



# Evaluating Health and Differentiation of Stem Cell Colonies from Unlabeled Images



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## Background

- Induced pluripotent stem cells (iPSCs) are extensively used in drug screening, human tissue modeling, understanding disease progression, and designing cell therapies
- While iPSCs offer immense potential for research, differentiating them into specific cell types or tissues is a time-intensive and delicate task
- Daily monitoring is essential to ensure that iPSCs remain viable, healthy, and on course for proper differentiation
- This research seeks to automate the quality control process for iPSCs by training a deep learning algorithm on unlabeled bright-field images of iPSC colonies
- A key objective is to accurately simulate the biological and physical aspects of iPSCs and optical imaging

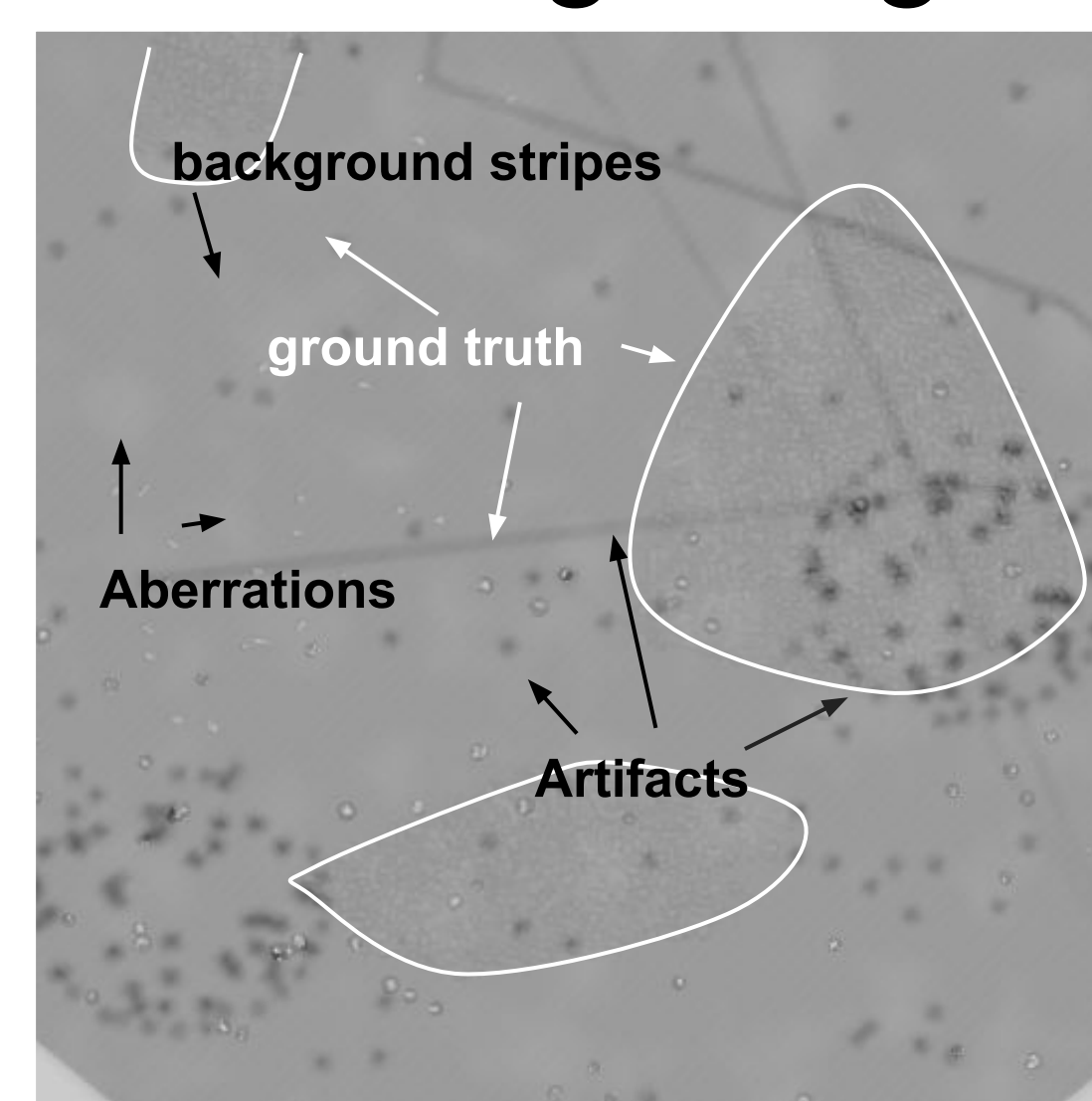
## Methods

- To enhance training accuracy and speed, physics-based ground truth images were generated using Blender, a 3D computer graphics software
- 8th version of the widely recognized pretrained object detection model, YOLO (You Only Look Once), was selected for training
- The model's performance was tested on images of iPSCs from the KOLF2.1J cell line, captured with a confocal microscope at 4x magnification
- Although 20x, 10x, and 4x magnification levels were tested, 4x was ultimately chosen due to the extended time required to capture images at higher levels
- Following the training of multiple model versions, additional elements—including visual artifacts, background intensity, and field of view—were simulated and randomized within the training set

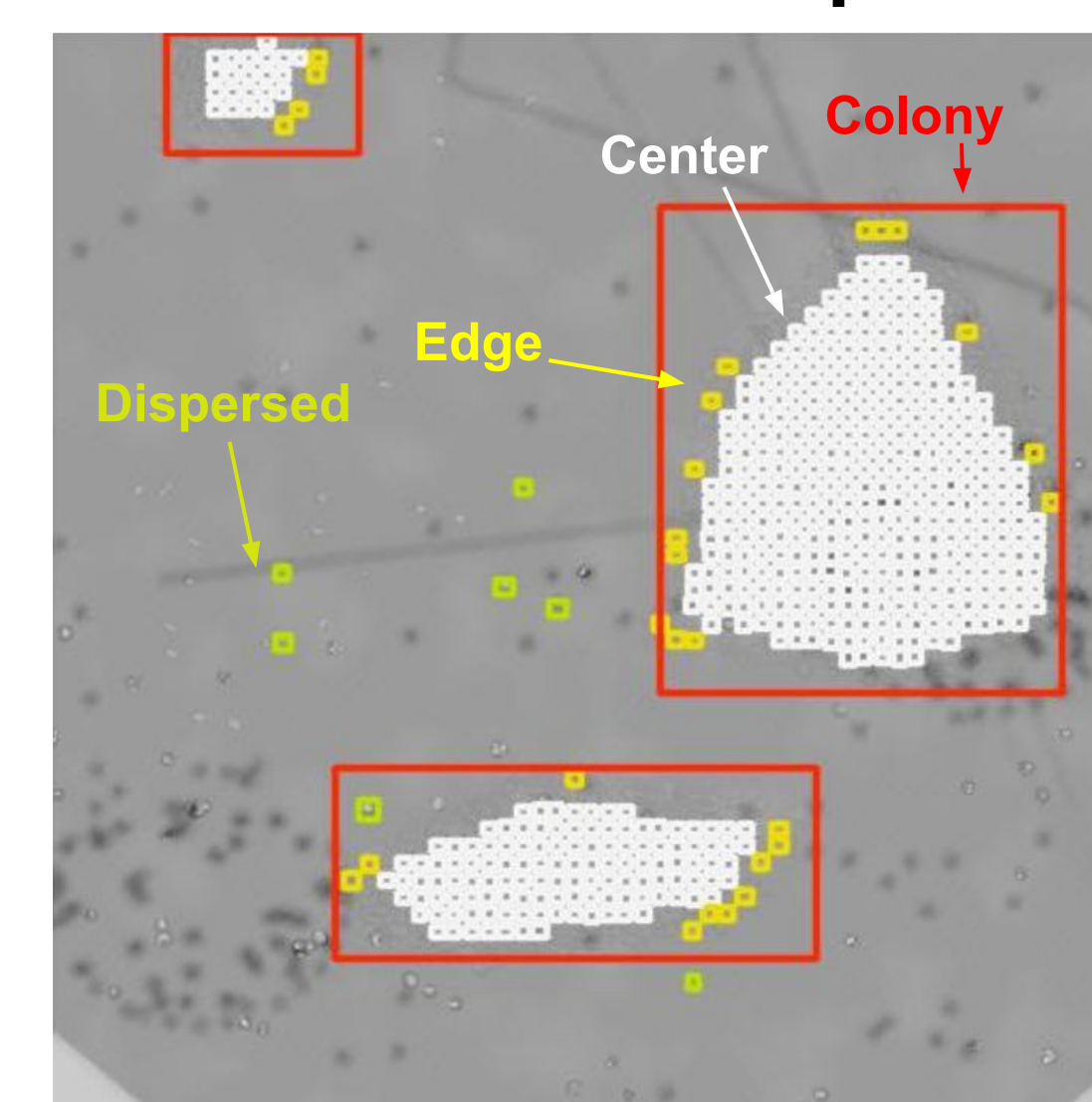
## Results

Batch Size = 1 (stochastic gradient descent); # of Epochs = 40;  
Training Data Size = 3674 ; Test Data Size = 100

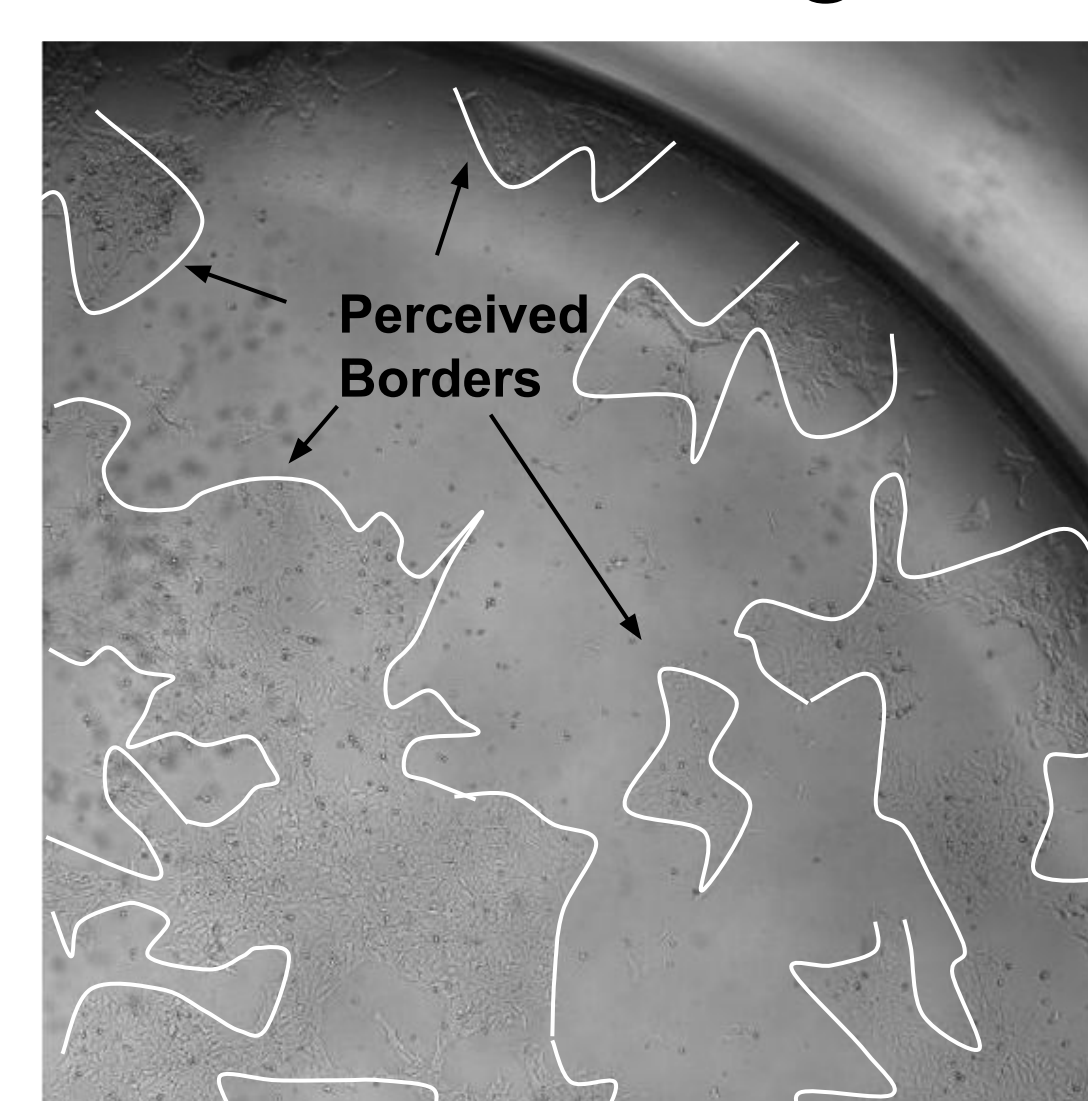
### Training Image



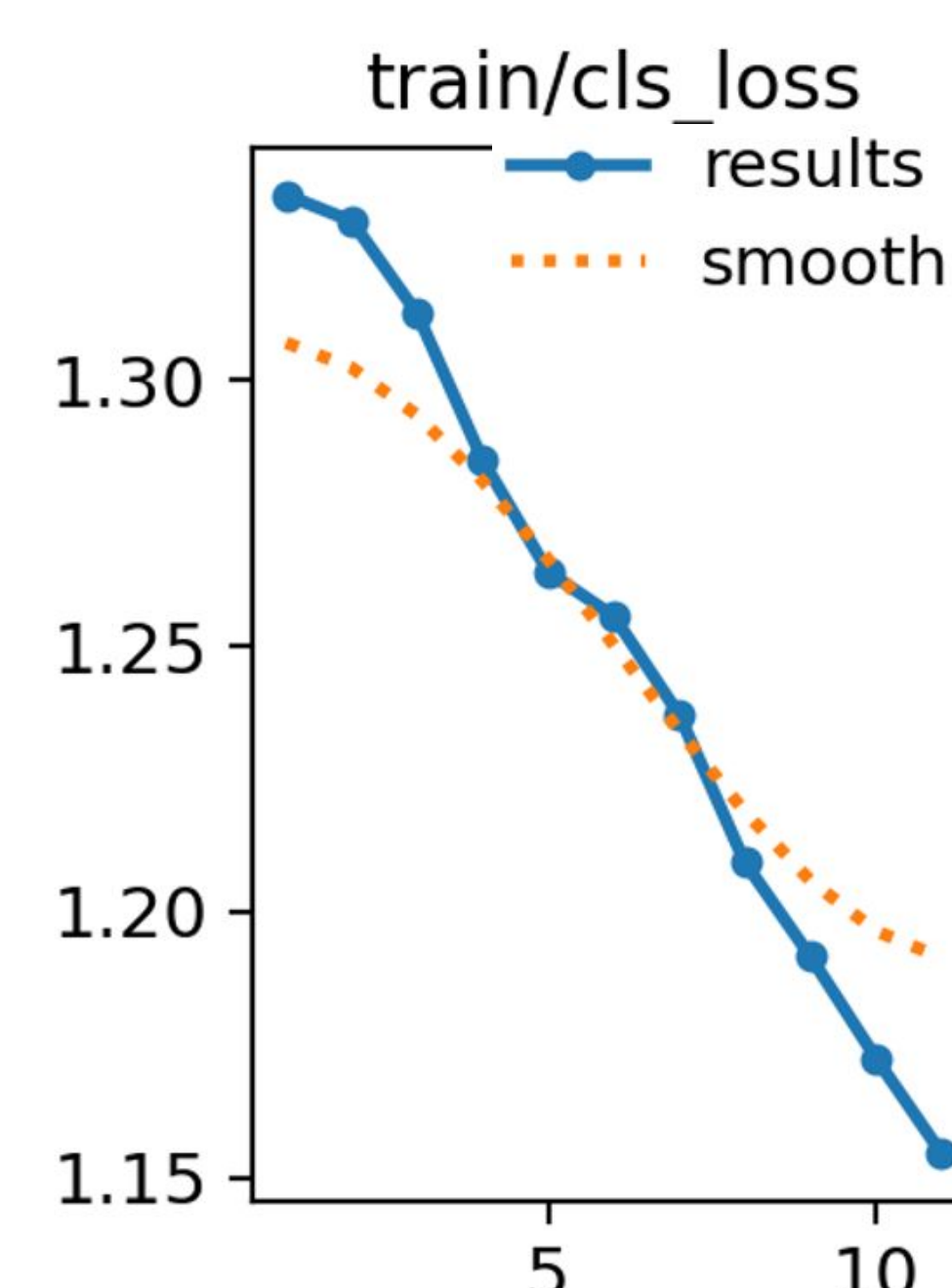
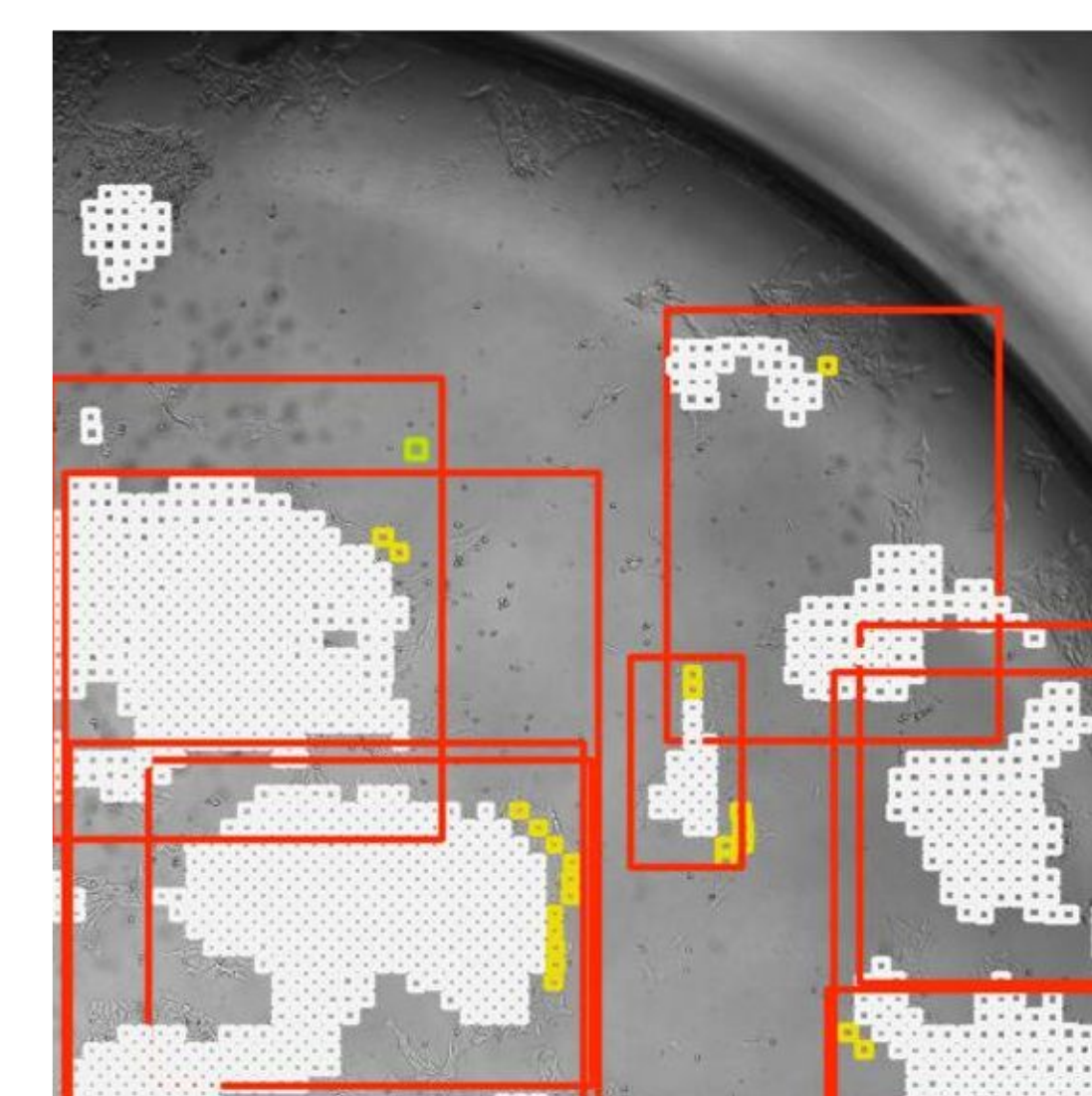
### Model Output



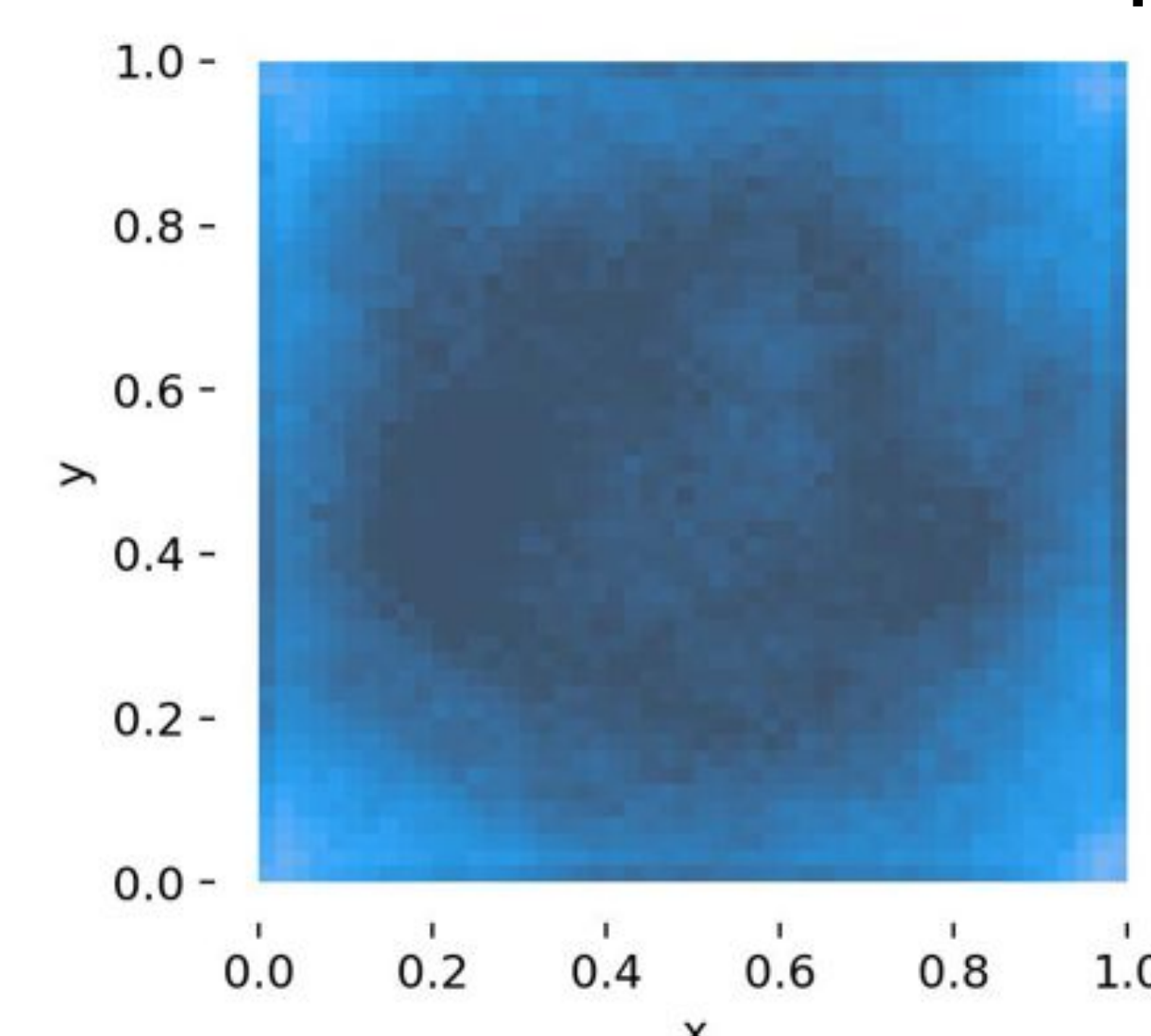
### Real Image



### Model Output



### Activation Heatmap



## Conclusion

- Blending of iPSC colony colors with the background, particularly at 4x magnification, made colony identification difficult, even by eye
- Adjustments to simulate the transparent, glass-like texture of iPSCs and incorporate well section boundaries in 96-well plate images improved detection accuracy
- Overlooked streaking patterns in images affected model performance, highlighting the need to account for these artifacts in the simulations

## Future Directions

- Eliminate differentiation between edge and inner cells, as only colony boundaries are needed and the model struggles with edge detection
- Include more physical aberrations in simulations to account for microscope limitations
- Utilize larger training and validation sets to enhance model robustness and generalization across various imaging conditions

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## Reference

Sekh, A.A., Opstad, I.S., Godtliebsen, G. *et al.* Physics-based machine learning for subcellular segmentation in living cells. *Nat Mach Intell* 3, 1071–1080 (2021).  
<https://doi.org/10.1038/s42256-021-00420-0>