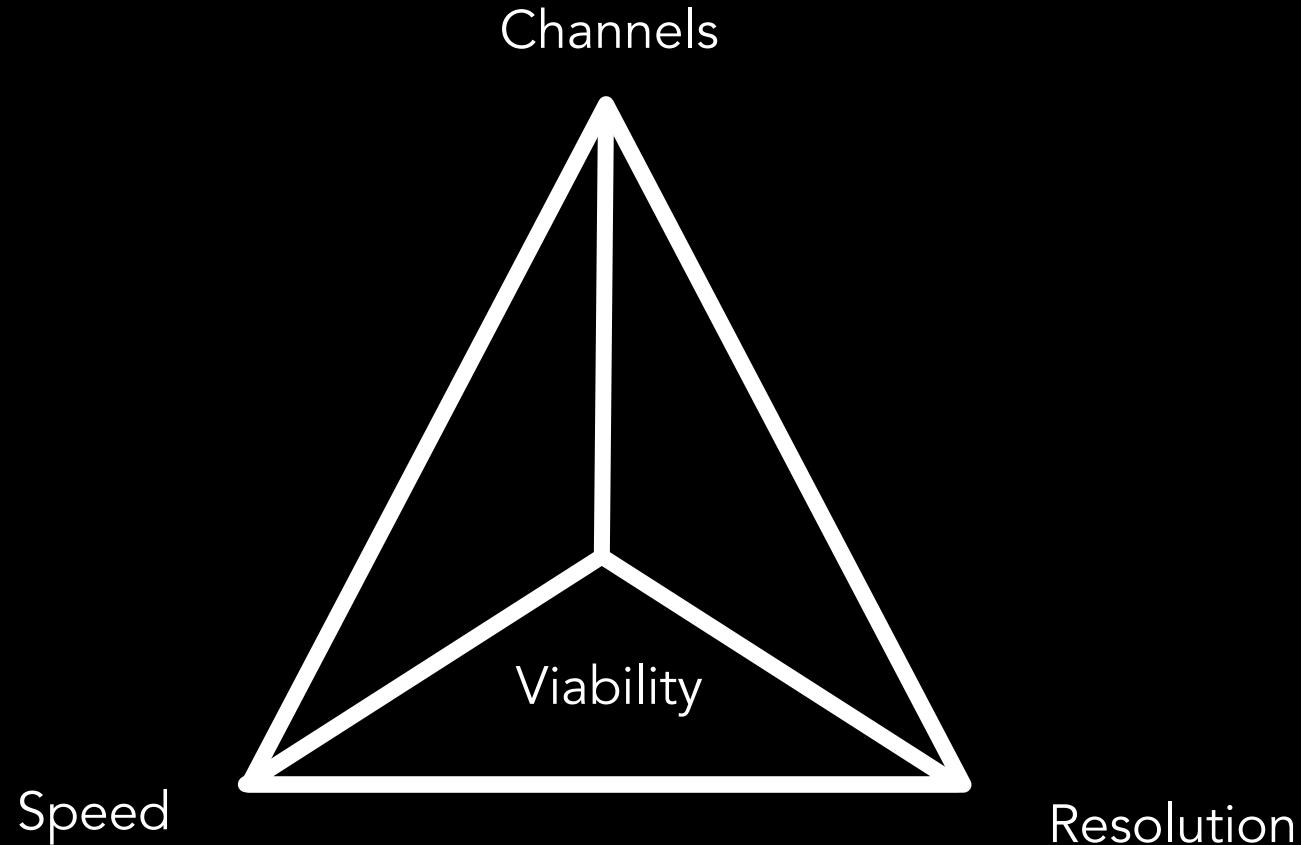
Reproducible staining!



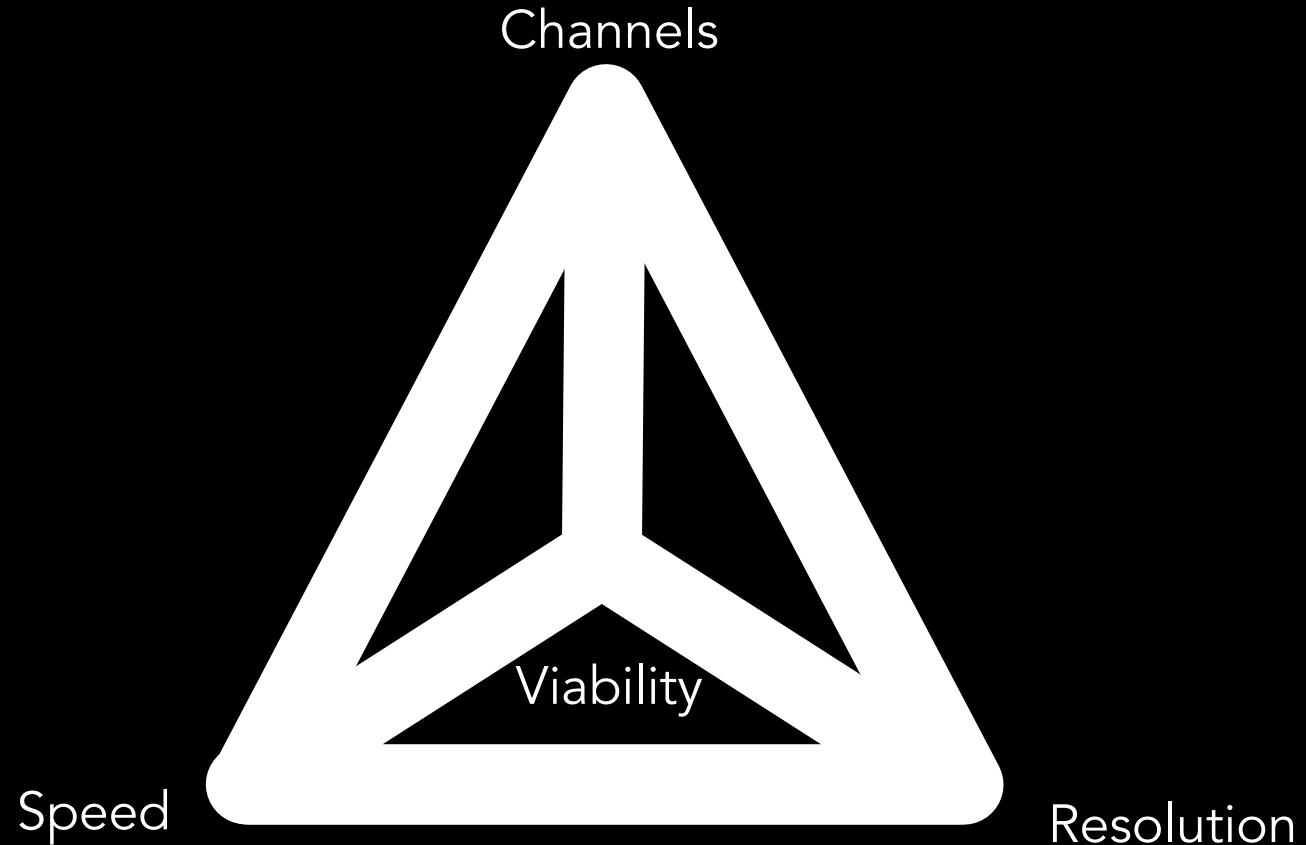
Guo, Yeh, Folkesson, et al., eLife 2020

Ounkomol et al., Nature Methods, 2018

Relax the experimental trade-offs with DL



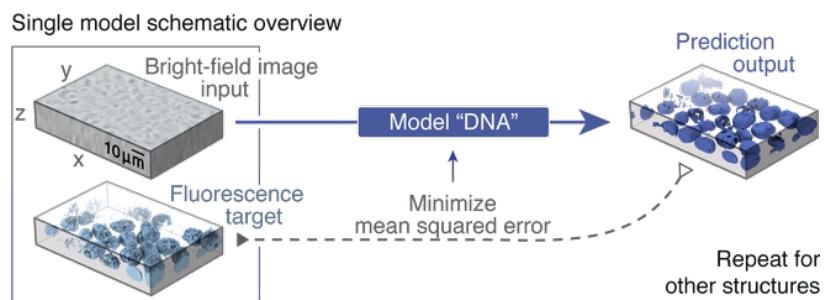
Relax the experimental trade-offs with DL



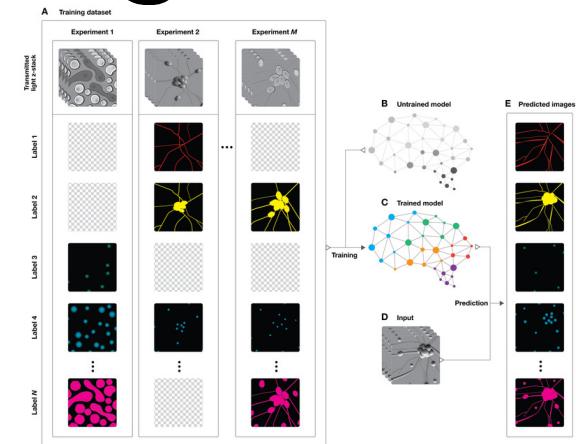
Data and algorithms for image translation



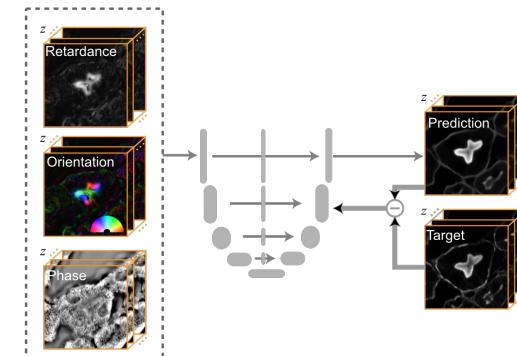
2D Pix-to-Pix (adversarial networks)
(Zhu et al., ICCV 2017; Isola et al., CVPR 2017)



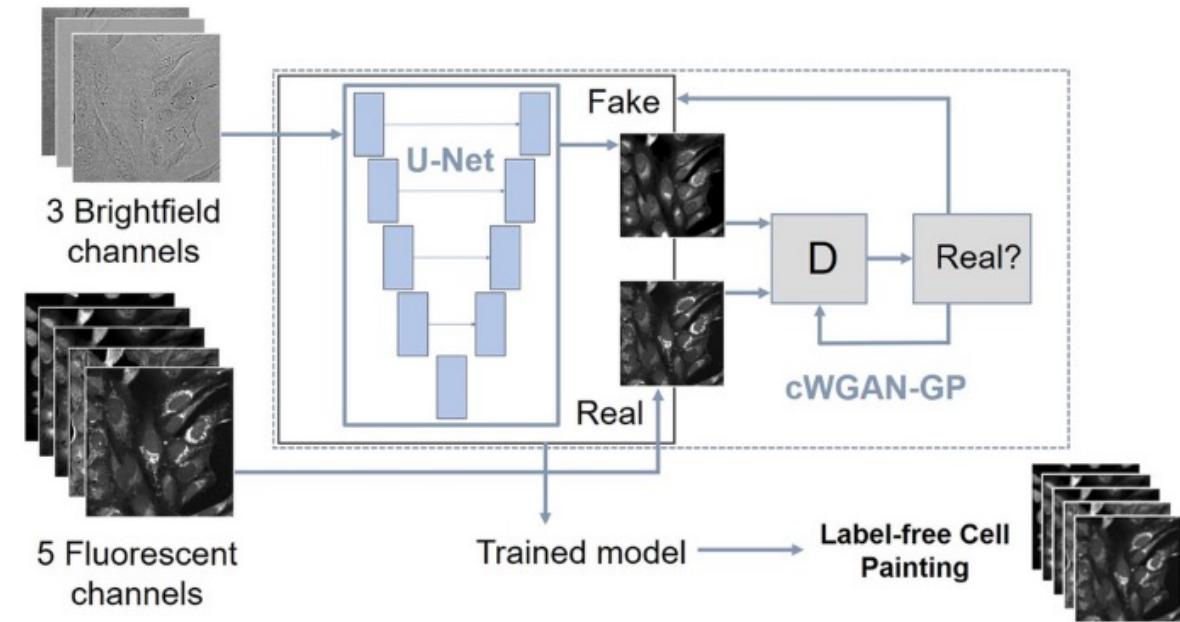
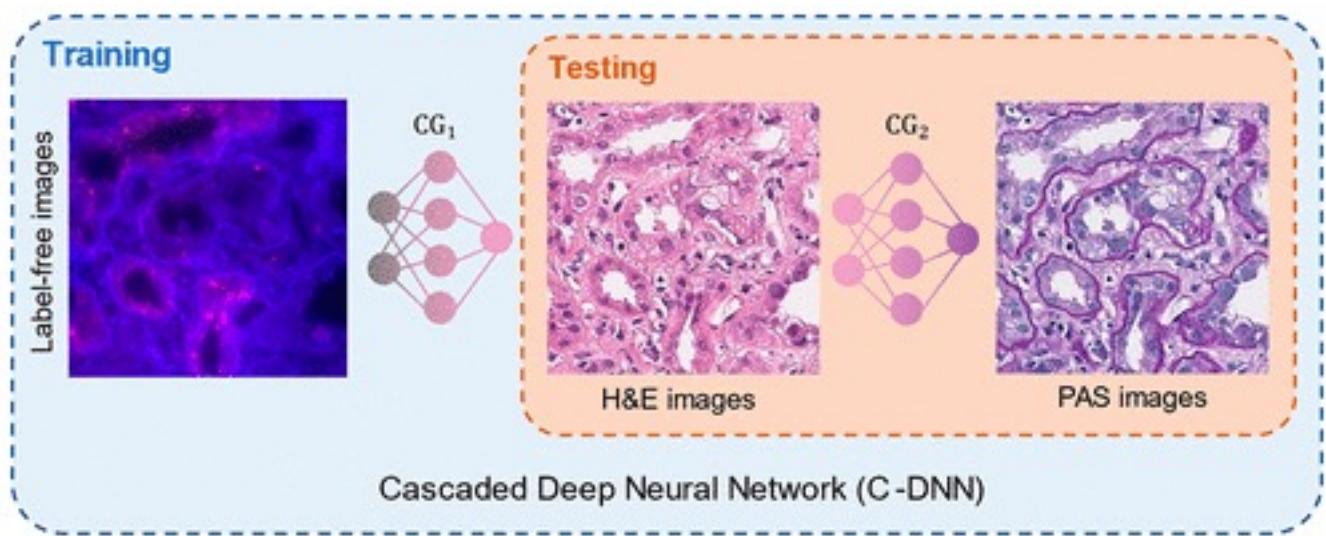
3D Label-free determination (3D U-Net)
(Ounkomol et al., Nature Methods, 2018)



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



3D image translation (2.5D U-Net)
(Guo, Yeh, Folkesson et al., eLife, 2020)

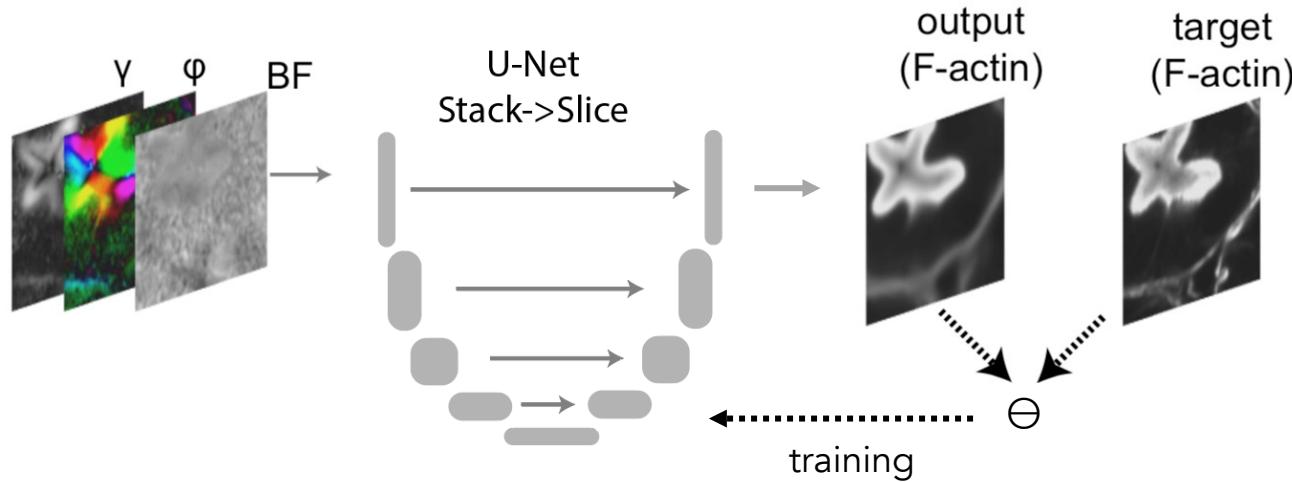


Yang...Ozcan ACS Photonics, 2022

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

3D virtual staining with multiple inputs

Predict molecular images from label-free images



Syuan-Ming



Anitha

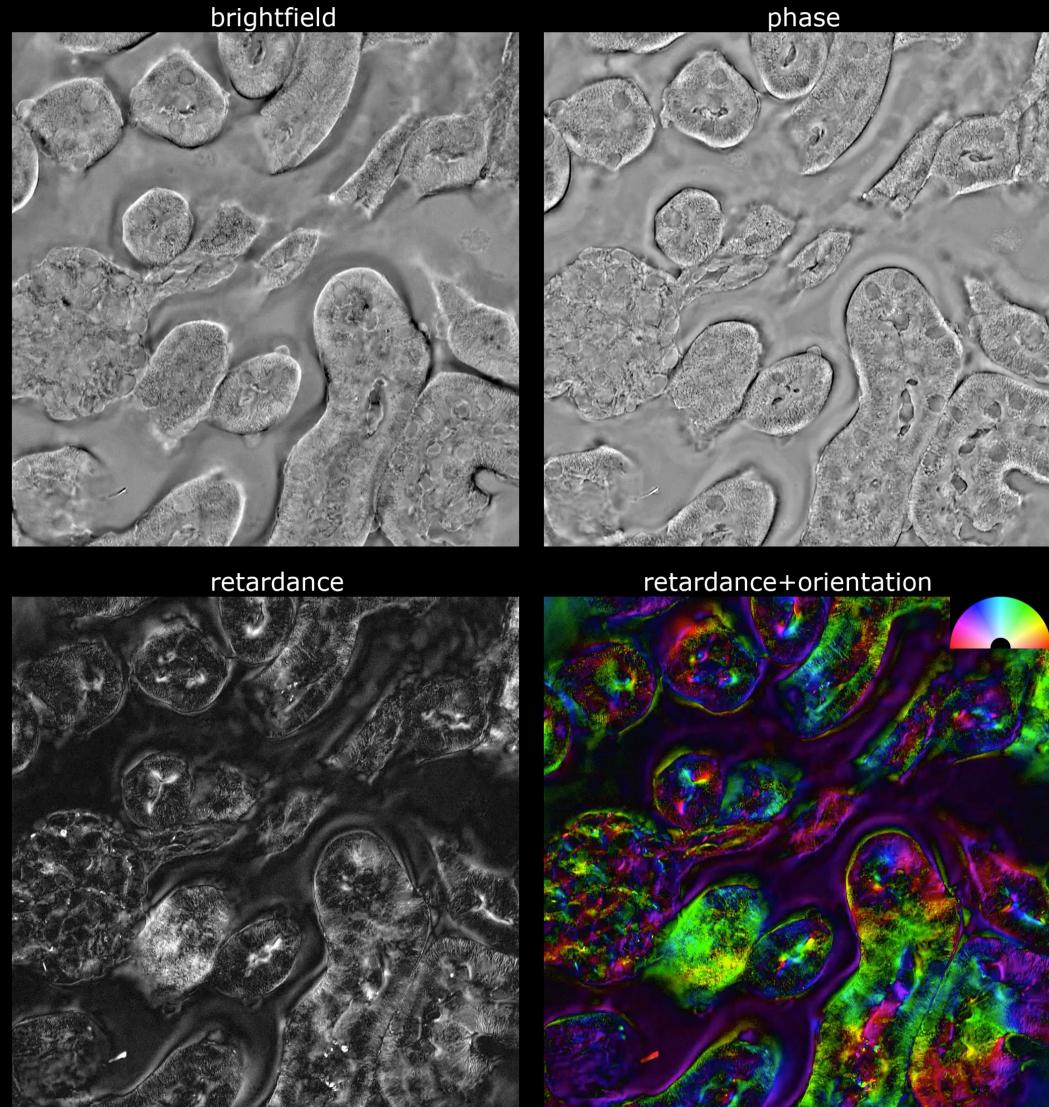


Jenny

[Guo, Yeh, Folkesson, et al., eLife 2020](#)

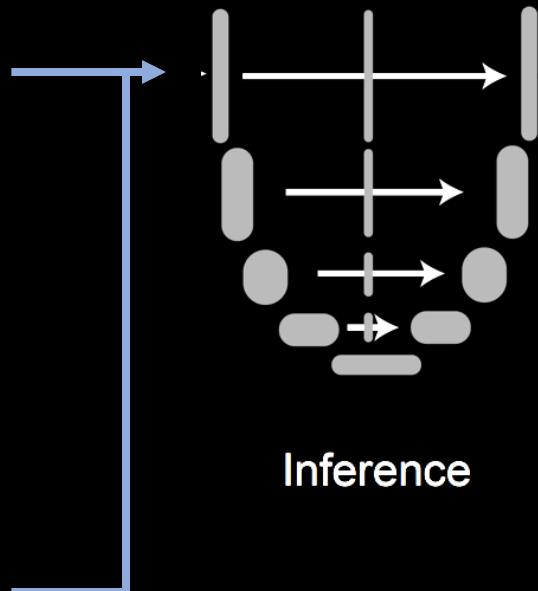
[https://github.com/mehta-lab/microDL
data](https://github.com/mehta-lab/microDL)

Efficient 3D virtual staining with 2.5D U-Net



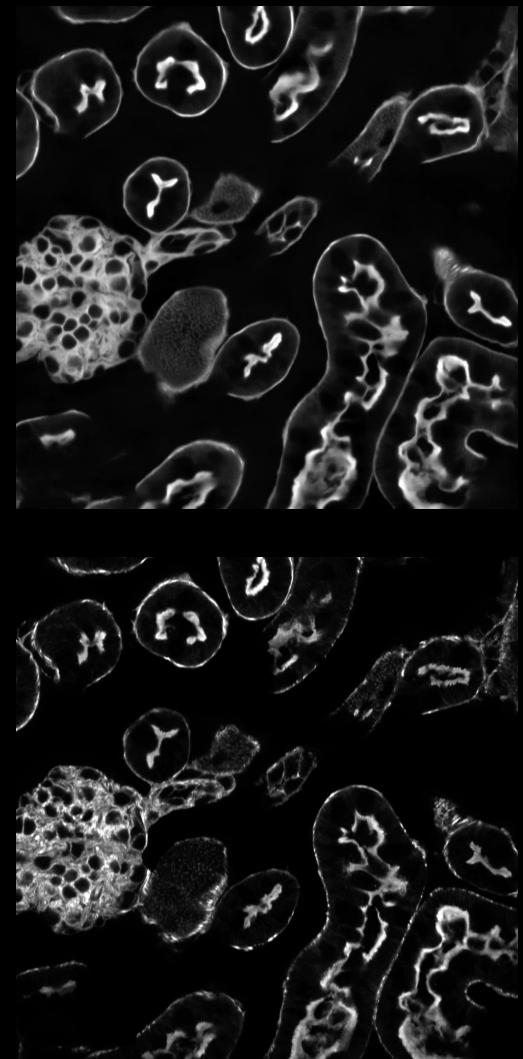
predicted F-actin

Multi-channel
2.5D U-Net



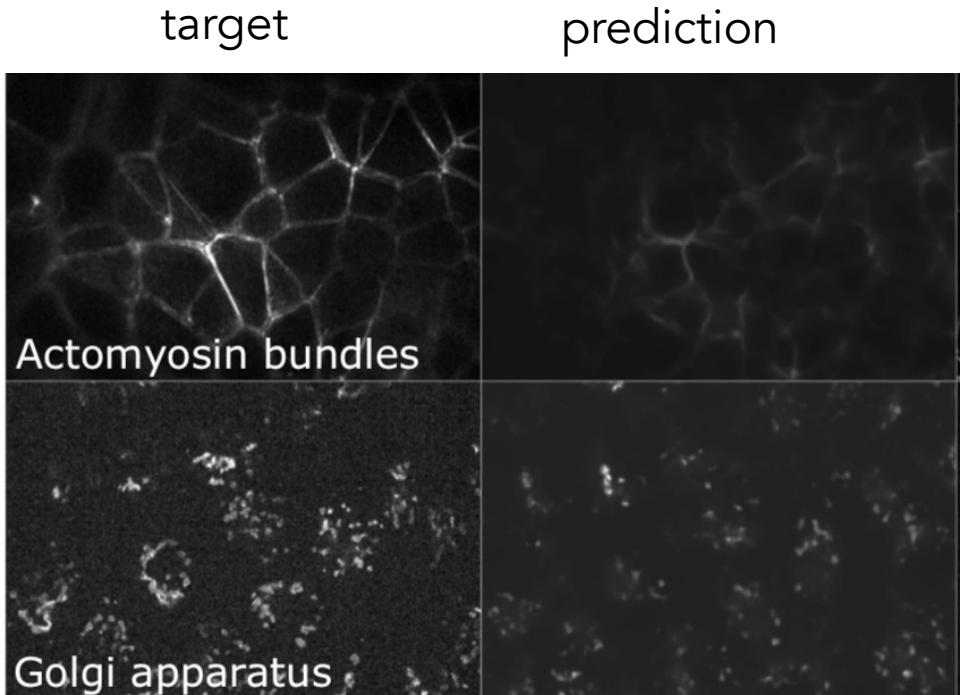
Inference

ground truth

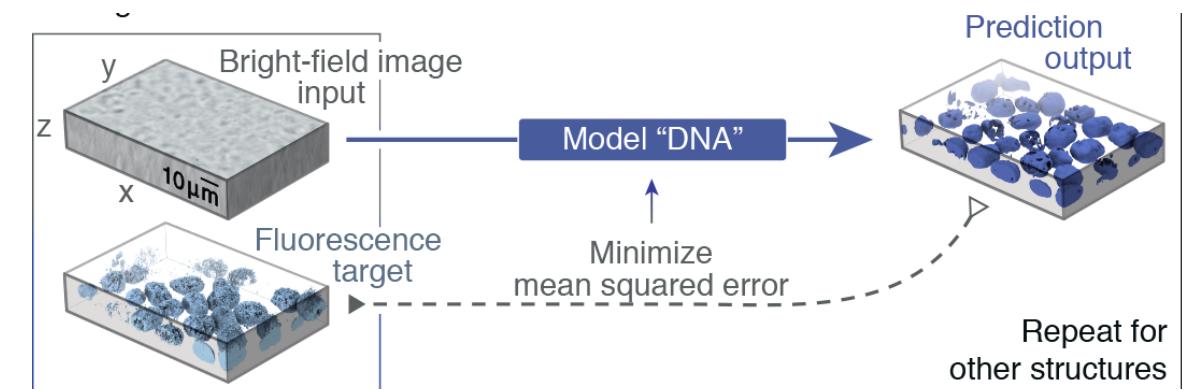


comparison with earlier methods

Machine cannot learn what microscope does not see



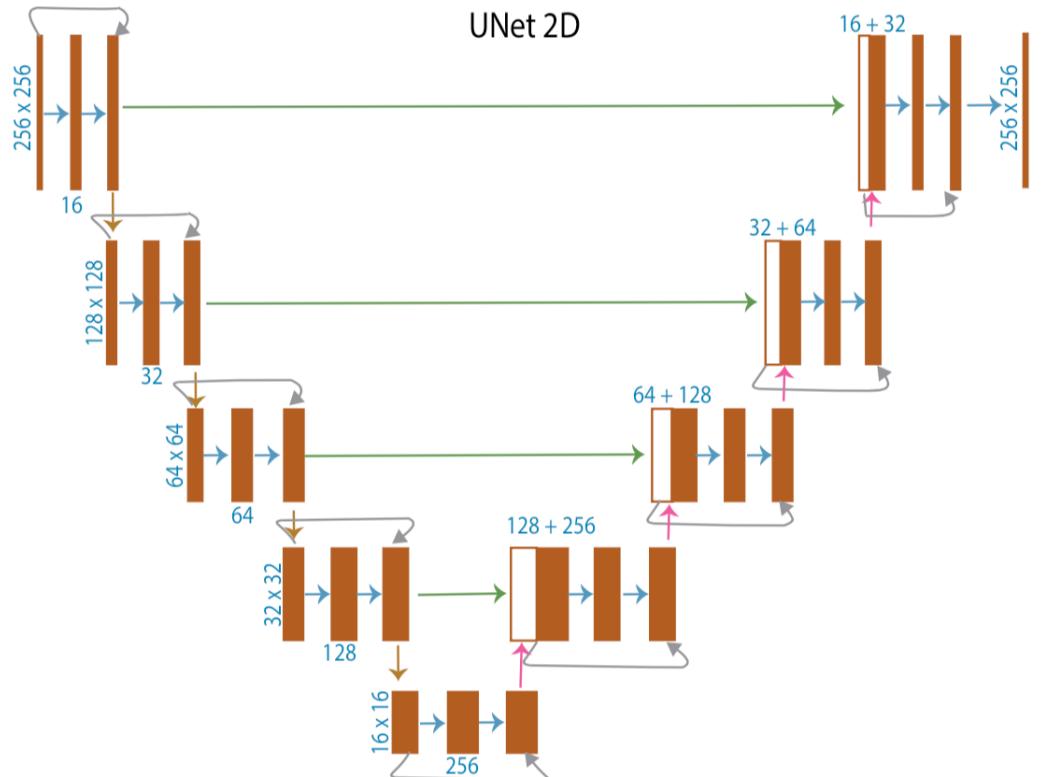
3D prediction is computationally expensive



Ounkomol,...,Johnson, 2018

Complex models (Inception, cycle GAN have remained limited to 2D images)

2D virtual staining



Residual connections enable faster convergence of deep model

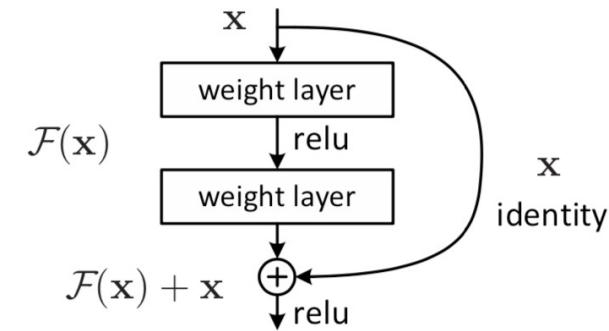
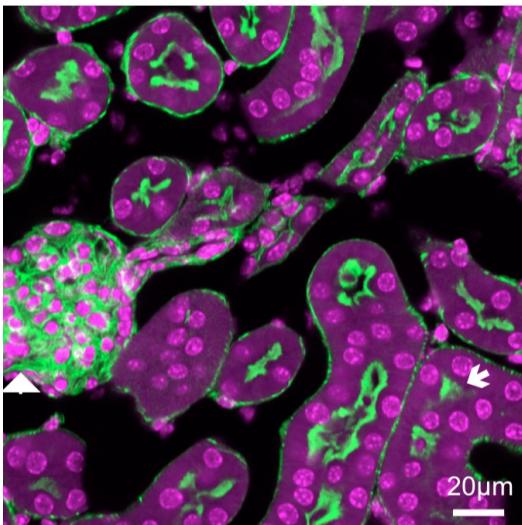


Figure 2. Residual learning: a building block.

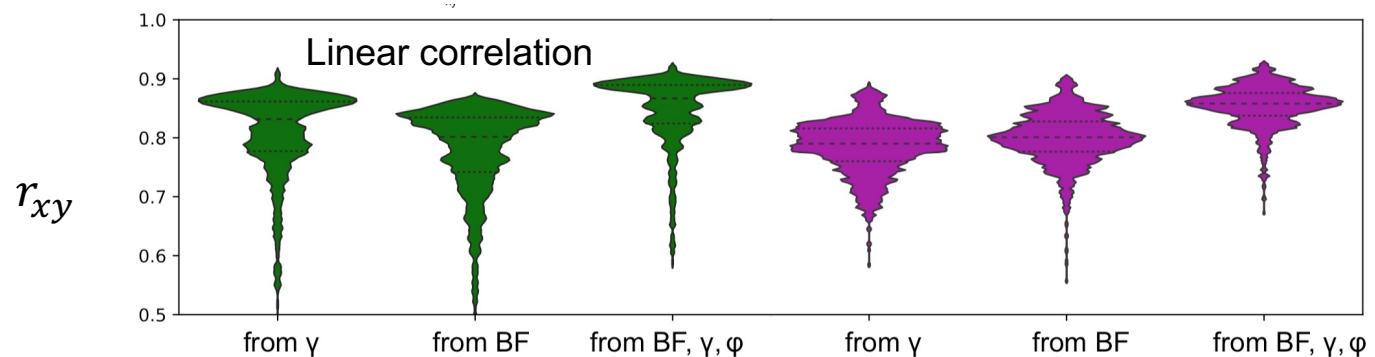
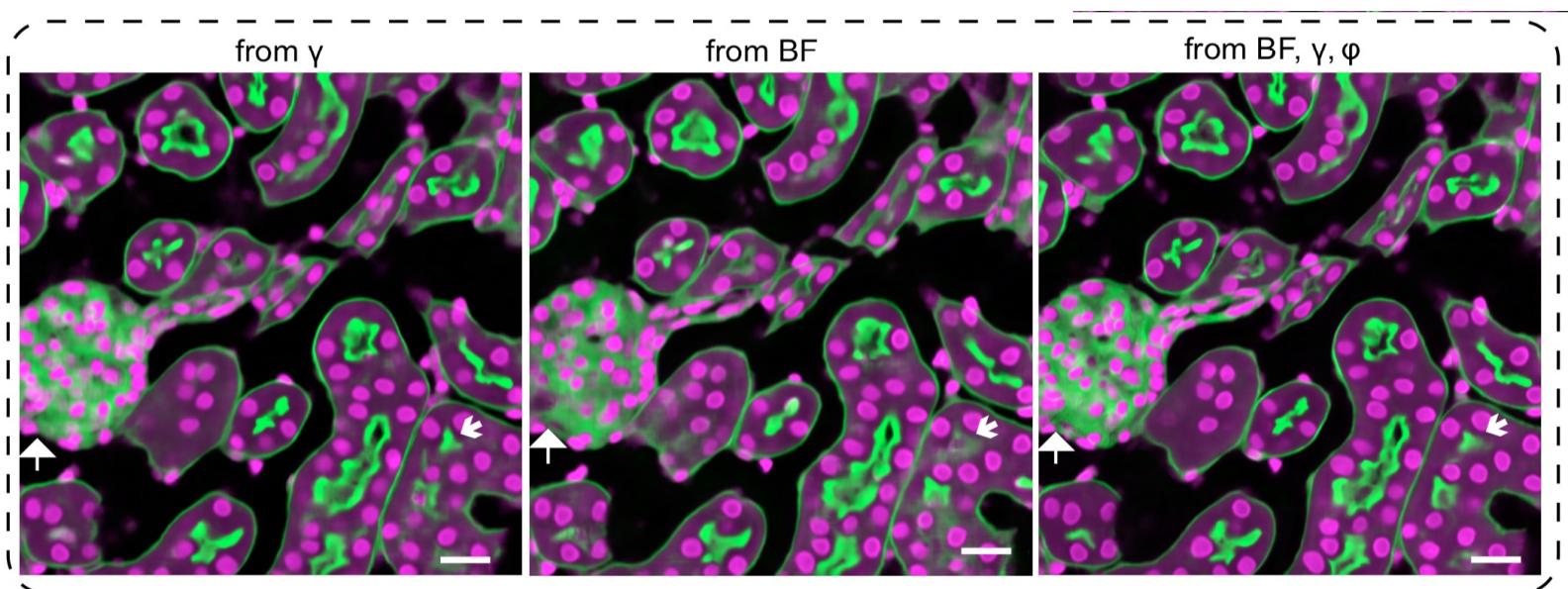
He et al, <https://arxiv.org/abs/1512.03385>

Multi-channel virtual staining

Ground truth (F-actin/DNA)

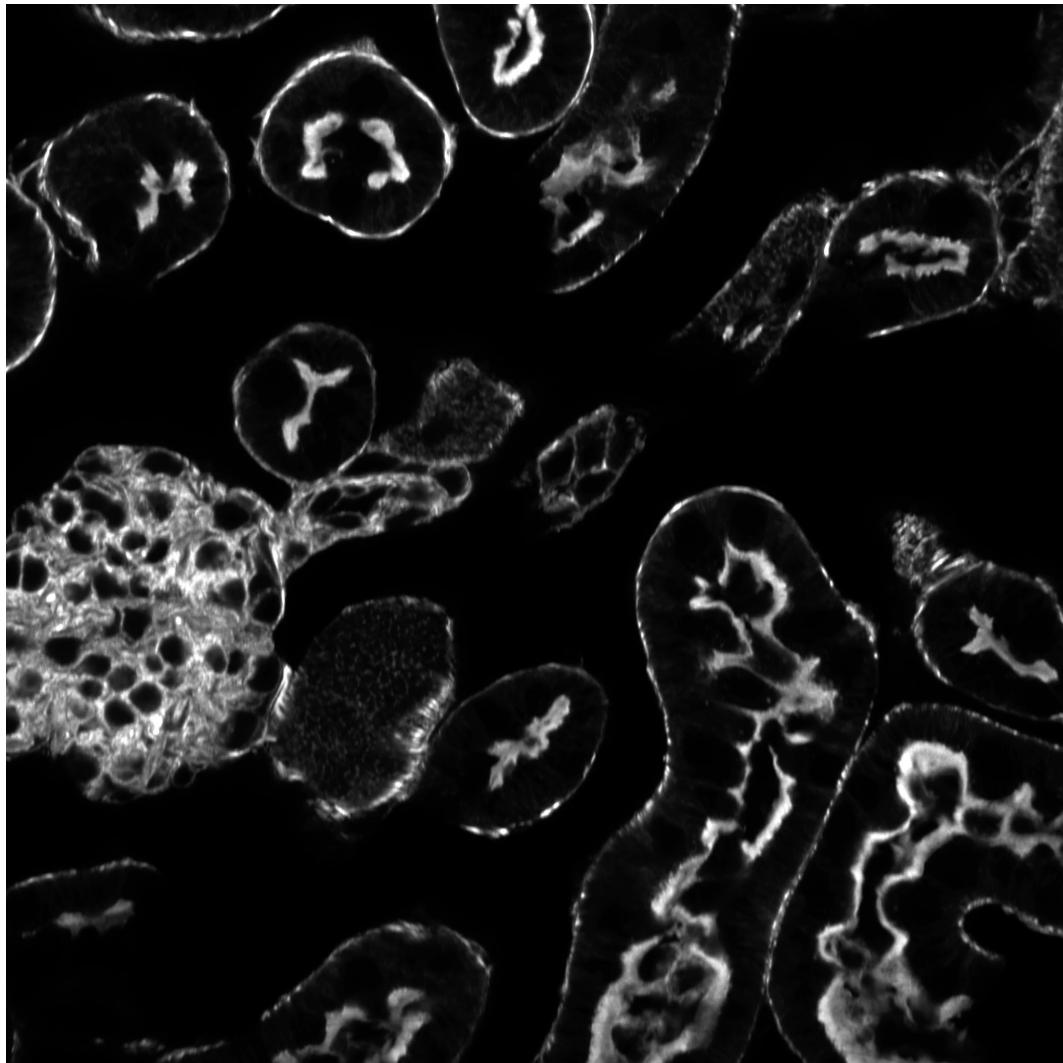


Predictions (F-actin/DNA)

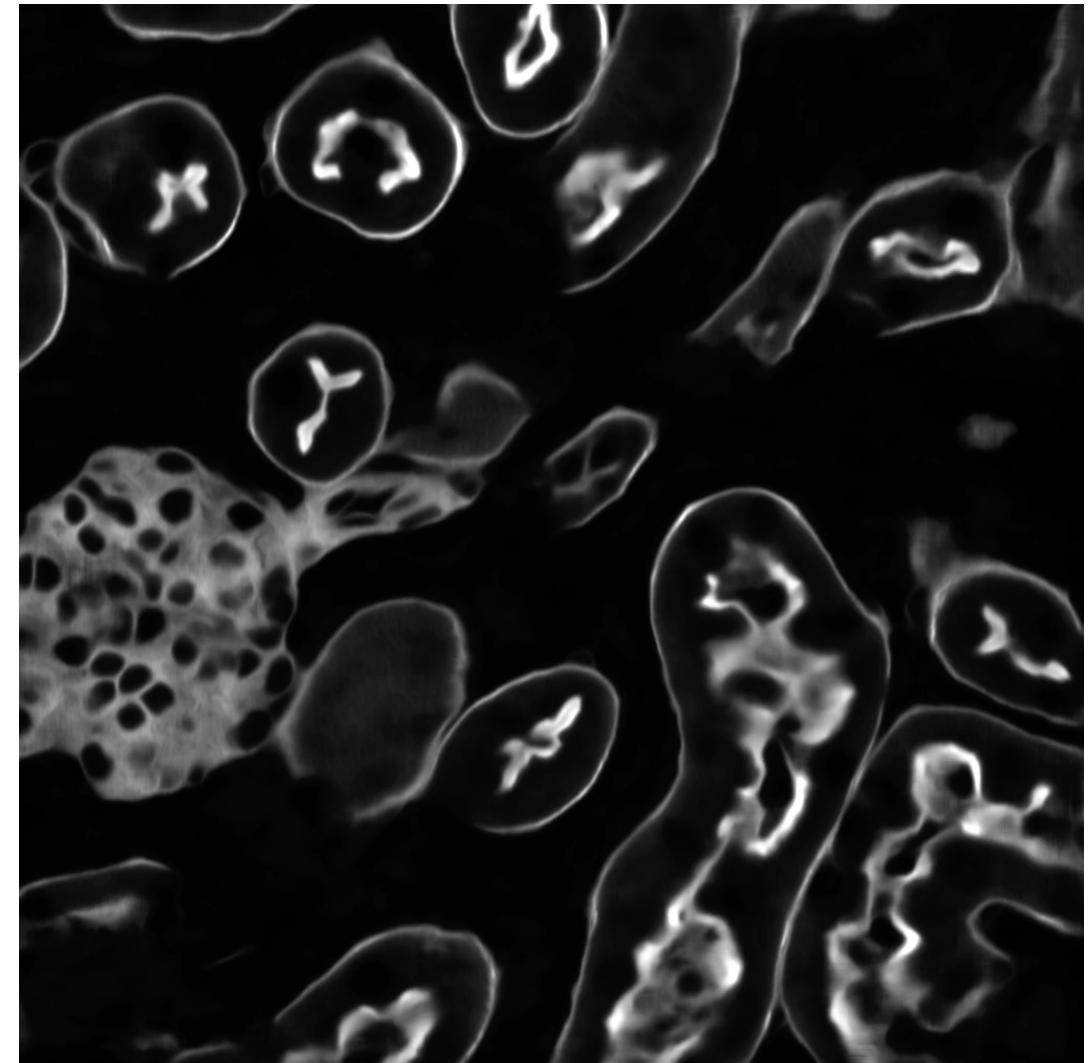


But, prediction along depth is not great

Ground truth

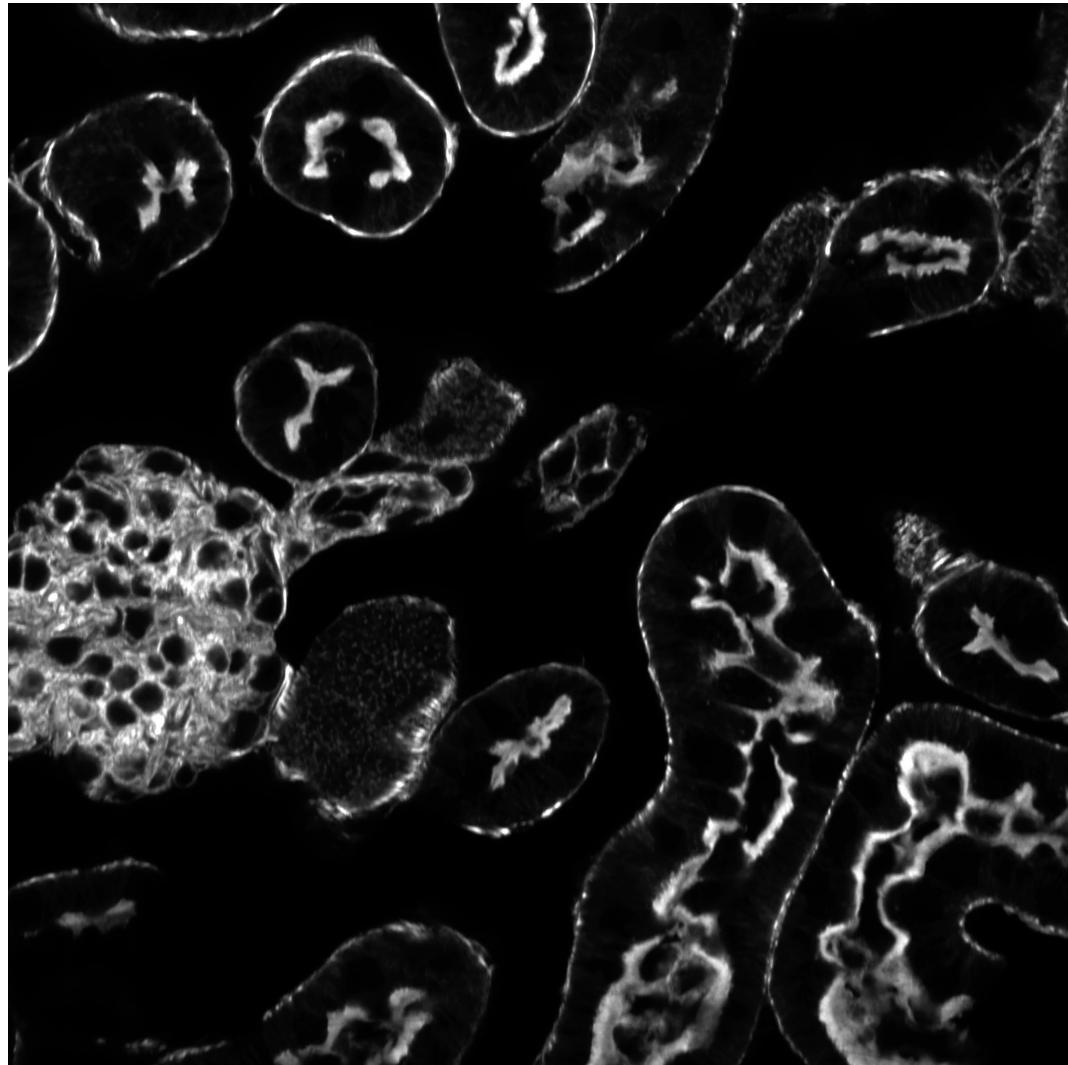


Predicted F-actin from retardance (2D model)

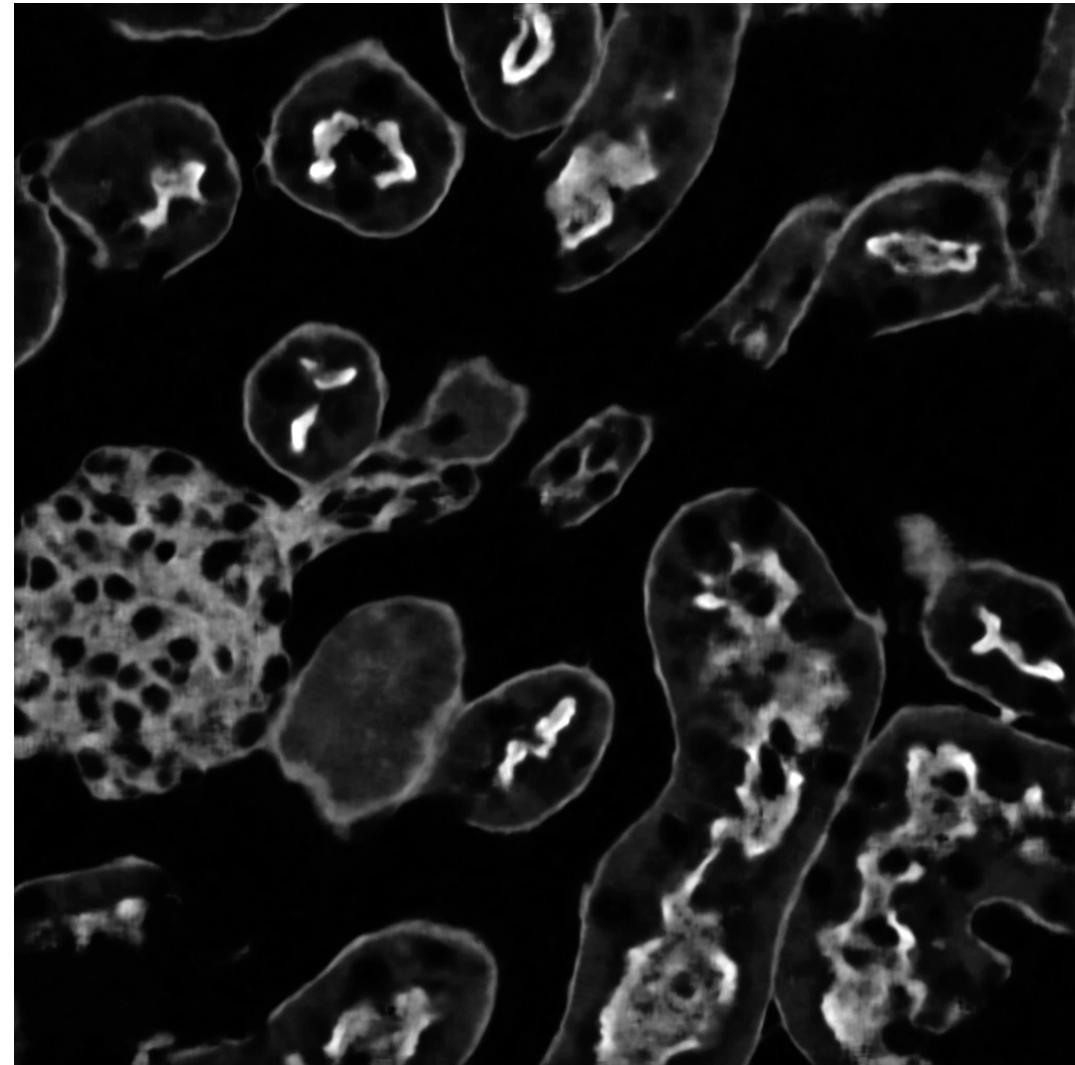


3D virtual staining improves continuity

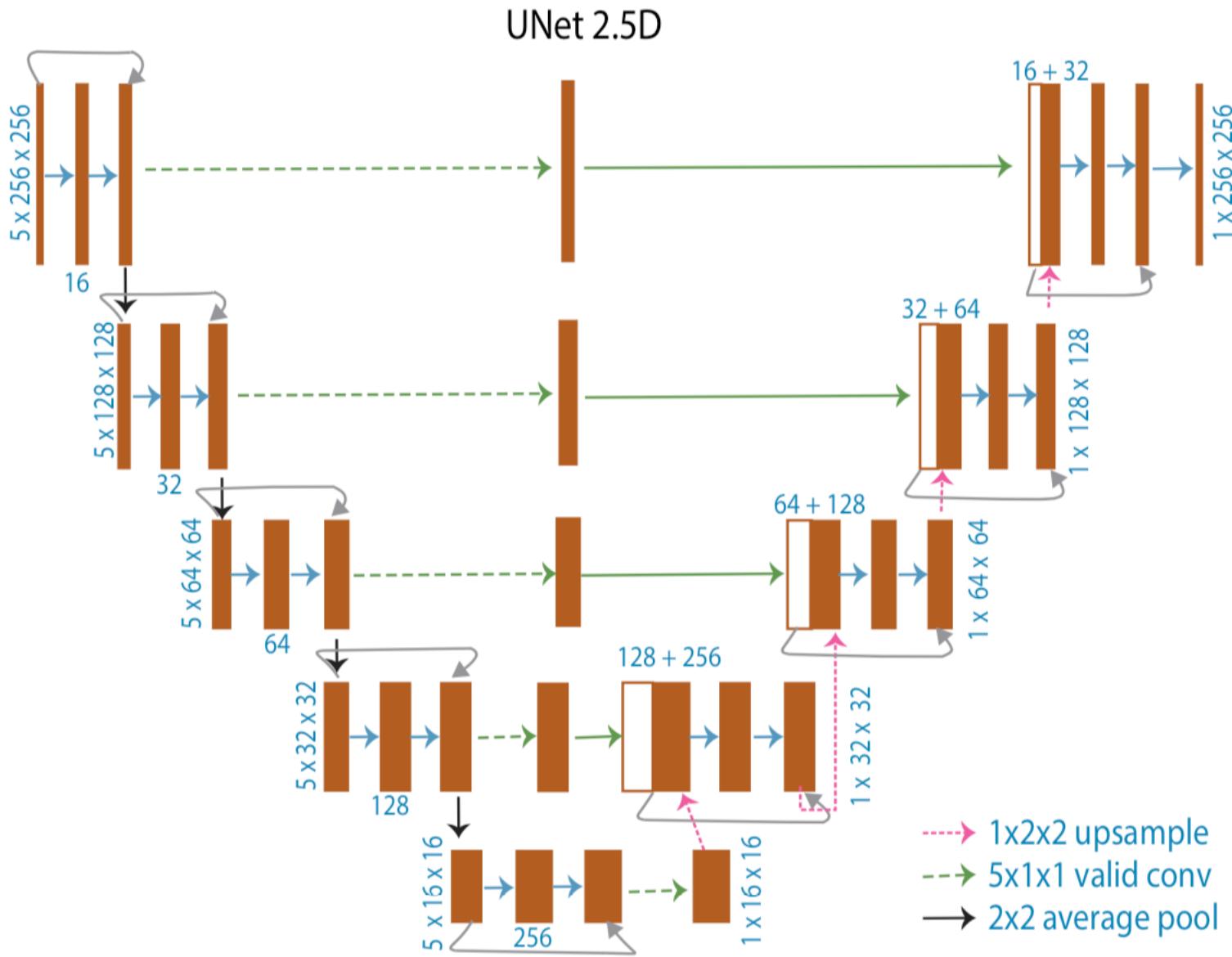
Ground truth



Predicted F-actin from retardance (3D model)

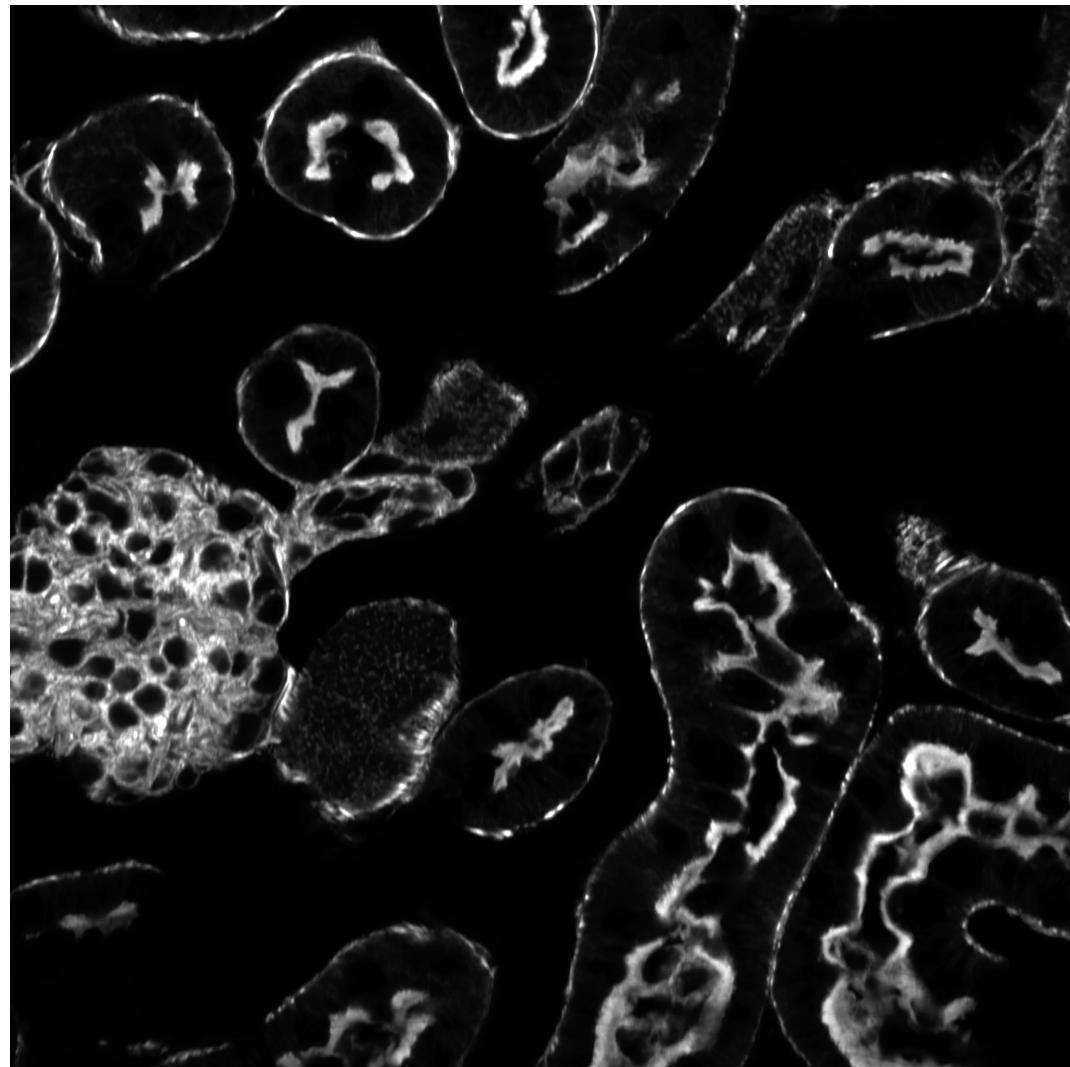


2.5D model

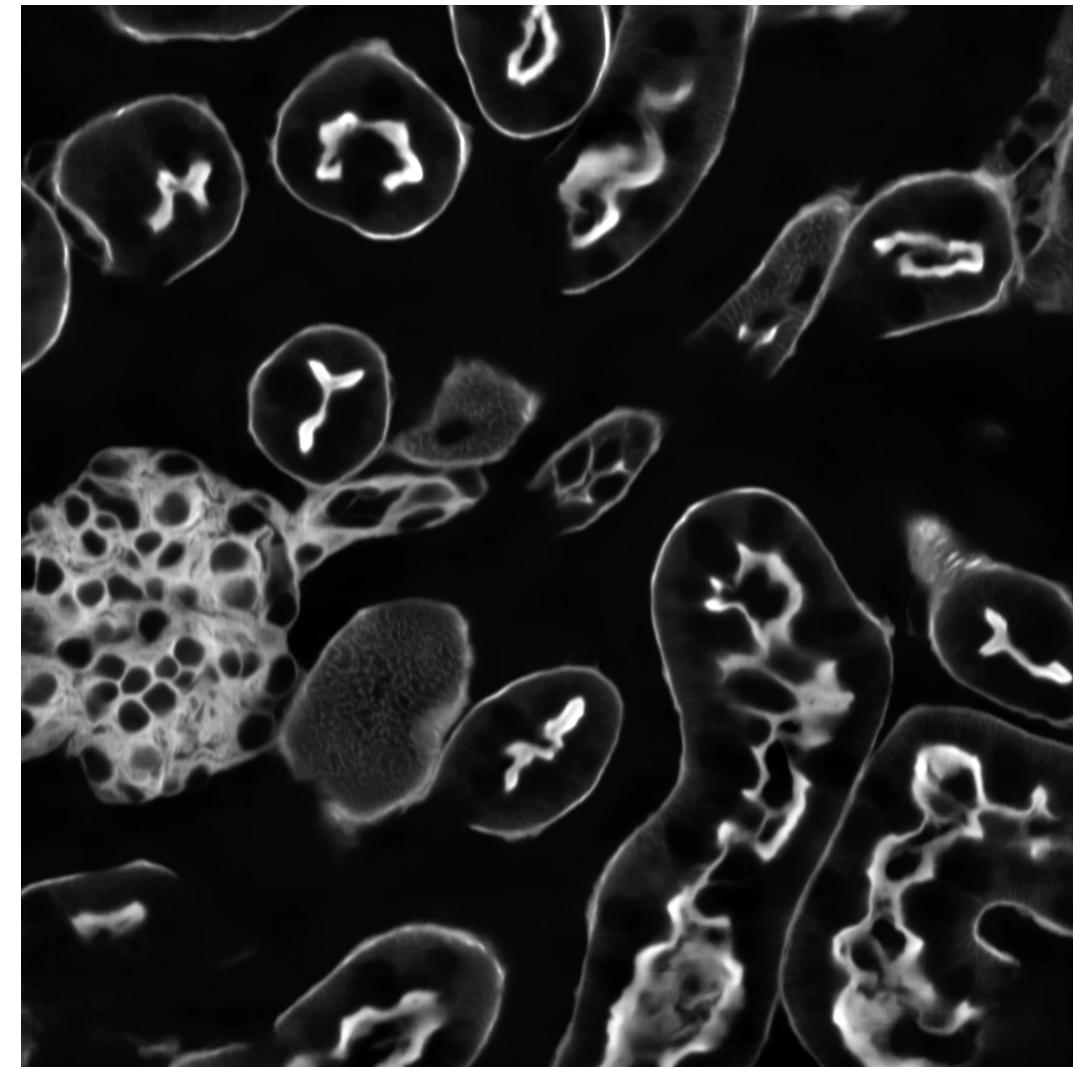


2.5D virtual staining

Ground truth

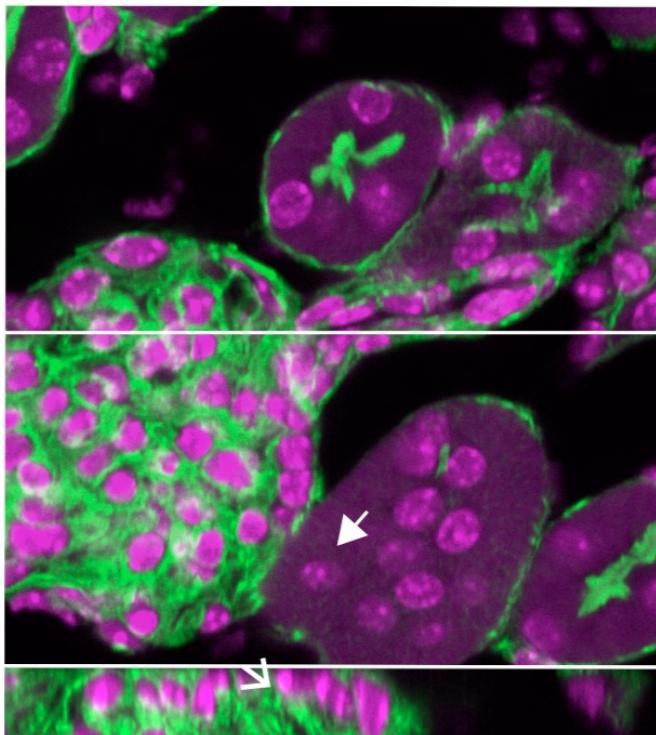


Predicted F-actin from γ (2.5D model)

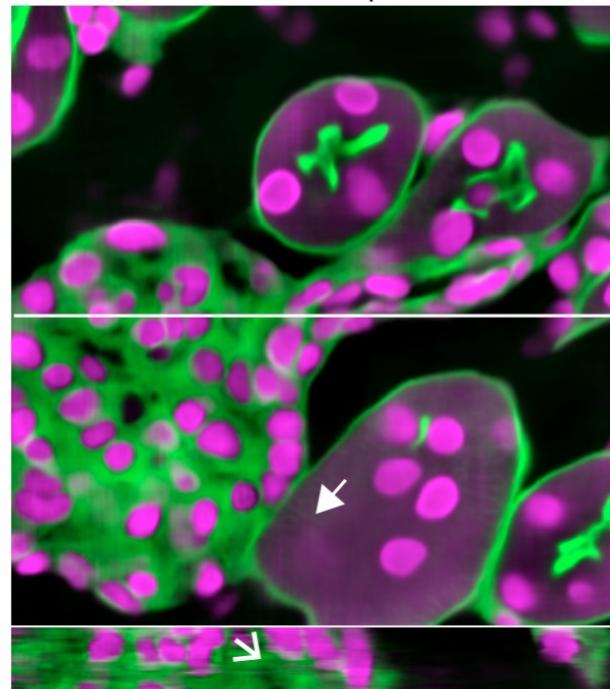


Multi-channel data improves accuracy

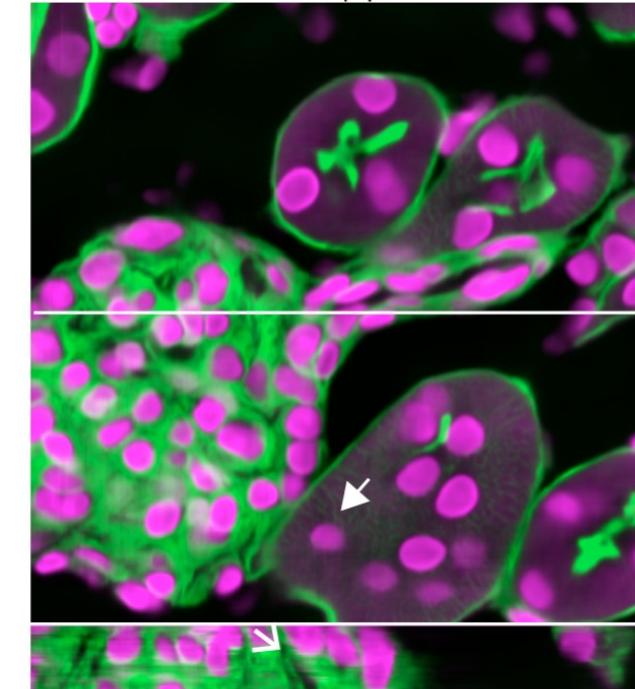
A ground truth (F-actin/DNA)



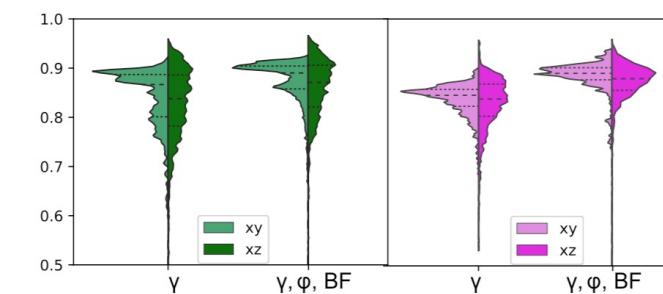
B predictions (F-actin/DNA)



from γ, φ, BF

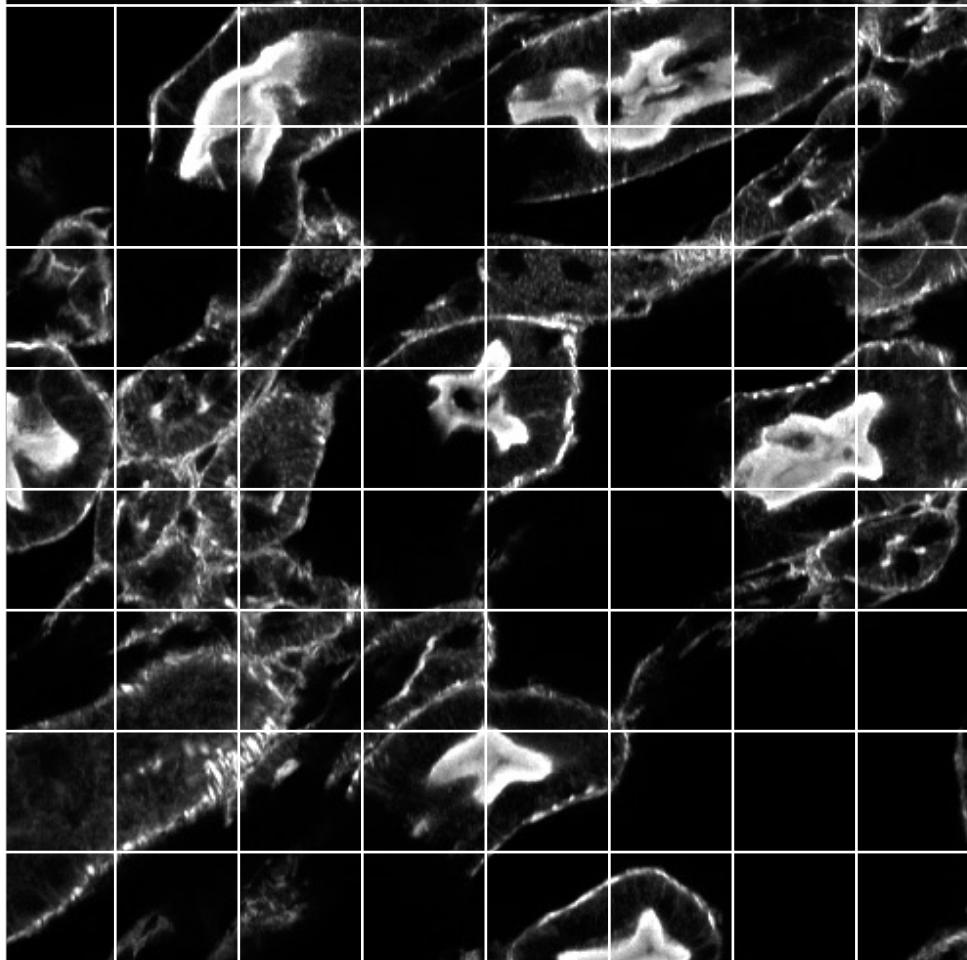


r_{xy}



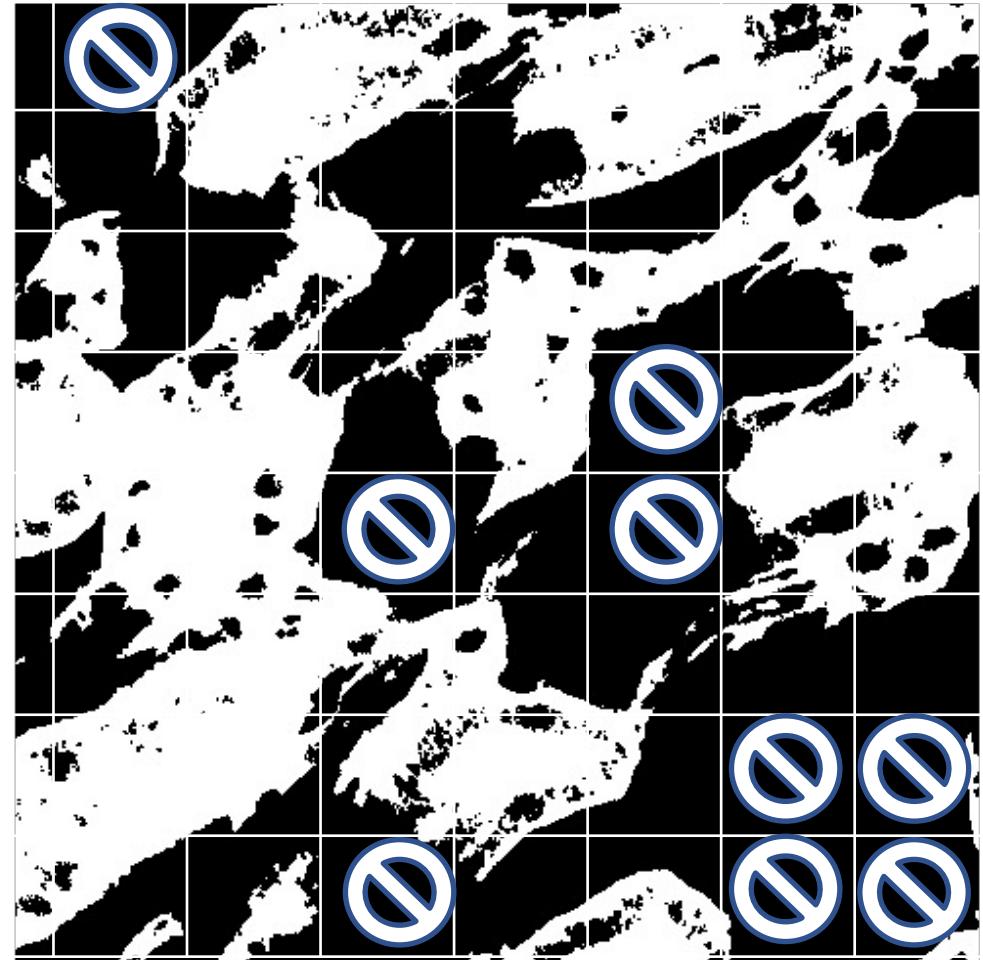
Mask background to balance classes

Masking



Tiling

Tile selection



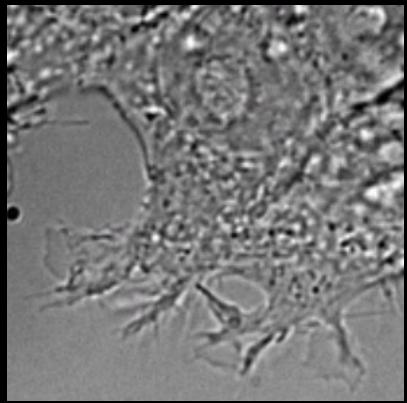
Important details

- **Registration is critical:** photolithographic fluorescent glass target visible in all label-free and fluorescent channels for precise 3D registration.



- **Regularization reduces overfitting:**
 - Dropouts: stochastically turn-off some fraction of weights.
 - Batch normalization: make sure that features are zero mean, unity variance

Agenda



$$y = H_j x S_i + n$$

computational
imaging

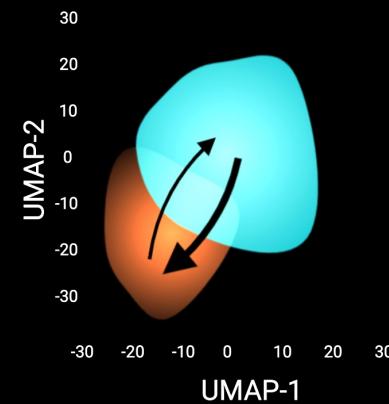


x

image
translation



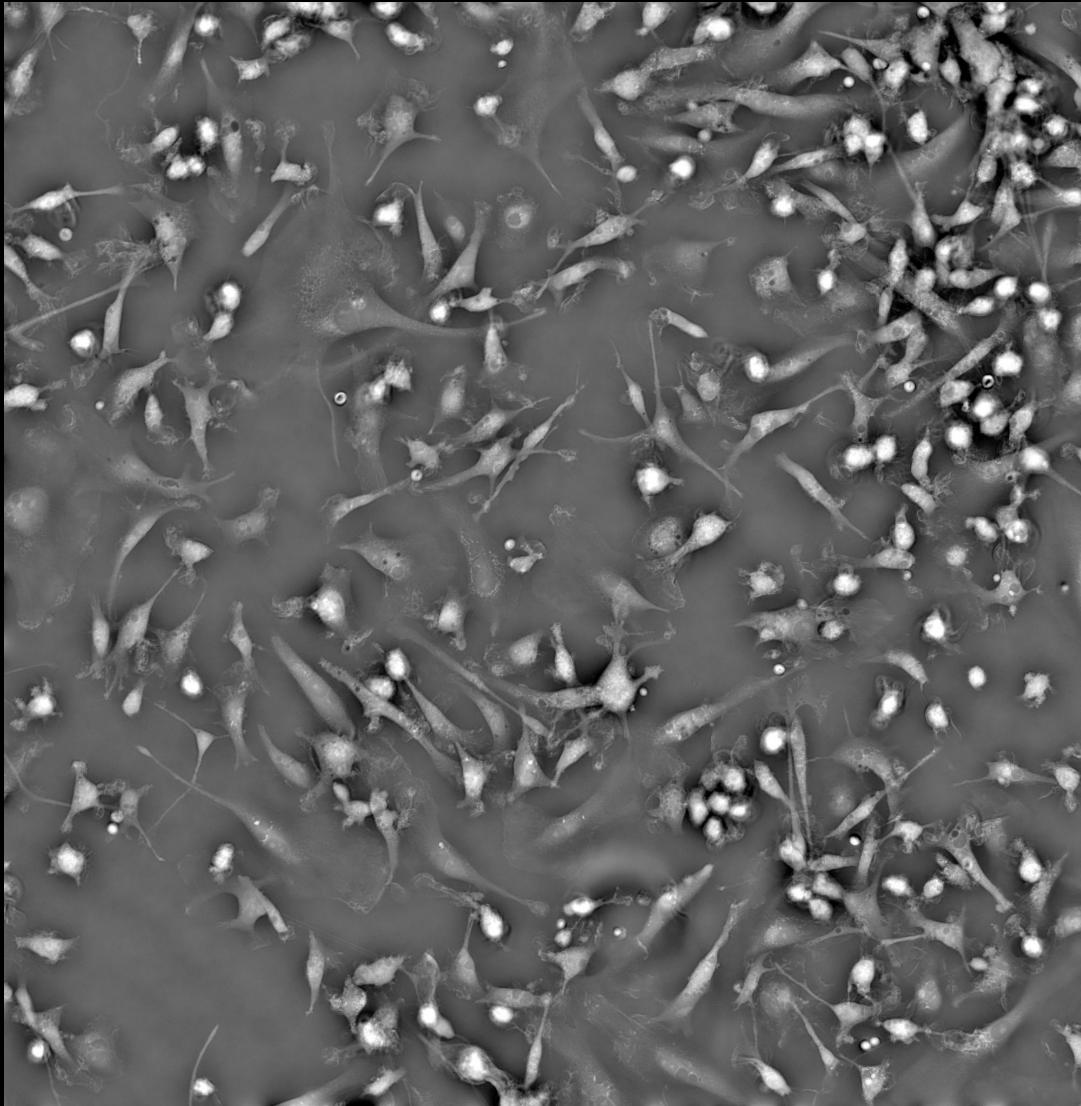
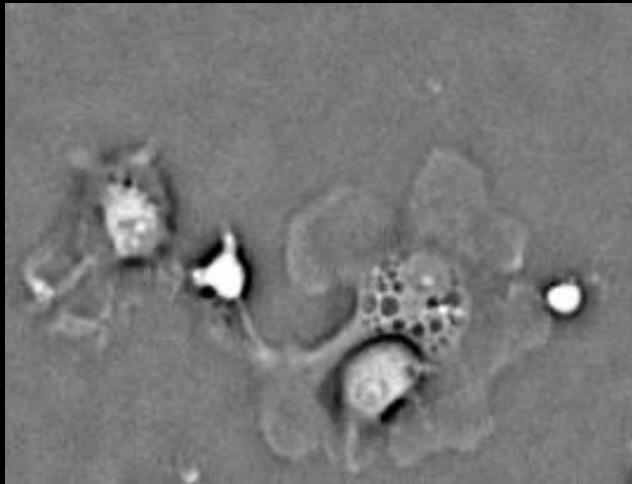
representation
learning



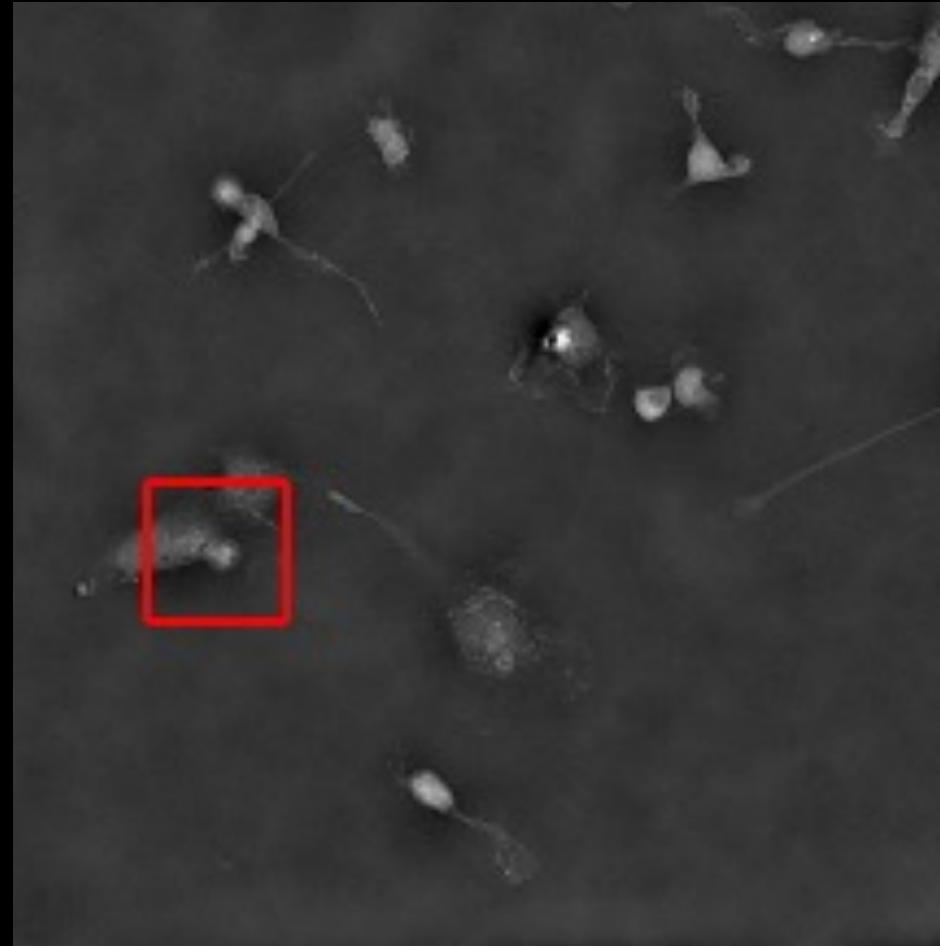
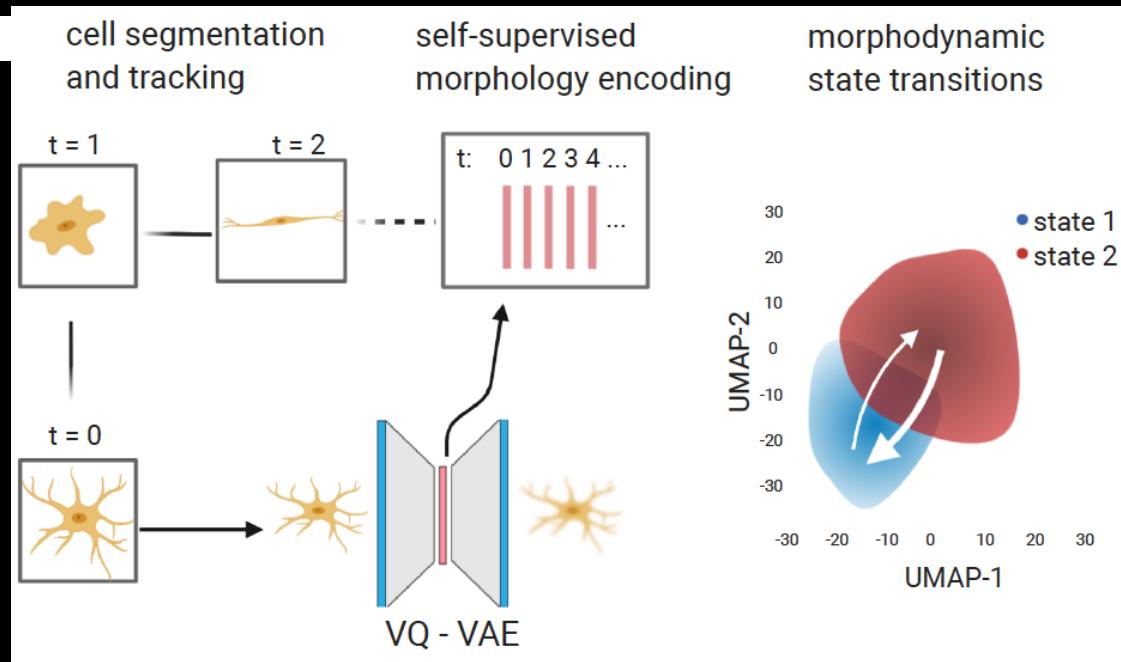
Learning from quantitative images without extensive annotations

- Detect complex states with single cell resolution
- Automated, principled dimensionality reduction.
- Annotations in latent space.
- Discover phenotypes that are not accessible to human vision.
- Measure intrinsic and perturbation-driven transients from live imaging data

Quantifying complex dynamics



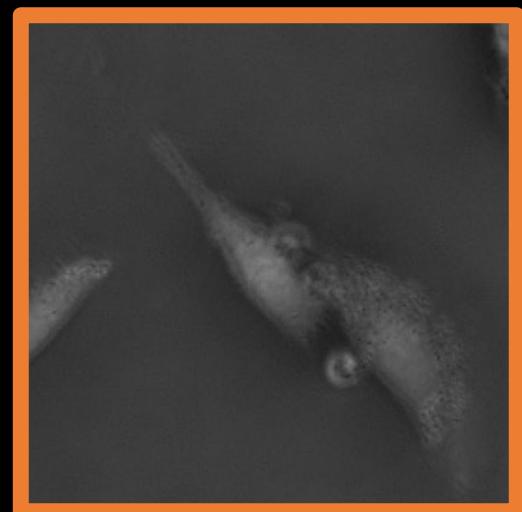
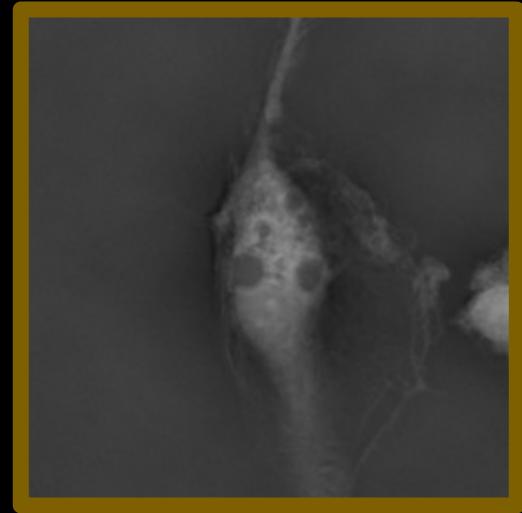
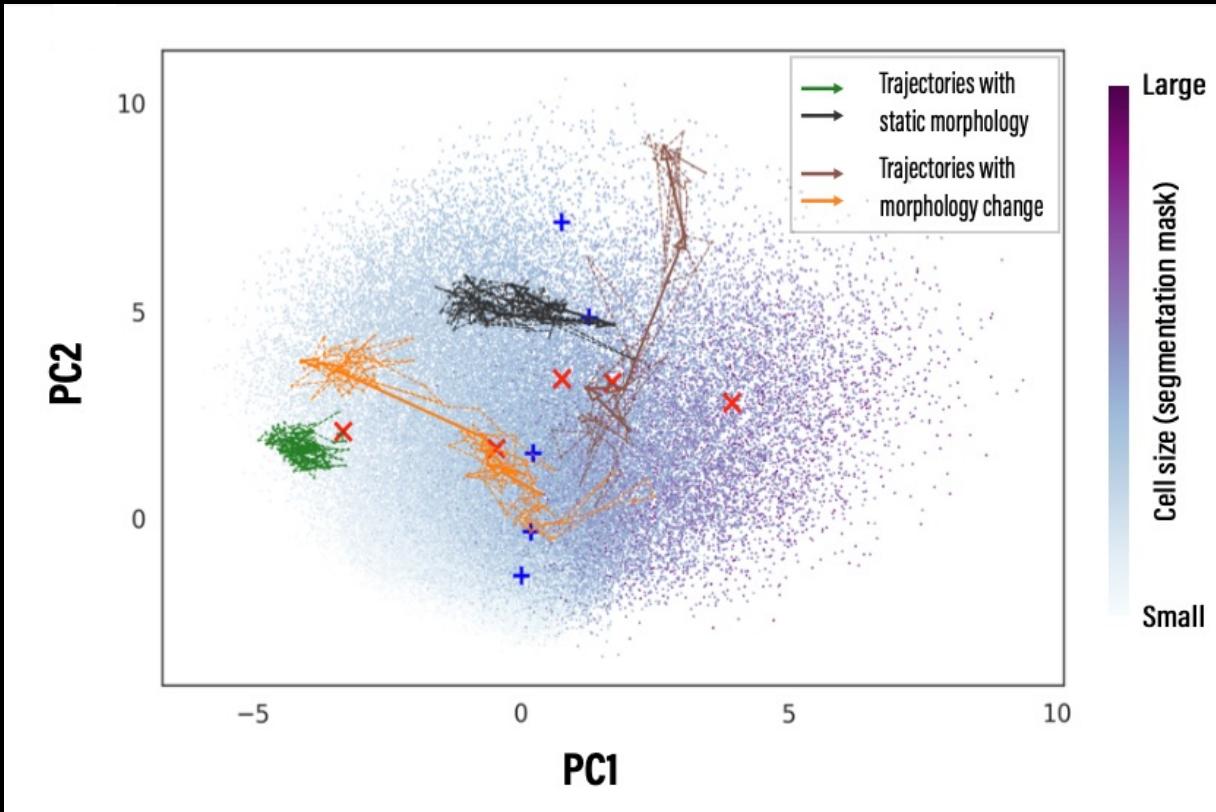
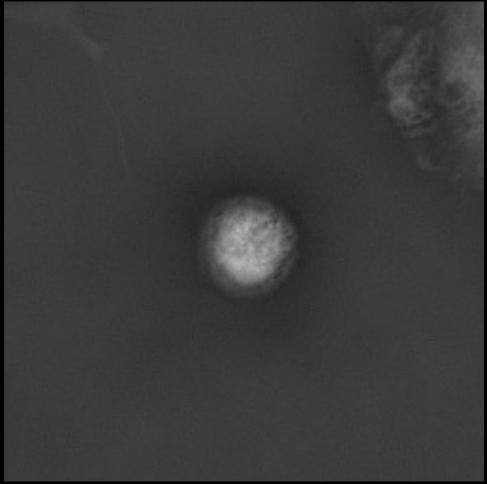
Learning temporally consistent representation



Wu et al., MBoC 2022

<https://github.com/mehta-lab/dynamorph>

Detecting transients in dynamics



Summary

- Quantitative label-free imaging provides physical specificity.
- Multi-channel 2.5D U-Nets are computationally efficient, almost as accurate as 3D U-Nets.
- Augmentations improve robustness & metrics are needed!
- Latent representation learned with self-supervision over time generalize well.

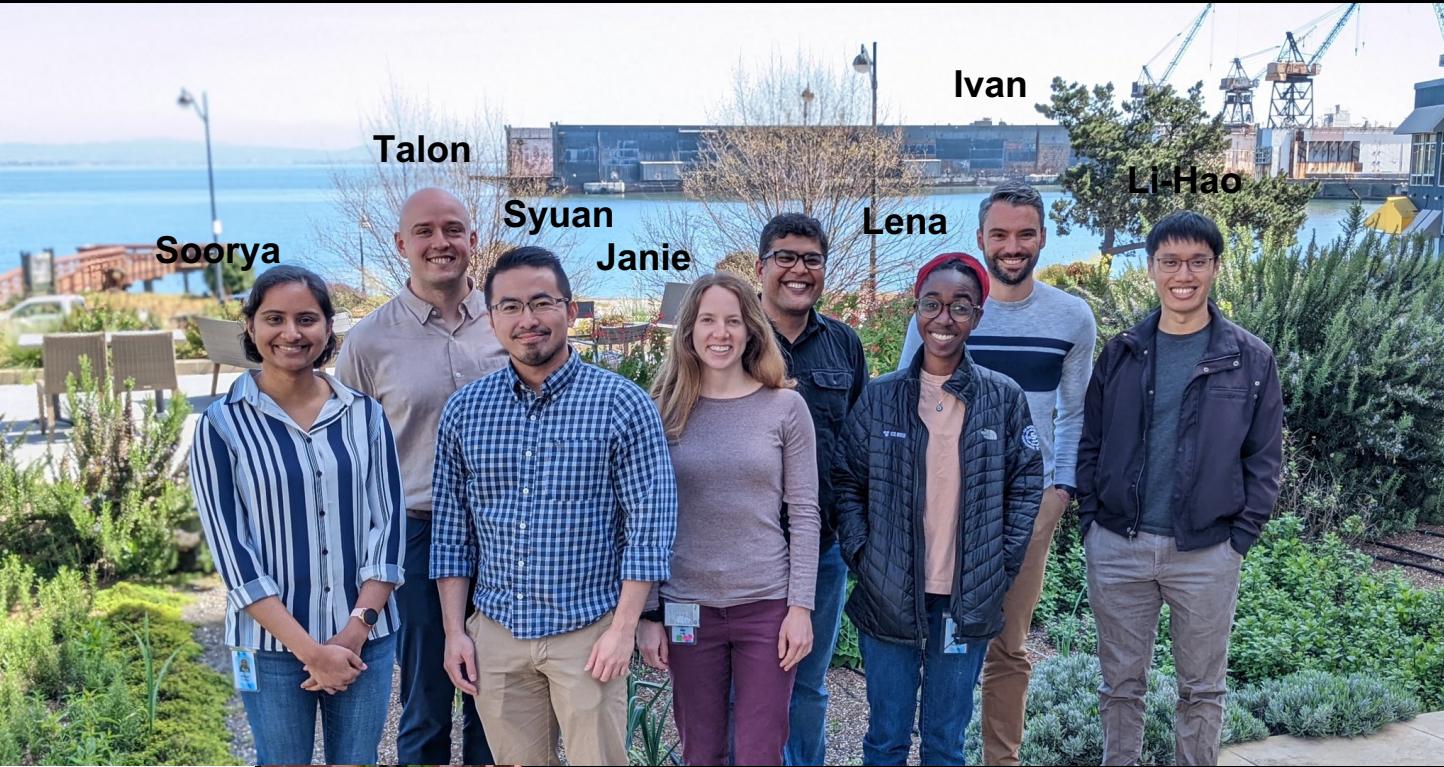
Next ...

- integrate physics-driven and data-driven models more frequently, more thoughtfully.
- develop metrics of accuracy when ground truth is incomplete.
- adopt practices for efficient development and deployment of models.

Project ideas:

- (courtesy: Talley) fast and accurate focus detection with physics-driven and data-driven algorithms.
- 3D segmentation, restoration, translation with 2.5D U-Net.
- virtual staining using CARE pipeline.
- generalizable virtual staining.

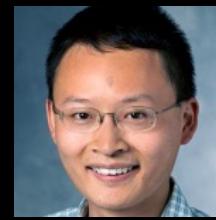
Thank you!



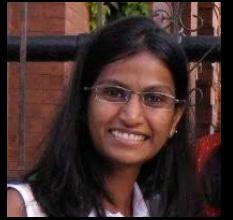
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